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Saccadic adaptation: cross-modal transfer and effect of spatial attention

Ali Batikh

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Ali Batikh

**Saccadic adaptation: cross-modal transfer and
effect of spatial attention.**

Devant le jury composé de :

Dr. Froment Caroline
Dr. Paeye Céline
Dr. Madelain Laurent
Dr. Montagnini Anna
Dr. PéliSSon Denis
Dr. Farnè Alessandro

Université Claude Bernard Lyon 1
Université Paris Cité
Université de Lille
CNRS
INSERM
INSERM

Présidente
Rapporteure
Rapporteur
Examinatrice
Directeur de thèse
Co-directeur de thèse

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ABSTRACT

Our brain continuously generates saccadic eye movements and maintains their accuracy thanks to saccadic adaptation (SA). Despite this plasticity-based mechanism has been widely studied since the late 20th century, many questions remain unanswered. For instance, in addition to visual targets, saccades can also be performed toward somatosensory and auditory stimuli, but **whether these ‘non-visual saccades’ can be subject to similar adaptive mechanisms as visual saccades is unknown.**

In the first part of this thesis, we investigated the possibility of adapting the amplitude of reactive saccades (RS) to tactile (Study 1) and auditory targets (Study 2) via the double target step paradigm, which has largely been used to induce adaptation of visual saccades since its introduction (McLaughlin 1967). We also investigated the bidirectional cross-modal transfer of adaptation between visual and tactile saccades, as well as between visual and auditory saccades, respectively. Our results revealed that tactile and auditory saccades can be adapted in much the same way as visual saccades. However, the transfer patterns were asymmetric: visual SA transferred fully to non-adapted tactile and auditory saccades, whereas tactile and auditory SA, despite complete generalization to saccades of the same modality but toward non-adapted locations, transferred only partially to the non-adapted visual saccades. On the one hand, the **full transfer of visual saccades adaptation further supports the current view of a motor adaptation locus for visual RS.** On the other hand, the **low adaptation transfers to visual saccades suggest the presence of adaptation loci specific to non-visual RS and situated upstream of the final motor pathway** common to all saccades.

Interestingly, both studies also demonstrate that SA can be elicited in darkness, thus, without the vision of the post-saccadic target location. This seems to contradict current theories on the nature of error signals driving adaptation, which all rely on post-saccadic visual feedback. One potential factor that might serve as an error signal for SA is the locus of spatial attention, as suggested by some previous studies. Spatial attention oriented covertly (no eye movement) and saccadic orienting responses both critically contribute to visual perception and involve overlapping neural substrates. In addition, recent studies show that SA modulates the orienting of spatial attention while the reverse effect, that is, the effect of spatial attention on SA, remains unsettled. In the second part of this thesis (Study 3), we aim to assess in depth the possibility of a modulatory effect of spatial attention on SA. We used a combination of the double-step target paradigm (to induce adaptation) and the cross-modal attentional-orienting paradigm to investigate the effect of tactile exogenous and endogenous spatial attention on the adaptation of reactive and voluntary saccades, respectively. Our results show **significant correlations between the amount and speed of saccadic adaptive changes and the amount of attention** allocated toward or away from the adapted saccade target. Thus, Study 3 brings

additional arguments in favor of a coupling between spatial attention and SA, possibly by means of an effect of spatial attention on the saccadic error signals at the level of the posterior parietal cortex. Overall, this work brings additional empirical insights on the control of accuracy of non-visual RS and further highlights the role of spatial attention in SA. Even though significant advances have been seen in models investigating the nature of the error signals driving SA, they currently do not consider the coupling between spatial attention and SA. Therefore, based on the available literature and the outcomes of this thesis, we suggest that future work should take into account the role of spatial attention in error processing.

Key Words: Saccades, Auditory saccades, Tactile saccades, Saccadic adaptation, Cross-modal transfer, Spatial attention.

RESUME

Thèse intitulée « **Adaptation saccadique: transfert intermodal et effet de l'attention spatiale** »

Notre cerveau génère continuellement des mouvements oculaires saccadiques et maintient leur précision grâce à l'adaptation saccadique (AS). Bien que l'AS ait été largement étudiée depuis la fin du 20^e siècle, de nombreuses questions restent ouvertes. Par exemple, en plus des cibles visuelles, les saccades peuvent également être effectuées vers des stimuli somatosensoriels et auditifs, mais on ne sait pas si ces 'saccades non visuelles' peuvent être adaptées comme les 'saccades visuelles'.

Dans la première partie de cette thèse, nous avons étudié la possibilité de modifier l'amplitude des saccades vers des cibles tactiles (Étude 1) et auditives (Étude 2) via le paradigme du double saut de cible, largement utilisé pour adapter les saccades visuelles (McLaughlin, 1967). Nous avons également étudié le transfert bidirectionnel et intermodal de l'AS entre les saccades réactives (SR) visuelles et tactiles, ainsi qu'entre les SR visuelles et auditives, respectivement. Nos résultats montrent que les saccades tactiles et auditives peuvent être adaptées d'une manière similaire aux SR visuelles. Cependant, les transferts étaient asymétriques : l'adaptation des SR visuelles transfère complètement aux saccades non adaptées tactiles et auditives, tandis que pour l'adaptation des SR tactiles et auditives, malgré leur généralisation aux saccades non adaptées de la même modalité, le transfert aux SR visuelles n'est que partiel. D'une part, le transfert complet de l'adaptation des SR visuelles soutient l'hypothèse actuelle d'un niveau moteur de l'adaptation de ces saccades. D'autre part, les faibles transferts d'adaptation vers les SR visuelles suggèrent l'existence de sites d'adaptation spécifiques aux SR non visuelles, situés en amont de la voie motrice finale commune à toutes les saccades.

La première partie de cette thèse montre que l'AS peut être déclenchée dans l'obscurité, sans information visuelle sur la position post-saccadique de la cible. Cela semble contredire les théories actuelles sur la nature des signaux d'erreur responsables de l'AS, qui reposent toutes sur ce *feedback* visuel post-saccadique. Un facteur potentiel qui pourrait servir de signal d'erreur pour l'AS est le locus de l'attention spatiale, comme le suggèrent certaines études précédentes. L'orientation *covert* (sans mouvement des yeux) de l'attention et les saccades contribuent ensemble à la perception visuelle et impliquent des substrats neuronaux communs. De plus, de récentes études montrent que l'AS module l'orientation de l'attention spatiale, tandis que l'effet inverse, de l'attention spatiale sur l'AS, reste indéterminé. Dans la deuxième partie de cette thèse (Étude 3), nous visons à évaluer en profondeur l'effet modulateur de l'attention spatiale sur l'AS. Nous avons utilisé une combinaison du paradigme du double saut de cible (pour induire l'adaptation) et du paradigme d'orientation intermodale de l'attention pour étudier l'effet de l'attention spatiale exogène et endogène tactile sur l'adaptation des

saccades réactives et volontaires, respectivement. Nos résultats montrent des corrélations significatives entre l'adaptation (taux et vitesse) et la quantité d'attention allouée vers ou à l'opposé de la cible saccadique adaptée. Ainsi, l'Étude 3 apporte des arguments supplémentaires en faveur d'un couplage entre l'attention spatiale et l'AS, possiblement via un effet de l'attention spatiale sur les signaux d'erreur saccadique au niveau du cortex pariétal postérieur.

Ce travail apporte de nouvelles perspectives sur le contrôle de la précision des SR non visuelles et met en lumière le rôle de l'attention spatiale dans l'AS. Bien que des progrès significatifs aient été réalisés par les modèles étudiant la nature des signaux d'erreur qui conduisent à l'AS, ces derniers ne prennent actuellement pas en compte le couplage entre l'attention spatiale et l'AS, ce qui devrait être le sujet de travaux futurs.

Mots clefs : Saccades, Saccades auditives, Saccades tactiles, Adaptation saccadique, Transfer intermodal, Attention spatiale.

RESUME SUBSTANTIEL

Les mouvements oculaires saccadiques amènent l'image rétinienne des objets d'intérêt au niveau de la fovéa, la région centrale de la rétine où l'acuité visuelle est maximale. Les saccades se classent en deux grandes catégories, les saccades réactives déclenchées par l'apparition soudaine de stimuli, et les saccades volontaires qui sont initiées par des processus endogènes (intention, prédiction, mémoire). La précision de nos saccades est maintenue tout au long de la vie grâce à un mécanisme basé sur la plasticité cérébrale, nommé adaptation saccadique (Pélisson et al., 2010). Par exemple, une lésion d'un muscle oculaire (ou bien de son innervation) chez l'humain et le singe affecte la précision des saccades effectuées par l'œil concerné en les rendant hypométriques. Dans cette situation, lorsque l'œil normal est couvert afin de restreindre les entrées visuelles à l'œil opéré, les saccades de ce dernier redeviennent normométriques avec le temps, révélant l'implication d'un mécanisme d'adaptation qui compense, dans ce cas, les effets des lésions neuromusculaires (Abel et al., 1978; Optican & Robinson, 1980). Heureusement, des techniques non invasives peuvent être utilisées pour étudier cette adaptation au laboratoire. La plus utilisée est le paradigme de double-saut de cible introduit par McLaughlin (McLaughlin, 1967), consistant à simuler une erreur de visée en déplaçant la cible visuelle vers une nouvelle position au cours de l'exécution de la saccade. Ce deuxième saut n'est généralement pas perçu par les participants, en raison du phénomène de suppression saccadique. Le décalage ainsi induit entre la position finale de la saccade et celle de la cible, va au cours des essais entraîner des changements progressifs dans les paramètres des saccades, principalement une diminution ou augmentation d'amplitude respectivement pour les sauts arrière (ou '*backward*') ou les sauts avant (ou '*forward*').

En plus des stimuli visuels, des stimuli somatosensoriels (par exemple, une mouche qui se pose sur la main) ainsi que des stimuli auditifs (par exemple, le bourdonnement de la mouche) peuvent entraîner des saccades. Quelle que soit la modalité sensorielle du stimulus, la saccade est produite par le même circuit moteur (voie finale commune) qui, par définition, génère des activités motrices dans un référentiel oculo-centré. Ce dernier est proche du référentiel rétino-centré dans lequel sont codées les cibles saccadiques visuelles, rendant la transformation visuo-oculomotrice relativement simple. A la différence des cibles saccadiques visuelles, les cibles non visuelles sont initialement codées dans des référentiels non rétino-centrés (céphalo-centré ou body-centré) pour aboutir, après une étape supplémentaire de transformation de coordonnées, aux commandes motrices encodées dans leur référentiel oculo-centré (Groh & Sparks, 1996b; Jay & Sparks, 1987a). Il est suggéré que l'adaptation des saccades réactives exerce ses effets sur la commande oculomotrice au niveau de la voie finale commune (Cotti et al., 2007). Cette hypothèse prédit que l'adaptation des saccades réactives visuelles transfère aux saccades réactives non visuelles (tactiles ou auditives), mais cette prédiction n'a jamais été testée concernant la modalité tactile et avec certaines limitations pour la modalité auditive (Collins

et al., 2010; Frens & van Opstal, 1994). De plus, les études sur l'adaptation saccadique se concentrent principalement sur les saccades visuelles si bien que jusqu'à présent, nous ne savons pas ce mécanisme de contrôle adaptatif des saccades bénéficie aussi aux saccades non visuelles.

La première étude de cette thèse (Etude 1) a pour objectif de répondre à ces questions. Pour ce faire, une première expérience a consisté à induire une adaptation '*backward*' des saccades visuelles réactives effectuées vers des diodes électroluminescentes (LED) placées sur les doigts de la main droite des participants (majeur et index) et à étudier le transfert de cette adaptation aux saccades tactiles effectuées vers une stimulation électro-tactile supraliminaire appliquée sur l'annulaire, le majeur, l'index et le pouce. Cette expérience réalisée sur 15 participants a révélé : 1) la généralisation de l'adaptation des saccades visuelles aux saccades visuelles non adaptées (vers l'annulaire et le pouce) et, 2) un transfert complet de cette adaptation aux différentes saccades tactiles. Dans une deuxième expérience (25 participants), nous avons testé la possibilité d'adapter les saccades tactiles elles-mêmes en exposant les participants à un paradigme de double saut de cible. Dans celui-ci, le participant effectuait des saccades vers une stimulation tactile sur le majeur ou l'index, au cours desquelles une seconde stimulation tactile simulant un saut arrière de la cible se produisait sur l'annulaire ou le majeur, respectivement. Cette 2^e expérience a montré une diminution significative du gain des saccades tactiles par comparaison à une session contrôle où la deuxième stimulation tactile était délivrée sur le doigt initialement stimulé au début de l'essai. Cette diminution était maintenue dans la phase post-exposition (où la cible disparaissait pendant la saccade), un effet consécutif qui caractérise les adaptations sensorimotrices. De plus, cette adaptation des saccades tactiles se généralisait aux saccades tactiles non adaptées (vers l'annulaire et le pouce), et transférait également, bien que partiellement, aux saccades réactives visuelles. Les résultats de cette première étude plaident donc en faveur de l'hypothèse d'un site d'adaptation des saccades réactives situé au niveau de la voie finale commune pour toutes les modalités de saccades. En plus, le transfert partiel de l'adaptation des saccades tactiles suggère l'existence d'un second site d'adaptation de ces saccades, situé en amont de la voie finale commune des saccades.

Dans la deuxième étude de cette thèse (Etude 2), nous avons abordé les mêmes questions que dans la première étude mais cette fois-ci pour les saccades auditives. Nous avons utilisé le paradigme de double saut de cible pour adapter les saccades réactives réalisées vers des cibles visuelles (Expérience 1, 15 participants) ou auditives (Expérience 2, 30 participants) situées à 15° d'un point de fixation central. Dans chaque expérience, le taux d'adaptation induite pour la modalité adaptée et le taux de transfert de l'adaptation vers la modalité non adaptée ont été comparés à ceux mesurés lors d'une session contrôle (sans adaptation). De plus, nous avons testé les deux types de modifications adaptatives de l'amplitude saccadique (*backward* et *forward*). Il a été suggéré que les adaptations '*backward*' et '*forward*' reposent, au moins partiellement, sur des mécanismes d'adaptation distincts et des substrats neuronaux différents (Ethier et al., 2008a; M. Panouillères et al., 2009a). Le transfert de l'adaptation '*backward*' des saccades visuelles réactives aux saccades auditives a déjà été rapporté

dans deux études distinctes (Collins et al., 2010; Frens & van Opstal, 1994). Dans l'Expérience 1 de cette étude, nous avons pu confirmer ces résultats, en montrant un transfert complet de l'adaptation '*backward*' aux saccades auditives. En plus, nous avons montré 1) une généralisation de l'adaptation aux saccades visuelles non-adaptées et 2) un transfert complet vers les saccades auditives effectuées vers des cibles non adaptés (cibles situées à 10° et 20° du point de fixation). En outre, nous avons observé que ce transfert 'visuel-vers-auditif' de l'adaptation '*backward*' existe aussi dans le cas de l'adaptation '*forward*', puisqu'après cette dernière l'amplitude des saccades auditives réalisées vers les différentes excentricités de cible était augmentée. Dans l'Expérience 2, nous avons pu montrer que, comme pour les saccades tactiles, un deuxième saut arrière des cibles auditives induisait une diminution progressive du gain saccadique qui était maintenue dans la phase post-exposition. De plus, cette adaptation '*backward*' des saccades auditives se généralise vers des cibles non adaptées et se transfère partiellement vers les saccades visuelles. Enfin, concernant l'adaptation '*forward*', nous n'avons pas obtenu d'augmentation significative du gain des saccades auditives en phase de post-exposition, même si ce gain augmentait progressivement et significativement durant la phase d'exposition, et donc les tests de généralisation spatiale et de transfert cross-modal n'ont pas été concluants.

Le transfert d'adaptation de la modalité visuelle vers les modalités tactile et auditive des saccades plaide en faveur d'un locus d'adaptation commun à toutes les modalités de saccades et situé à un niveau fonctionnel moteur. Bien que nous ayons pu démontrer pour la première fois les capacités adaptatives oculomotrices à corriger les imprécisions des saccades non visuelles tactiles et auditives, le transfert partiel d'adaptation de ces deux modalités de saccades non visuelles vers les saccades de la modalité visuelle plaide en faveur de l'existence de sites d'adaptation '*backward*' spécialisés pour les modalités non visuelles et situés en amont de la voie motrice finale. L'absence d'adaptation '*forward*' des saccades auditives dans l'Etude 2 peut être rapprochée au fait que l'adaptation '*forward*' est en général plus difficile à induire (M. Panouillères et al., 2009a).

Dans tous les modèles actuels, les informations visuelles post-saccadiques sont essentielles à l'élaboration des signaux d'erreur qui déclenchent l'adaptation saccadique (Masselink & Lappe, 2021). Néanmoins, les Études 1 et 2 nous ont permis de montrer qu'une adaptation '*backward*' des saccades non-visuelles peut être induite en l'absence d'informations visuelles post-saccadiques, les participants réalisant l'expérience dans l'obscurité complète. Comment sont élaborés les signaux d'erreurs dans ces situations ? L'un des facteurs potentiels pouvant jouer un rôle est l'attention spatiale (Khan et al., 2014). Comme les mouvements oculaires saccadiques, l'orientation de l'attention spatiale peut être réalisée de deux manières différentes : l'orientation endogène se produit en fonction de nos objectifs, intentions et informations mémorisées, tandis que l'orientation exogène est automatique et résulte de l'apparition soudaine de stimuli (Corbetta et al., 2008; Corbetta & Shulman, 2002). Plusieurs études ont montré que l'adaptation saccadique renforce l'orientation de l'attention spatiale (Nicolas, Bidet-Caulet, et al., 2019; Nicolas et al., 2020), tandis que l'effet inverse, c'est-à-dire de

l'attention spatiale sur l'adaptation saccadique, reste incertain. Dans l'Étude 3, nous avons étudié l'effet de l'attention spatiale exogène (expérience 1, 20 participants) et endogène (expérience 2, 20 participants) sur l'adaptation des saccades réactives et volontaires, respectivement. Dans la phase d'exposition de chaque expérience, nous avons adapté (adaptation '*backward*') les saccades vers des cibles visuelles situées à 15° du point de fixation. Simultanément, l'attention spatiale tactile était orientée systématiquement soit vers la cible de la saccade adaptée (session '*ipsi*'), soit vers le côté opposé (session '*contra*'). Nous émettons l'hypothèse que, par son effet cross-modal sur l'attention visuelle (C. Spence et al., 1998, 2000), l'attention spatiale tactile va renforcer l'adaptation saccadique lorsqu'elle est orientée vers la cible adaptée et, à l'inverse, va réduire l'adaptation lorsqu'elle est orientée loin de la cible de la saccade. En accord avec cette hypothèse, nous avons trouvé dans chaque expérience des corrélations significatives entre la quantité d'orientation attentionnelle et nos deux mesures principales de l'adaptation (la vitesse de changement d'amplitude saccadique et l'effet consécutif). L'Étude 3 apporte ainsi des arguments supplémentaires en faveur d'un couplage entre l'attention spatiale et l'adaptation saccadique. Ces résultats nous amènent également à suggérer que cet effet facilitateur de l'attention spatiale pourrait impliquer le traitement du signal d'erreur, potentiellement au niveau du cortex pariétal postérieur.

Sur la base du travail réalisé au cours de cette thèse, nous proposons que l'attention spatiale soit prise en compte dans les recherches futures sur la nature du signal d'erreur à l'origine de l'adaptation saccadique. Une autre possibilité, non exclusive de la précédente, est que l'adaptation des saccades non-visuelles pourrait résulter d'un signal d'erreur reposant sur des informations non-visuelles post-saccadiques codées dans un cadre de référence centré sur les yeux. De plus, comme les adaptations des saccades volontaires et réactives semblent reposer au moins partiellement sur des mécanismes différents (Pélisson et al., 2010), des travaux futurs pourraient examiner si un transfert d'adaptation visuel-vers-auditif et visuel-vers-tactile se produirait pour les saccades volontaires et si les saccades volontaires non-visuelles elles-mêmes peuvent être adaptées. Finalement, des études futures devront déterminer le rôle exact de l'attention sur l'adaptation saccadique, plus précisément si l'attention spatiale module les mécanismes de plasticité oculomotrice ou de traitement des signaux d'erreurs, ou bien les deux.

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LIST OF ABBREVIATIONS

| | |
|--------------|--|
| BBG | Brainstem Burst Generator |
| CD | Corollary Discharge |
| cFN | Caudal Fastigial Nucleus |
| CN | Caudate Nucleus |
| DLPFC | Dorsolateral Prefrontal Cortex |
| EBN | Excitatory Burst Neurons |
| EEG | Electroencephalography |
| ERP | Event-Related Potential |
| FEF | Frontal Eye Fields |
| fMRI | Functional Magnetic Resonance Imaging |
| FOR | Fastigial Oculomotor Region |
| Gpe | External Segment Of The Globus Pallidus |
| IBN | Inhibitory Burst Neurons |
| IC | Inferior Colliculus |
| IFG | Inferior Frontal Gyrus |
| INC | Interstitial Nucleus Of Cajal |
| IPL | Inferior Parietal Lobule |
| ipRGC | Intrinsically Photosensitive Retinal Ganglion Cells |
| IPS | Intraparietal Sulcus |
| IT | Inferior Temporal Cortex |
| La | Latch Interneurons |
| LGN | Lateral Geniculate Nucleus |
| LIP | Lateral Intraparietal |
| LLBN | Long Lead Burst Neurons |
| LOC | Lateral Occipital Cortex |
| LTD | Long Term Depression |
| MD | Medial Dorsal Nucleus Of The Thalamus |
| medRF | Medullary Reticular Formation |
| MFG | Middle Frontal Gyrus |
| MN | Motor Neurons |
| MRF | Mesencephalic Reticular Formation |
| MT | Middle Temporal Are |

| | |
|--------------|--|
| MVN | Medial Vestibular Nuclei |
| NPH | Nucleus Prepositus Hypoglossi |
| NRTP | Nucleus Reticularis Tegmenti Pontis |
| OMV | Oculomotor Vermis |
| OPN | Omnidirectional Pause Neurons |
| PEF | Parietal Eye Field |
| PET | Positron Emission Tomography |
| PPC | Posterior Parietal Cortex |
| PPRF | Paramedian Pontine Reticular Formation |
| riMLF | Rostral Interstitial Nucleus Of The Medial Longitudinal Fasciculus In The Mesencephalon |
| SC | Superior Colliculus |
| SEF | Supplementary Eye Fields |
| SLBN | Short Lead Burst Neurons |
| SNpr | Substantia Nigra Pars Reticulata |
| SOA | Stimulus Onset Asynchrony |
| SPL | Superior Parietal Lobule |
| STG | Superior Temporal Gyrus |
| STN | Subthalamic Nucleus |
| TMS | Transcranial Magnetic Stimulation |
| TN | Tonic Neurons |
| TPJ | Temporo-Parietal Junction |
| Tr | Trigger Interneurons |
| VFC | Ventral Frontal Cortex |
| VL | Ventrolateral Nucleus Of The Thalamus |
| VOR | Vestibulo Ocular Reflex |

A. INTRODUCTION

Chapter 1: Vision

These days, with the vast amount of knowledge humans have acquired over decades and scientific questions becoming increasingly precise and restricted, we sometimes seem to have lost track of the first questions humans ask: Who am I? Why do I exist? And where do I exist?

The first question about who we are and our survival instincts made us increasingly curious about the nature of our bodies, how they function, and the methods of treatment we can use to fight injuries, pain, and deadly diseases and, therefore, to live yet another day. When we look back to some discoveries made by our ancestors hundreds or even thousands of years ago, we might sometimes sit back and say, “That is not hard to know! Why did it take them that long ?” Of course, we might say that while sitting on a comfortable chair, in a cozy room under the air conditioner without worrying about growing corn to eat while ancient scientists and philosophers were chased by angry people calling them sorcerers and witches, traveled hundreds of kilometers for months and even years to discover new civilizations and bring back their knowledge, and even got killed for daring to practice science and discovering new stuff.

“The eyes are our door to the external world.” We probably read this quote several times in many places, and we might even have lost track of the first person to write it. Studying the visual system started a long time ago, and history is full of remarkable people who constituted the triggers of the domino effect in the advancement we are living in neurosciences, more precisely in the studies of visual perception. As far as we know, the ancient Greek philosopher Aristotle thought that light emits from our eyes and interacts with external objects. Another Greek philosopher, Plato, described visual perception as a passive process where light from objects enters the eyes and forms an image on the retina. In his *Book of Optics*, Ibn Al-Haytham proposed a more accurate model of vision involving light rays entering the eyes through the pupil and forming inverted images on the retina. Among his anatomical studies in the 15th century, Leonardo da Vinci (Gross, 1997) brought additional information on the structural and functional aspects of the eyes. In the 18th and 19th centuries, vision studies underwent significant advances, especially with Thomas Young and Hermann von Helmholtz, who proposed the Young-Helmholtz theory of color vision, suggesting that the eyes contain three color receptors specific to different light wavelengths. The 19th century included significant progress in understanding vision's physiological and neural basis, such as the discovery of the visual processing area in the brain, (Wade, 2000) which continued in the 20th century with the development of psychophysics, the study of visual illusions, and the discovery of specialized visual processing pathways in the brain. Today, thanks to the advancements made in all scientific fields, and with

techniques such as electrophysiology, neuroimaging, and molecular biology, the study of vision has reached a peak of discoveries and inventions and continues to provide deeper insights into the neural mechanism underlying vision. In this chapter, we will describe the anatomy of the eyes, the component of the retina, how light's photons are transformed into electric signals in the retina, and how the latter are transported to specific brain regions to create the world's visual representation we experience.

1.1. The eye's anatomy

The eyes are ball-shaped organs that allow the conversion of light rays into electric signals to be processed by several brain regions. It contains three layers of tissues, as indicated in Figure 1:

1. The sclera:

It is the white, tough outer layer of the eye that provides structural support and protection to the inner parts. Its anterior part is transformed into the cornea, a transparent, dome-shaped surface at the front of the eye, which allows light to reach the eyes' anterior chamber.

2. The uveal tract:

It is the intermediate tissue layer of the eye and is divided into two main components:

- a. The choroid: it constitutes the largest component of the uveal tract and is situated between the sclera and the retina. The choroid is rich in blood vessels that nourish the retina and contains the pigment epithelium which is in contact with the retinal photoreceptors layer. From the choroid extends the ciliary body, which encircles the lens (a transparent flexible structure allowing to focus the light on the retina) and contains a muscular component (ciliary muscles) that maintains the lens's refractive power and a vascular component (ciliary processes) that produces fluids (aqueous humor) that fills the anterior chamber situated between the cornea and the lens as well as the posterior chamber located between the iris and the lens. Extending from the ciliary processes, the zonule fibers maintain the lens's position and shape within the eye.
- b. The iris is the colored and anterior component of the uveal tract. It constitutes two sets of opposing-action muscles that regulate the size of the pupil (the black circular opening at the center of the iris), controlling the amount of light entering the eye.

3. The retina:

It is the innermost layer of the eye where light rays are projected. The retina is part of the central nervous system and comprises different cell layers, including photoreceptors. Photoreceptors are of two types: the cones responsible for high-resolution vision and color vision, and the rods, which are the most sensitive photoreceptors to light but have a low spatial resolution. The optic nerves, as well as the blood vessels that nourish the retina, leave it through the optic disk, also called optic papilla, where no photoreceptors can be found and, therefore, represent the blind spot in each eye. Above the optic disk is the macula lutea, a region with a high concentration of cones. At the center

of the macula, the area with the highest concentration of cones is called the fovea, which forms a small depression in the retina and accounts for the sharpest vision and highest color perception. The space between the lens and the retina is filled with vitreous humor, a thick, gelatinous liquid that maintains the eye's shape (For reviews: (Prasad & Galetta, 2011; Purves et al., 2018)).

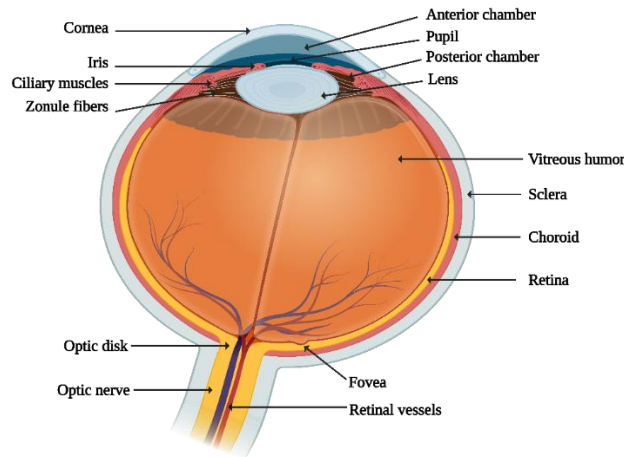


Figure 1: Schematic representation of the human eye. Created with BioRender.com.

1.2. The retina's cell layers

The light must reach the cones and rods' outer segments (photoreceptors' outer segments layer) buried in the innermost part of the retina under the pigment epithelium, to trigger the fabulous cascade allowing its conversion into electric signals via a process called phototransduction. Therefore, the light passes through several layers containing different cell types (Prasad & Galetta, 2011; Purves et al., 2018), as represented in Figure 2:

- a. The nerve fiber layer is situated at the retina's surface and consists of the axons of ganglion cells, axons which assemble at the level of the optic disk to form the optic nerve leaving the eye.
- b. The ganglion cell layer is named after the ganglion cells forming it and constitutes the retina's output neurons.
- c. The inner plexiform layer contains the processes of amacrine cells and constitutes a site of synaptic connection between ganglion, amacrine, and bipolar cells.
- d. The inner nuclear layer contains the bipolar cells, which receive inputs from photoreceptors and transmit signals to the ganglion cells. Bipolar cells connected to rods and cones differ in morphology, connectivity, synaptic organizations, and functional properties. This layer also contains the bodies of horizontal and amacrine cells.

- e. The outer plexiform layer contains the processes of horizontal cells which enable lateral connections between photoreceptors and bipolar cells and synaptic connections between horizontal, photoreceptors, and bipolar cells.
- f. The outer nuclear layer where the cell bodies of photoreceptors are located.

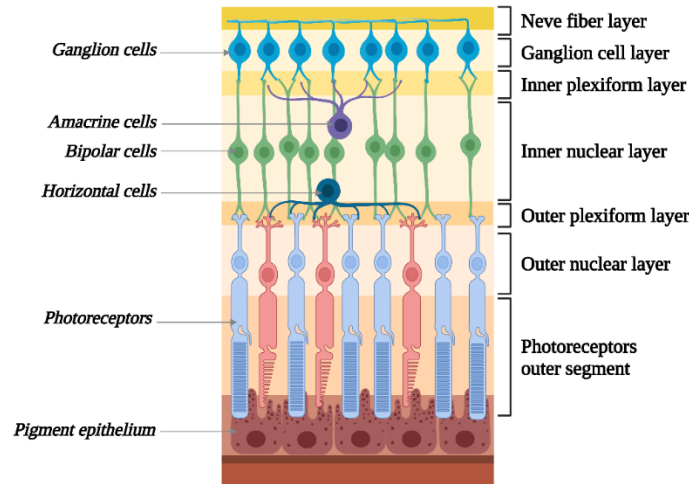


Figure 2: Schematic representation of the human retina. Created with BioRender.com.

1.3. Rods and Cones

The retina contains two types of photoreceptors: rods and cones. Both photoreceptors have an elongated outer segment containing packs of membranous disks stacked on top of each other, as represented in Figure 3. Those disks are rich in photopigment molecules embedded in their membranes. The rod system is extremely sensitive to light at the cost of a low spatial resolution, and in darkness, its activation leads to perception called scotopic vision. The cone system is more specialized for acuity at the cost of sensitivity, and under normal indoor or outdoor lightning, it is responsible for photopic vision, in which rod-mediated perception is null. Mesopic vision represents an intermediate state to which both cones and rods contribute.

The number of rods in the humans' retinas far exceeds the number of cones (approximately 90 million vs. 4.5 million). However, the distribution of those two photoreceptors types is not the same across the retina. The highest cone density in the retina is found in the fovea, the central part of which being the foveola, a rod-free avascular area with the sharpest vision. Three types of cones can be defined according to the wavelength of their photopigment, called opsin. The S-cones, or short-wavelength cones, also called blue cones, are sensitive to blue light. Medium-wavelength cones (M-cones), known as green cones, respond to green light. And finally long-wavelength cones (L-cones), also known as red cones, react to red light. Those three types of cones make the cone system responsible for color vision, which is trichromatic in normal humans (Gegenfurtner & Kiper, 2003). In

rods, we can only find a single type of photopigment called rhodopsin, a specific type of opsin sensitive to a broad range of light wavelengths, making the rods highly sensitive to light. The rods are highly concentrated at the periphery of the retina and the more we approach from the fovea the less is this concentration.

While bipolar cells driven by cones are directly connected to the ganglion cells, bipolar cells activated by rods do not have such direct connections (Masland, 2001). Instead, rods transmit electric signals to ganglion cells via the amacrine cells at the inner plexiform layer. A significant difference exists in the degree of convergence in the cones and rods circuitry. In the cones system, a ganglion cell receives inputs from one bipolar cell, which receives inputs from only one cone, therefore, contributing to the high acuity of this system. In contrast, in the rods system, many rods converge onto the same bipolar cell, and many rod bipolar cells converge on a single amacrine cell. This convergence both results in the low spatial resolution found in the rod system and in the rod system's high sensitivity to light, as small signals derived from multiple rods can add-up into a supra-threshold one.

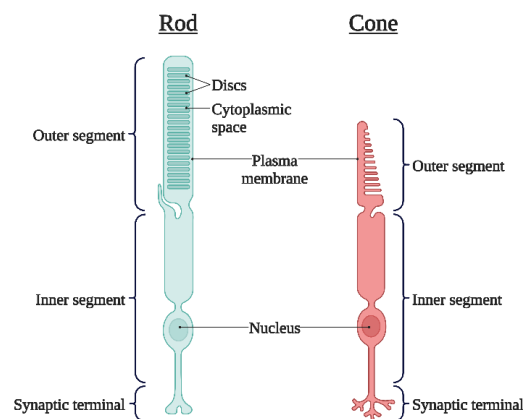


Figure 3: Schematic representation of the retina's photoreceptors, the rods, and the cones. Created with BioRender.com.

1.4. The retinal circuitry

Opsin is a G protein-coupled receptor with seven transmembrane domains with the N-terminus located at the intradiscal side and the C-terminus at the cytoplasmic side (Shichida & Matsuyama, 2009). In our visual system opsins bind in their seventh transmembrane a light-sensitive molecule (chromophore) called retinal (11-cis retinal) responsible for initiating the phototransduction. When the light hits the chromophore retinal, it leads to the isomerization of retinal from 11-cis to all-trans, which dissociates from the opsin protein, triggering a conformational change along its structure. This leads to activating an intracellular messenger G protein called transducin. One activated rhodopsin molecule can activate hundreds of transducin. This later activates an enzyme called phosphodiesterase situated at the cytoplasmic side of the disk membrane which triggers the hydrolyzation of cyclic guanosine

monophosphate (cGMP) into guanosine monophosphate (GMP). The reduction of cGMP in the cytoplasm and leads to the closure of cyclic nucleotide-gated (CNG) ion channels in the photoreceptor cell membrane (allows the influx of Ca^{2+} and Na^{+} into the photoreceptor's outer segment), leading to the hyperpolarization of the cell due to the reduced concentration of Ca^{2+} , therefore reducing the release of the neurotransmitter Glutamate (Terakita, 2005). Photoreceptors in the retina exhibit a graded membrane potential rather than an action potential in other receptors, as it is not required for the signal being generated in the photoreceptors to travel a long distance. In darkness, the membrane potential is around -40 mV, while in the presence of light, this potential becomes more negative and can go up to -65 mV (Purves et al., 2018).

To ensure a sufficient amount of chromophore retinal in the membranous disks, all-trans diffuse into the cytoplasm, where it undergoes conversion to all-trans retinol, transported via interphotoreceptor retinoid-binding protein (IRBP) to the pigment epithelium where it converts back to 11-cis retinal, and finally transported back to the photoreceptors disks. This so-called retinoid cycle is vital for vision and emphasize the role of the pigment epithelium. Additionally, the pigment epithelium nourishes photoreceptors and removes old membranous disks as the photoreceptors keep fabricating new ones, pushing the old disks from the inner part of the outer segment toward the outer part. Finally the pigment epithelium absorbs the intraocular light that escape the photoreceptor layer and therefore reduce the backscatter of light which might impact the vision's acuity.

The decrease in Ca^{2+} concentration inside the cell after exposure to light triggers the activation of rhodopsin kinase (a protein that block the activity of rhodopsin), increases the affinity of CNG ion channels to cGMP, and activates the cGMP synthesizing enzyme, which increases the concentration of cGMP, all in order to open the CNG ion channels, therefore increasing Ca^{2+} influx and preventing the saturation of the activated rhodopsin molecules (Purves et al., 2018).

Several types of bipolar and ganglion cells exist in the retina (Wienbar & Schwartz, 2018) among which are the ON-center and OFF-center cells. The ON-center bipolar cells hold on their dendrites mGluR6 receptors (G protein-coupled metabotropic glutamate receptor) whereby glutamate released by photoreceptors leads to their hyperpolarization. Symmetrically, the reduction of Glutamate released by photoreceptors after their hyperpolarization in the presence of light results in freeing the mGluR6 receptors and, therefore, the depolarization of ON-center bipolar cells, which will in turn release Glutamate at the level of their synaptic connections with ON-center ganglion cells resulting in their depolarization. The OFF-center bipolar cells have ionotropic receptors on their dendrites, and therefore, glutamate has an excitatory effect on those cells. In the light, the reduction of glutamate release results in the hyperpolarization of OFF-center bipolar cells, and in the hyperpolarization of their target OFF-center ganglion cells. Based on their role in signal transmission, ON-center bipolar cells are called sign-inverting, while OFF-center bipolar cells are called sign-conserving (Masland, 2001).

1.5. Ganglion's receptive field

The receptive field of a ganglion cell represents the area in the visual field in which light affects the firing rate of this particular ganglion cell. Ganglion cell's receptive field has central and surrounding annular regions, as seen in Figure 4. ON-center ganglion cells increase their discharge when the luminance increases in their receptive field's center, whereas the increase of discharge of OFF-center ganglion cells occurs when the luminance decrements in their receptive field's center. For both types of ganglion cells, the surrounding area of their receptive field exerts an effect antagonist to their response to stimulation of the central region. Thus, for ON-center ganglion cells, the absence (presence) of light at their receptive field's surroundings increases (decreases) their firing rate whereas opposite modulations take place for OFF-center ganglion cells (presence of light in the surrounding area of the receptive fields increases discharge and vice versa). With a uniform illumination throughout the receptive field, responses to the center and to the surrounding of the receptive field add together and cancel each other. Hence, ganglion cells are sensitive to luminance contrast, which is the difference in illumination levels between the receptive field's center and surroundings. Thus, they are sensitive to the object's boundaries.

Horizontal cells, as mentioned previously, connect photoreceptors. whereas, as noted above, the response to stimulation of the central part of ganglion cell receptive field results from the response of the spatially-coincident receptor transmitted vertically via the bipolar cell, the response to stimulation of the peripheral part of ganglion cell receptive field results from the response of surrounding receptors transmitted indirectly through horizontal cells (see figure 4) (Masland, 2001; Purves et al., 2018).

It is important to note that a large variety of ganglion cells (over 30 types) have been identified in the retina, differing in their physiology and morphology. The majority of ganglion cells present in the retina are Midget cells known also as P (Parvocellular) ganglion cells and constitutes around 80% of retinal ganglion cells. Midget cells reside mostly in the fovea and are sensitive to color and fine details and have high spatial frequencies. Around 10% of retinal ganglion cells are parasol cells also known as M (Magnocellular) ganglion cells characterized by their large cell bodies and dendritic fields and they are involved in motion procession and have low spatial frequencies. Furthermore, a relatively small amount of ganglion retinal cells called K (koniocellular) ganglion cells can also be found in the human retina. Those cells are small and less understood and they have a role in color processing. It is important to note that not all ganglion cells transport the same types of information to the brain. For example, some ganglion cells do not depend on cones and rods for phototransduction. Instead, they have their own photopigments called melanopsin. Those types of ganglion cells project to specific brain areas responsible for regulating pupil size and the circadian rhythm.

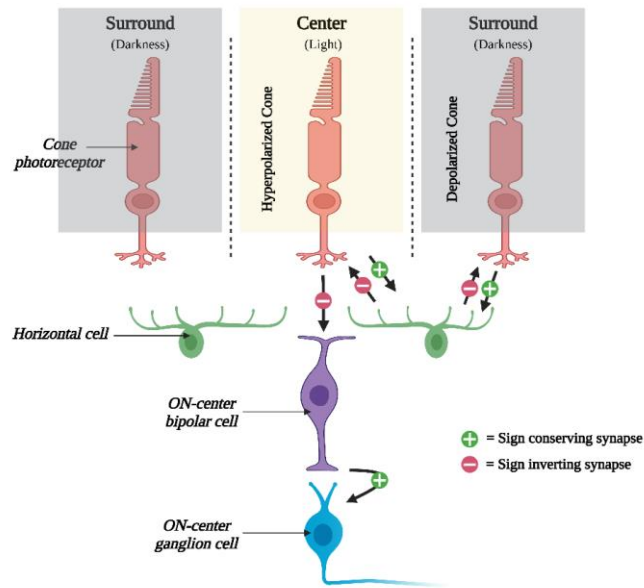


Figure 4: Schematic representation of horizontal cells' role in the human retina. Horizontal cells connect neighboring photoreceptors. A cone photoreceptor in the surroundings of a ganglion cell's receptive field depolarizes due to the absence of light. It triggers the depolarization of horizontal cells at its post-synaptic location via glutamate. This first synaptic connection is considered a sign conserving. In turn, a depolarized horizontal cell triggers the hyperpolarization of the cone cell present in the center of the ganglion cell receptive field. This synapse is a sign inverting and reinforces the decrease of glutamate release by the center cone cell, increasing the responses of On-center bipolar and ganglion cells to illumination of the receptive field center. Created with BioRender.com.

1.6. The visual pathways

Each of our eyes sees a part of the visual space representing its visual field. The image is inverted and left-right reversed on the retina, as described in Figure 5A. Suppose we virtually draw two perpendicular lines (meridians) centered at the fixation point (the location sensed by the fovea), dividing the visual field into four quadrants. Then, an image presented in the superior temporal quadrant for example, projects onto the inferior nasal part of the retina. When the fovea of both eyes are directed to the same visual target, a portion of the visual field of both eyes overlaps, resulting in an area of the space both eyes see. This binocular field consists of two symmetrical hemifields (left and right). The right binocular hemifield projects to both the nasal part of the retina in the right eye and the temporal part of the retina in the left eye, and the left binocular hemifield projects to both the nasal part of the retina in the left eye and the temporal part of the retina in the right eye.

This retinotopic organization is maintained in the optic nerve formed by the Ganglion cells' axons leaving the retina. At the level of the optic chiasm (situated at the base of the brain near the hypothalamus), around 60% of the fibers, mainly coming from the nasal part of the retina, cross to the

opposite side (decussation), while the remaining 40% coming from the temporal part of the retina continue on the same side (see Figure 5B). Due to this partial decussation, the optic track originating from the optic chiasm, regroups fibers from both eyes concerned with the contralateral hemifield (left hemifield in right optic tract and vice versa) ; the optic tract projects ipsilaterally to the thalamus's lateral geniculate nucleus (LGN).

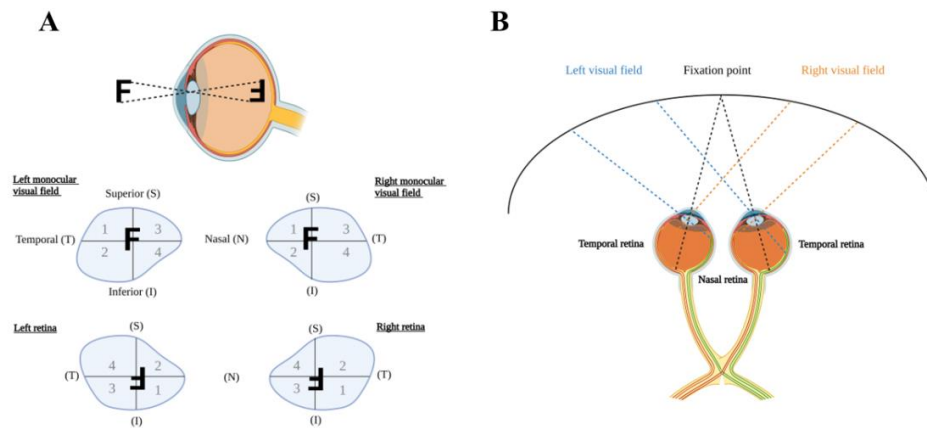


Figure 5: The image on the retina. A schematic representation describing : (A) How the retinal image of a specific visual feature is inverted and left-right reversed and (B) The visual field areas seen by each of the temporal and nasal parts of the left and right retina during fixation. Created with BioRender.com.

The LGN comprises six different layers in which the axons of retinal ganglion cells terminate in an orderly fashion, thus generating an ordered map of the contralateral hemifield. Even though LGN receives inputs from both eyes, retinal axons from the left and the right eyes terminate in different layers, making individual LGN neurons monocular. Ganglion cells axons from temporal retina (ipsilateral eye) terminates in layers 2, 3 and 5 while those from the nasal retina (contralateral eye) terminate in layers 1, 4 and 6 (De Moraes, 2013). As mentioned previously, several types of retinal ganglion cells have been identified. At the level of the LGN, three types of retinal ganglion cells can be differentiated according to the specific layers to which they project and to the type of information they carry. In layers 1 and 2 of the LGN (ventral layers), magnocellular neurons receive inputs primarily from parasol ganglion cells sensitive to motion and low spatial frequencies. Therefore, magnocellular neurons receive and process information related to motion detection, depth perception, and the perception of fast-moving objects. Layers 3 to 6 (dorsal layers) contain parvocellular neurons and receive inputs from Midget ganglion cells, sensitive to color, fine details, and high spatial frequencies. Therefore, parvocellular neurons in the LGN receive and process information related to spatial acuity, color vision, and form perception (shape and size). Between the six layers of the LGN,

in the interlaminar zones, resides koniocellular neurons, which receive inputs from a specific type of small bistratified ganglion cells (K-cells) and have a role in color vision (Prasad & Galetta, 2011).

Neurons in the LGN send their axons to the primary visual cortex (V1 or striate cortex) through the internal capsule, thus forming the so-called optic radiation. Compared to the LGN, there is around a 400-fold increase in the number of neurons in V1 (De Moraes, 2013). The map of the contralateral visual field established in the LGN is preserved in the primary visual cortex. According to this retinotopic organization, neighboring locations in the visual field (activating neighboring loci in the retina) are represented by adjacent neurons in V1 (Grill-Spector & Malach, 2004). The fovea is mapped in the posterior part of V1, and the more we progress into the anterior parts, the more peripheral the retinal representations are. The lower visual field is represented above the calcarine sulcus, while the upper visual field is below it. However, not all parts of the retina are represented at the cortical areas level by the same weight, in contrast, cortical areas mapping the macula are much broader and contain more neurons than those mapping the peripheral parts of the retina, a characteristic known as the cortical magnification of the central visual field.

The primary visual cortex constitutes a 2 mm thick sheet containing six cellular layers. Layer 1 constitutes the most superficial layer and contains horizontal connections with higher visual areas, while from layers 5 and 6, originate descending projections to the superior colliculus and the LGN respectively. Layers 2 and 3 receive axons from LGN's koniocellular cells and project to cortical areas. Finally, layer 4 receives direct inputs from the LGN and is divided into sublayers (4A, 4B, and 4C (α and β)): axons of LGN's magnocellular cells terminate in layer 4C α , while parvocellular cells axons terminate in layer 4C β . Layer 4 represents the first stage of cortical processing of the visual information; thus, neurons in this layer, like neurons in the LGN, are monocular, in addition they form columns representing each a neighboring visual field area. Beyond layer 4, axons originating from this layer start converging onto neurons in other layers that become binocular, receiving inputs from both eyes, which provide them the capability to process depth, so-called stereopsis. Neurons in the primary visual cortex respond mainly to the orientation of edges, the direction of stimulus motion, the variation of contrast, and its rate of change. They can be classified into two broad classes: the spiny neurons, also called pyramidal neurons, which have an excitatory effect via the glutamate neurotransmitter and constitute the source of the projections into cortical and subcortical areas, and the smooth neurons, which are local interneurons that represent the source of cortical inhibition via the secretion of GABA (Purves et al., 2018).

Two main principles govern the organization of cortical visual areas, their functional specialization and hierarchical processing (Grill-Spector & Malach, 2004). First, the pattern of projections of the primary visual cortex onto extrastriate cortical areas suggests a functional specialization into two cortical visual systems: 1) The ventral stream, or the "what" pathway, leads from layer 4C β in V1 to the temporal lobe and includes V2, V4, and the inferotemporal cortex (IT). Those areas are responsible for object recognition and high-resolution forms of vision. 2) The dorsal

stream, or the “where/how” pathway, leads from layer 4Ca in V1 to the posterior parietal cortex (PPC) and includes V2, V3a, and the middle temporal area (V5/MT). This pathway processes the spatial aspect of vision, like motion and the positional relationship between objects, and constitutes a place of multisensory integration, mainly at the level of the PPC (Maunsell, 1992; Mishkin et al., 1983). Second, visual perception is thought to unfold progressively through a step-by-step journey of activation across hierarchically organized processing units. Starting with information depicted in a specific and basic manner, this information undergoes over successive stages a series of transformations, evolving into broader, more complex, and potentially multimodal representations. For example, the sensitivity to contrast has been found to decrease from V1 to the lateral occipital complex (LOC), a region belonging to the ventral stream and specialized in objects and faces recognition, with an intermediate contrast sensitivity found in V4. These and similar findings highlight the hierarchical and gradual progression from initial retinotopic regions to more advanced ones such as abstract object representations (Avidan et al., 2002). Furthermore, it is important to note that activities in the visual cortex not only originate from bottom-up processing of visual information from the LGN but also by top-down modulations from areas higher in the visual hierarchy and coping with cognitive processes like attention, memory and expectations (Driver et al., 2001; Macaluso et al., 2000).

The visual pathway described so far constitutes the primary visual pathway or the retinogeniculostriate pathways, which allow visual perception of about most of what we see. But retinal ganglion cells also project to other locations in the brain. First, ganglion cell axons project onto the suprachiasmatic nucleus of the hypothalamus via the retinohypothalamic pathway, carrying essential information for regulating and maintaining the circadian rhythm. Those so-called intrinsically photosensitive retinal ganglion cells (ipRGC) (Pickard & Sollars, 2012) have their own photopigments called melanopsin and do not depend on photoreceptors. They also provide essential information for regulating the pupillary light reflex mediated by the pretectum, a nucleus located between the midbrain and the thalamus. Finally, some retinal ganglion cells also project directly to the superficial layers of the superior colliculus, vital in controlling eye and head movements.

1.7. Conclusion

The light enters the eye and reach the retina where it is transformed by the retinal photoreceptors into an electric signal. This signal passes through different neuronal populations of the retinal layers to reach finally the ganglion cells layer. Ganglion cell's axons in each eye form the optic nerve which exit the retina and decussate at the level of the optic chiasm before forming the optic tracts. The optic tract fibers containing information of the contralateral visual hemifield terminates in the different layers of the LGN which send projection via the optic radiation to the primary visual cortex. The retinotopic representation of the visual field is maintained throughout this retino-geniculo-cortical pathway, as well as from the primary visual cortex onward to extra-striate areas. Visual signals are further transmitted to extrastriate areas through two main pathways, the ventral and the dorsal stream, all in order to create the image of the external world that we experience in our daily life.

Chapter 2: Saccadic eye movements

As pointed out in the previous chapter, the cones system (cones photoreceptors and their corresponding bipolar and ganglion cells) has high spatial resolution and is responsible for color vision; in contrast, the rods system (the rods and their corresponding bipolar and ganglion cells) has low spatial resolution and is highly sensitive to a broad range of light wavelengths. Also, the repartition of photoreceptor types (cones and rods) is not even along the retinal surface. Therefore, the fovea, constituting the center of the retina where most cones are located, prioritizes acuity over sensitivity. In contrast, the peripheral retina has the inverse characteristics, prioritizing sensitivity over acuity thanks to the rods system. Thus, to process a particular object in our visual scene in detail, it is crucial to bring its retinal image to the fovea by reorienting gaze through head and/or eye movements.

2.1. Eye movement types

Eye movements can be classified into five basic types. Some of them serve to shift the gaze direction (saccades, smooth pursuit movements, and vergence movements), and the others maintain the alignment between the fovea and the object of interest during head or visual field movements (vestibulo-ocular and optokinetic movements).

Saccades are rapid and conjugate ocular movements (both eyes move in the same direction and to the same extent) responsible for directing the gaze from one point of interest to another, changing the point of fixation. They are performed endlessly during our daily activities to explore our visual environment in search for new information, such as during reading, driving, watching movies, playing sports.... They are characterized by their high velocity and short duration and can be performed voluntarily, based on our internal goals and motivation, or they can be reflexively triggered by sudden events (reactive or automatic).

Smooth pursuit movements are also conjugate but slow eye movements that allow the eyes to continuously track moving objects. Those movements are voluntary, and unlike saccades, which rapidly shift gaze, they involve a steady pursuit of a moving target to maintain its image on the fovea.

Vergence movements are coordinated but disconjugate ocular movements, maintaining binocular vision, with both eyes moving in opposite directions to modify the fixation focus in depth. These movements include convergence, where both eyes turn inward to focus on nearby objects, and divergence, where both eyes turn outward to focus on distant objects. Thus, vergence movements allow the brain to integrate the visual information from both eyes into a single three-dimensional perception, which is essential for depth perception and stereoscopic vision.

Vestibulo-ocular movements are reflexive eye movements from vestibular origin that stabilize gaze during head movements: the vestibulo-ocular-reflex (VOR) generates compensatory eye movements (i.e., of the same speed as head motion but in the opposite direction). By preventing the sliding of the visual image on the retina's surface, the VOR is critical to avoid blurring and maintain

visual stability. The VOR, driven by signals from the vestibular system, which senses head motion and position relative to gravity, usually takes the form of nystagmus, the succession of slow compensatory eye movements in the direction opposite to the head motion and of quick eye movements (saccades) which reset eye position in orbit.

Finally, optokinetic movements are also reflexive eye movements critical for maintaining visual stability, but as compared to the VOR, they occur in response to moving visual stimuli, even when the head is stationary, such as a passing train or scrolling text. The optokinetic response is a nystagmus with slow compensatory eye movements in the direction of the moving visual stimulus and quick eye movements in the opposite direction. Such optokinetic nystagmus are essential for stabilizing the visual image on the retina during sustained motion and maintaining spatial orientation during self-motion (Nikolov, 2020; Purves et al., 2018).

In this chapter, and for the purpose of this thesis, we will focus on saccadic eye movements, their effectors, neural correlates, characteristics, and how they can be directed to visual but also to non-visual (auditory and tactile) stimuli.

2.2. Saccadic eye movement categories and metrics

As mentioned in the previous section, saccades are rapid eye movements that allow the image of objects of interest to be brought into the fovea. Saccades can be triggered in the laboratory by presenting a visual target at a certain location relative to a fixation point and instructing the subject to simply ‘look’ at the target.

The amplitude of saccades represents the distance between the saccade endpoint and the initial eye position. As a measure of the accuracy of saccades, the gain is calculated as the ratio between the saccade’s amplitude and the retinal error, which is the distance between the location of the target and the initial eye position. A saccade is considered normometric when its gain equals 1, meaning that the eye has reached its target. In normal physiological conditions, our saccades tend to be hypometric, with a gain of around 0.95 on average or less for large target eccentricities. When the gain is higher than 1, the saccade is considered hypermetric, which mostly occurs under pathological conditions. The saccade's duration represents the time between the saccade's beginning and end. The peak velocity represents the maximum speed that a saccade reaches during its trajectory. Both the duration and the peak velocity increase in a nonlinear fashion with amplitude, as represented in Figure 6. These two relationships together are known as the saccade’s main sequence (Catz & Thier, 2007). The main sequence represents a fundamental characteristic of oculomotor control, reflecting an optimized balance between speed, accuracy, and energy expense. It ensures that within the physical (the mechanics of the orbit) and neural constraints of the ocular motor system, saccades reach their goal accurately and with minimal visual disruption (the time spent with poor vision when the eye is in flight), facilitating seamless visual perception and interaction with the environment (M. Harris & Wolpert, 2006).

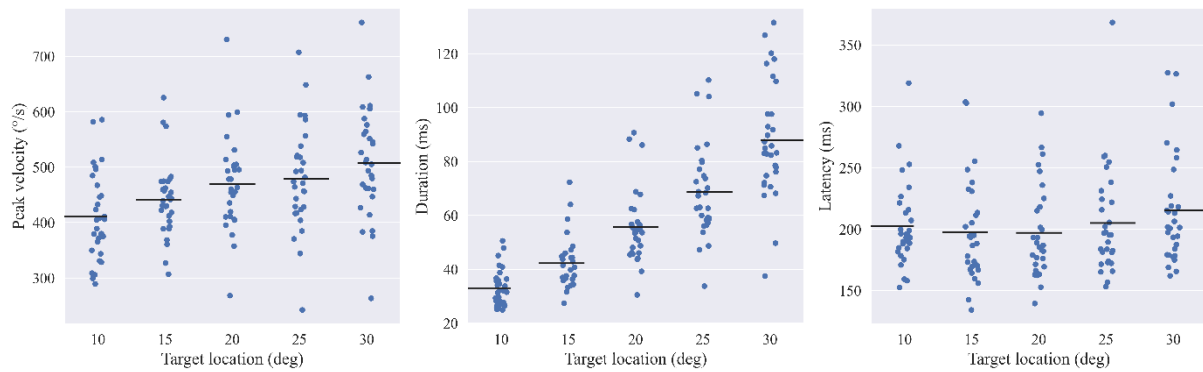


Figure 6: Saccade’s metrics. Relationships between visual saccades peak velocity (left panel), duration (middle panel), and latency (right panel) as a function of target eccentricity. Each dot represents the mean value for the corresponding parameter in one participant (30 participants in total). The mean values for all participants are shown as black lines. These data were taken from one of the experiments done during this thesis.

The saccade latency, the delay of saccade initiation relative to the go signal (target presentation for reactive saccades), represents the time our brain requires to program and initiate the saccade. The more volitional the saccade is, the higher the latency, as it takes the brain more time to make decisions. Reactive (reflexive or automatic) saccades have latency values of around 150–200 ms, and voluntary saccades latencies larger than 250 ms. Generally, the latency tends to increase with increasing eccentricity (see Figure 6).

Reactive saccades are triggered by the sudden appearance of an object in the periphery. In the laboratory, reactive saccades can be induced by presenting a target at the periphery and simultaneously extinguishing the fixation point the participants were looking at. They are instructed to perform the saccade as fast and accurately as possible toward this new target. If the fixation point disappears prior to the appearance of the peripheral target (“gap paradigm”), the so-called express saccades can be observed and they are characterized by a latency varying between 80 and 130 ms (Hamm et al., 2010). The extremely short latency of express saccades is attributed to the removal of fixation and/or disengagement of attentional focus related to the disappearance of the fixation point prior to target presentation.

Voluntary saccades can be divided into subclasses. First, scanning saccades are the most common in daily life, being performed whenever subjects naturally explore their environment. They can be studied in the lab by asking participants to look sequentially at a set of simultaneously presented targets, with or without specifying a certain scanning order. Although their latency cannot be strictly measured due to the absence of an external triggering event, scanning saccades are characterized by an inter-saccade interval longer than the latency of reactive saccades, varying around 430 ms (Alahyane et al., 2007). A second subclass of voluntary saccades is delayed saccades, which can be investigated using an “overlap paradigm”. In such tasks, when the peripheral target is

presented, the fixation point does not disappear immediately but instead remains visible for some time, and participants are requested to maintain fixation and delay their saccade to the target until an instructed cue appears (modification of the target or fixation point, or disappearance of fixation point) a few hundreds of milliseconds after target onset (overlap interval). Saccades latencies in overlap paradigms vary depending on the overlap interval (Vencato et al., 2022). Third, memory-guided saccades are saccades performed toward the memorized location of a target that disappears a certain delay before the instruction to initiate the movement is provided. Fourth, predictive saccades occur when we track a visual target that regularly jumps between two peripheral locations. Participants quickly adapt to this situation by initiating saccades directly toward the location where the target will re-appear, revealing the capabilities of our saccadic system to anticipate the target location based on expectations (Nikolov, 2020). Finally, the anti-saccade tasks consist of generating a saccade toward the target mirror (opposite) location. These tasks represent a particularly efficient tool to investigate the volitional control of saccades. Indeed, to be successful, participants must first suppress the reflexive saccade toward the visual target, and the rate of failure to inhibit this visual grasp reflex - erroneous pro-saccades made to the target- quantifies the ability of our cognitive system to inhibit responses (Munoz & Everling, 2004). Secondly, as anti-saccade tasks spatially decouple the target stimulus from the saccade response, they allow for better access to the target encoding and the response preparation processes of saccade planning, requiring our brain to flip the target vector representation resulting from sensory processes into a motor vector representation driving the saccadic efferent pathways.

In the following sections, we present the neural basis and substrate of saccadic eye movements.

2.3. Extraocular muscles

Eye movements and positioning are allowed thanks to three pairs of antagonist muscles (Figure 7). First, the medial and the lateral rectus muscles are responsible solely for horizontal movements, allowing each eye to be brought toward (adduction) or away (abduction) from the nose, respectively. Torsional movements are mediated by both the superior and the inferior oblique muscles, which respectively allow bringing the top of the eye toward (intorsion) or away (extorsion) from the nose. When the eye is abducted, vertical movements are performed thanks to the superior and the inferior rectus muscles, which are responsible respectively for the elevation and the depression of the eye. However, when the eye is adducted, the oblique muscles mediate vertical movements, an elevation for the inferior oblique muscle, and a depression for the superior oblique muscle. Finally, when the eye is straight ahead, both oblique and rectus pairs of muscles contribute to vertical movements (Purves et al., 2018).

Three cranial nerves innervate the extraocular muscles. First, the trochlear nerve (cranial nerve IV) originates from the trochlear nucleus in the caudal midbrain, decussates in the superior medullary

velum, and enters the orbit via the superior orbital fissure to innervate the superior oblique muscle contralateral to the trochlear nucleus. Second, the abducens nerve (cranial nerve VI) originates from the abducens nucleus in the caudal pons, exits from the inferior pontine sulcus, enters the orbit via the superior orbital fissure, and innervates the lateral rectus muscle ipsilaterally. Third, the oculomotor nerve (cranial nerve III) contains axons originating from the oculomotor nucleus in the rostral midbrain, exit in the interpeduncular fossa, and enter the orbit via the superior orbital fissure in order to innervate all four remaining extraocular muscles. This nerve also contains parasympathetic axons originating from the Edinger-Westphal nucleus in the rostral midbrain, innervating the iris and the ciliary muscle for pupillary constriction (Fix & Brueckner, 2009).

Motor neurons (MN) in the 3 oculomotor nuclei (abducens, trochlear, oculomotor nuclei) present a pulse-step pattern of discharge in relation to every saccade. The pulse component is a high-frequency and brief burst of action potentials providing the initial force to move the eye quickly against the visco-elastic forces due to the orbital mechanics. The burst lasts for the duration of the saccade, its frequency of discharge correlates with the saccade's velocity, and the total number of spikes in the burst correlates with the saccade amplitude. The burst of MN is directionally specific, i.e., it is observed only for the neuron's on-direction (the pulling direction of the innervated muscle) but not for other directions and notably for the off-direction, where a pause is observed instead. The step component of MN discharge is a low-frequency and sustained discharge of action potentials that maintains the eyes stable after the saccade in their new eccentric position against the passive elastic force generated by the stretched muscle. This tonic activity is linearly related to eye position also in a direction-specific way, increasing in the on-direction and decreasing in the off-direction. The activity of motor neurons is mediated by the brainstem burst generator (BBG), which consists of pre-motor neurons located in the mesencephalic, pontine, and medullary regions (Catz & Thier, 2007; Munoz, 2002).

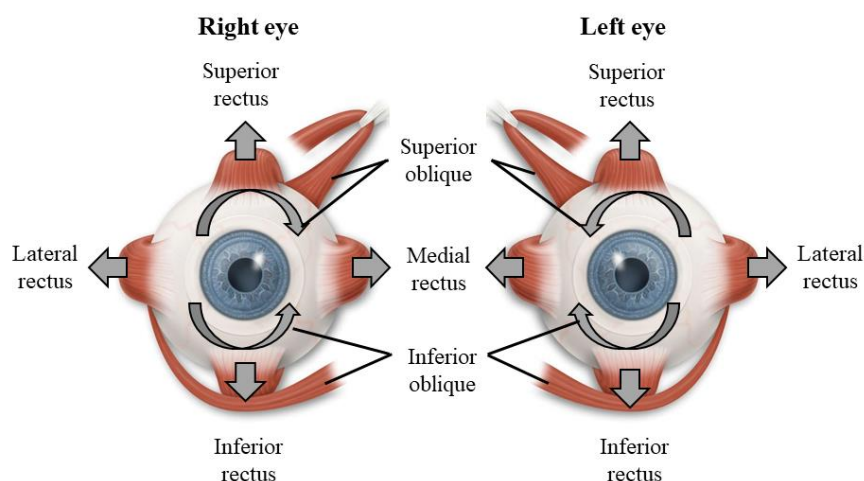


Figure 7: Schematics of the human extraocular muscles and of their direction of action.

2.4. Brainstem burst generator

The brainstem burst generator (BBG) contains different sets of neurons that operate collectively to generate the pulse-step discharge of the MN (Figure 8). We detail below the four main categories of neurons of the horizontal burst generator: the short lead burst neurons (SLBN), omnidirectional pause neurons (OPN), long lead burst neurons (LLBN), and tonic neurons (TN).

1. SLBN constitute the source of MN pulse discharge, contributing to trigger all saccades in the on-direction (ipsiversive) by displaying a burst starting around 10 ms before the saccade and stopping slightly before its end (Highstein & Baker, 1978; Luschei & Fuchs, 1972). They include excitatory burst neurons (EBN) and inhibitory burst neurons (IBN). EBNs have excitatory monosynaptic connections with the MN of the ipsilateral abducens nucleus; thereby, the EBN burst of activity contributes to triggering saccades by activating agonist muscles of the ipsilateral eye. In addition, EBNs also activate in the abducens nucleus, inter-nuclear neurons that indirectly innervate, via the oculomotor nucleus MN, the medial rectus muscle of the contralateral eye. Thus, EBNs are responsible for the contraction of the agonists of both eyes (Scudder et al., 2002). In contrast, the IBN's main role is to relax the antagonists of both eyes (Scudder et al., 1988). Indeed, IBN make monosynaptic inhibitory connections with the MN and inter-nuclear neurons of the contralateral abducens nucleus, such that the IBN burst contributes to ipsiversive saccades by generating a pause of activity in these neurons, resulting in the relaxation of antagonist muscles. IBN also make monosynaptic inhibitory connections with the contralateral burst neurons (EBN and IBN), shutting down the antagonist burst generator and thus re-enforcing the 'push-pull' control of agonist vs antagonist motor commands during saccades. While EBN and IBN responsible for horizontal saccades are located in the paramedian pontine reticular formation (PPRF), EBN and IBN responsible for vertical saccades are located in the rostral interstitial nucleus of the medial longitudinal fasciculus in the mesencephalon (riMLF) and the interstitial nucleus of Cajal (INC). IBN can also be found in the medullary reticular formation (medRF). Both EBN and IBN receive excitatory projections directly from the superior colliculus (SC) and indirectly via the LLBN (note that IBN also receive excitatory projections from ipsilateral EBN) (Scudder et al., 2002).

2. OPN are found in the PPRF; they have a tonic discharge during fixation while pausing during saccades in all directions. OPN have inhibitory monosynaptic connections with both EBN (Curthoys et al., 1984) and IBN (Sparks, 2002), allowing them to act as a brake by keeping the saccadic pulse generator permanently silent during fixation periods. Their pause of activity, allowing saccade triggering, comes from two main sources: first, OPN receive indirect inhibitory connections from the SC (more precisely from fixation neurons in rostral SC) via Trigger (Tr) interneurons, which, combined with a possible direct inhibition by the LLBN, contributes to launch the saccade by releasing OPN inhibition on the pulse generator; second, OPN are also indirectly inhibited from EBN via Latch (La) interneurons, this circuit being thought to maintain the OPN brake released until the

end of the saccade. It is suggested that OPN contribute to oblique saccades by synchronizing the onset of EBNs responsible for both horizontal and vertical saccades (Moschovakis et al., 1996; Sparks, 2002).

3. LLBN are found among EBN and IBN in the PPRF and the medulla and have different roles and characteristics. Some LLBN have been found to burst for a preferred or on-direction, similar to EBN and IBN. In contrast, others called vectorial LLBN have been found, similarly to collicular neurons, to fire for specific saccade vectors (size and direction specific). LLBN receive excitatory projection from the SC and send excitatory projection to EBN, and therefore, LLBN serve as a relay between those two. It is also suggested that LLBN may have inhibitory connections with OPN, thus contributing to silencing them during saccades. In addition, some LLBN found in the PPRF and the nucleus reticularis tegmenti pontis (NRTP) send projections to the cerebellum (Moschovakis et al., 1996; Scudder et al., 2002).

4. The step discharge of MN allowing to maintain the eye at an eccentric position at the end of a horizontal saccade is triggered by excitatory projections from tonic neurons (TN) in the nucleus prepositus hypoglossi NPH and the medial vestibular nuclei MVN, while neurons in the INC provide vertical and torsional eye position signals. It has been found that neurons in the NPH discharge robustly for saccades in the on-direction and pause for saccades in the off-direction. Their inactivation does not affect the amplitude of saccades but instead results in an incapability to maintain the eye in an eccentric position at the end of horizontal saccades. Similarly, the inactivation of neurons in the INC results in an incapacity to hold the eye position after vertical or oblique saccades. NPH and MVN receive excitatory projection from EBN, and it has been suggested that in addition to contributions from cerebellar areas, eye position signals are created by mathematical integration of EBN discharges. (Catz & Thier, 2007; Munoz, 2002; Scudder et al., 2002; Sparks, 2002).

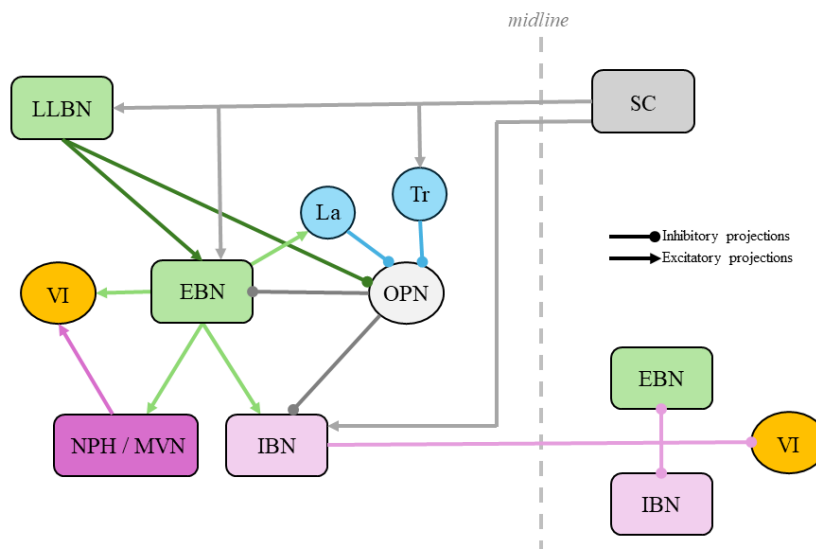


Figure 8: The brainstem burst generator. Schematics of the different types of neurons and connections composing the brainstem burst generator responsible for horizontal eye movements. SC:

Superior colliculus, LLBN: Long-lead burst neurons, EBN: Excitatory burst neurons, IBN: Inhibitory burst neurons, OPN: Omnidirectional pause neurons, VI: Abducens nuclei, La: Latch neurons, Tr: Trigger neurons, NPH: nucleus prepositus hypoglossi, MVN: medial vestibular nuclei.

2.5. Superior colliculus

The Superior colliculus (SC) is a multilayered structure in the midbrain, with superficial, intermediate, and deep layers characterized by distinct neurons, inputs, outputs, and functions. This structure is critical for eye movements, coordinated head-and-eye movements, and head-eye-and-body movements and plays an important role in multisensory integration and the orienting of attention. For the purposes of this thesis, we will discuss solely the role of the superior colliculus in head-restrained saccadic eye movements.

The superficial layers receive direct inputs from the retina and the primary visual cortex. They contain visual neurons involved in target detection and localization, encoding visual information in a retinotopic frame of reference. The intermediate layers receive cortical multisensory (auditory, visual, and somatosensory) information; they also receive information from the collicular superficial layers. The intermediate layers constitute a site of multisensory integration and contain buildup neurons exhibiting gradual increases in activity before saccade onset. Finally, the deep layers receive inputs from cortical saccadic areas and from the SC intermediate layers; together with the latter, they generate the motor commands for saccadic eye movements and send them to the brainstem pulse generator (Liu et al., 2022).

The deep layers contain buildup and burst neurons, which both exhibit a high-frequency burst of action potentials a few milliseconds before and during saccades in a spatially specific manner: for each neuron, the burst depends on the saccade's amplitude and direction, being present only when the saccade ends in a certain region of the retinotopic space, the so-called movement field, with a maximal firing rate for an optimal saccade vector within the movement field. The arrangement of neurons with such spatially selective burst activity defines a retinotopic map in the deep and intermediate layers: neurons responsible for small-amplitude saccades (small and perifoveal movement fields) are located rostrally within the SC, while neurons with large and eccentric movement fields responsible for large-amplitude i) horizontal saccades are located more caudally ii) vertical upward/downward saccades are located more medially/laterally. It is important to note that the number of burst neurons responsible for small saccades and the surface of the SC dedicated to them are proportionally higher than for larger saccades. The repartition of neurons involved in the vertical component of saccades along the mediolateral areas of the SC tends to be more linear (Gandhi & Katnani, 2011; Sparks, 2002; Sparks et al., 1976).

The rostral pole of the SC also houses fixation neurons, which fire tonically during fixation and pause during saccades. Fixation has been proposed to be an active motor state involving the direct projection of these SC fixation neurons to the brainstem OPNs. However, several studies showed that

the discharge properties differ between OPNs and SC fixation neurons, notably the later discharge also for contraversive micro-saccades and small amplitude saccades. Therefore, it is suggested that neurons in both rostral SCs act together to provide a balance of activity capable of maintaining fixation through inhibitory projections on caudal SC neurons, a hypothesis arguing against the presence of “literally” fixation neurons. (Hafed et al., 2009; Hafed & Krauzlis, 2010).

As indicated above, individual SC neurons burst maximally for their optimal saccade vector, but they also burst for a wide range of saccade vectors insofar as they terminate in the neuron’s movement field. Since this movement field is broad, the pre-saccadic burst sent by the SC’s deep layers to the brainstem results from a large population of neighboring burst neurons, whose movement field encompasses the saccade vector. How the global brainstem motor command results from the discharge of all activated SC neurons is an issue known as the spatio-temporal transform. Two commonly discussed models are debated in this area. The vector averaging model states that the global population burst results from summing all individual neurons’ bursts and then dividing the sum by the number of active neurons; in other words, the global activity encodes the vector average of all elementary vectors encoded by individual neurons. In contrast, in the vector summation model, the global activity encodes the weighted sum of all individual neuron vectors, resulting from a simple summation of the activity of individual neurons (Gandhi & Katnani, 2011).

SC burst neurons project directly to IBN and EBN as well as indirectly through LLBN, present in pontine and mesencephalic regions. They further project to the central mesencephalic reticular formation (cMRF), which further projects back to the SC. Therefore, it was suggested that cMRF constitutes a brainstem feedback source to the SC (Waitzman et al., 2000). Neurons in the deep and intermediate layers of the SC also indirectly project to the cerebellum through the nucleus reticularis tegmenti pontis NRTP. This projection allows further processing and refining of the saccade motor command by the cerebellum, which is crucial for the mechanism of saccadic adaptation, maintaining our saccade precision throughout life and constituting the central interest of this thesis. Furthermore, the deep and intermediate layers of the SC receive feedback from the cerebellum, as will be described in the next section. As mentioned in Chapter 1, visual information travels via the dorsal stream and reaches the posterior parietal cortex. This later projects to frontal areas, including the frontal and the supplementary eye fields (FEF and SEF). The deep layers of the SC receive inputs from the lateral intraparietal (LIP) as well as from the FEF, the SEF, and the dorsolateral prefrontal cortex (DLPFC) directly or indirectly through the basal ganglia (Gandhi & Katnani, 2011; Liu et al., 2022; Munoz & Everling, 2004; Scudder et al., 2002; Sparks, 2002). Therefore, cortical and subcortical information that reaches the SC is integrated within its sensorimotor map, allowing the selection of the proper target and, once the activity of saccades build-up neurons surpasses a certain threshold, the triggering of the saccade. Once the motor command is generated, a copy of the motor command (efference copy, also termed corollary discharge) is sent from the SC to the FEF through the mediodorsal nucleus (Zimmermann & Lappe, 2016).

2.6. Cerebellum

The cerebellum, located at the back of the brain underneath the occipital lobe, plays a crucial role in motor control, coordination of voluntary movements, balance and posture control, and learning motor skills. In the context of saccadic eye movements, the cerebellum is involved in fine-tuning (motor planning and timing) and adapting (amplitude control) those movements. The cerebellum receives indirect inputs from the FEF, SEF, and the SC via neurons in cerebellar relays located in the NRTP as well as in parts of the pontine nuclei, which project bilaterally via Mossy fibers to lobules VIc and VII, also called the oculomotor vermis. This later contains Purkinje cells, which have an inhibitory projection to the caudal end of the fastigial nucleus, also called the fastigial oculomotor region (FOR). The FOR, via its contralateral projections to the BBG, has excitatory effects on SLBN and LLBN. FOR was shown to discharge a few milliseconds before and during contraversive saccades and to start discharging around 30 ms before the end of ipsiversive saccades. In addition, unilateral inactivation of the FOR in awake animals has repeatedly led to hypermetric ipsiversive saccades and hypometric contraversive saccades (cat: (Goffart et al., 1998), monkey :(F. R. Robinson et al., 1993)). Therefore, FOR activity is crucial for accelerating contraversive saccades and decelerating the ipsiversive ones through its projections to the brainstem burst generator. The FOR projects also to the deep and the intermediate layers of the SC, therefore constituting a source of cerebellar feedback to the SC, which can also contribute to modulating the saccade command (Munoz & Everling, 2004; Scudder et al., 2002). Purkinje cells receive excitatory inputs via climbing fibers originating at the level of the inferior olive, which receives inputs from the SC. Those fibers and the complex spikes they produce in Purkinje cells play a crucial role in motor learning, supposedly by generating the error signal driving saccadic adaptation (Iwamoto & Kaku, 2010). In the next chapter, we will discuss the role of the cerebellum in saccadic adaptation.

2.7. Basal ganglia

The basal ganglia form an indirect relay between structures in the frontal cortex (FEF, SEF, and DLPFC) and the superior colliculus, contributing to the performance of voluntary saccades based on our internal goals and motivations and the inhibition of unwanted reactive saccades performed toward the sudden appearance of stimuli in the environment. Therefore, it is a site for integrating motivation and reward information into the saccade motor command. The basal ganglia's caudate nucleus (CN) receives excitatory inputs from the frontal cortex. The activation of CN triggers either a direct inhibition or an indirect excitation of the Substantia nigra pars reticulata (SNpr). The indirect pathway between the CN and the SNpr involves two inhibitory connections: the first is between the CN and the external segment of the globus pallidus (GPe), and the second is from the GPe to the subthalamic nucleus (STN). The SNpr, in its turn, has inhibitory projections to the intermediate layers of the SC and thalamic nuclei projecting to the frontal cortex (Catz & Thier, 2007; Munoz & Everling, 2004).

2.8. Cortical areas

At this point, it is already mentioned that several cortical areas are implicated in saccadic eye movements. The contribution of cortical regions to saccades has been studied extensively in both humans and monkeys.

Electrical stimulations of FEF in monkeys were shown to produce both head and eye movements (Tu & Keating, 2000). Pre-target preparatory activity predicting both the direction and the time of saccade occurrence has been seen in the FEF, and the higher this activity, the lower the saccade reaction time (J. D. Connolly et al., 2005). The FEF has efferent projections to the SC either directly or through the basal ganglia. Single neuron recordings in monkeys SC and FEF show that, similar to the SC, FEF also contains saccade-related neurons and fixation neurons. It was suggested that FEF neurons projecting directly to the SC carry the preparatory activity for pro-saccades and anti-saccades (Everling & Munoz, 2000), as supported by the attenuated preparatory and stimulus-related activity in the SC to avoid unwanted pro-saccades in anti-saccades tasks in monkeys (Everling et al., 1999). It also projects to the NRTP, which sends inputs to the cerebellum. In addition, FEF has been shown to have weak (Hanes & Wurtz, 2001) but numerous projections to brainstem areas, including the cMRF, riMLF, PPRF, NPH, and INC. Further, it has been shown that the stimulation of FEF activates LLBN and inhibits OPN (Scudder et al., 2002). In humans, fMRI shows that the FEF, along with the SEF and the precuneus, are more activated in anti-saccade tasks than in tasks involving reactive pro-saccades (Dyckman et al., 2007). In fact, another fMRI study showed that the contribution of the FEF to voluntary saccades is more linked to its mediolateral part, while the lateral part of FEF shows activation during both reactive and voluntary saccades (Jamadar et al., 2013).

Furthermore, the DLPFC, the SEF, and the anterior cingulate cortex (ACC) contribute to the volitional control of saccadic eye movements either by the initiation of voluntary saccades or by suppressing unwanted saccades (Hamm et al., 2012; Jamadar et al., 2013). Both DLPFC and SEF project to the FEF and the SC, and it was also shown that SEF has projections to the brainstem similar to those of the FEF (Munoz & Everling, 2004). A decrease in the activity of the FEF and the SEF over time has been found in anti-saccade tasks as subjects' efficiency increases, which might be associated with fewer neural resources being necessary to achieve the task (Lee et al., 2013). The DLPFC, along with the ventrolateral prefrontal and the inferior frontal cortex, also show increased activity in anti-saccades tasks compared to pro-saccades ones, which was attributed to the role of those areas in the suppression of erroneous saccades. Furthermore, based on a negative correlation of their activity, the DLPFC has been shown to exert top-down control on the occipital visual cortex (Clementz et al., 2007, 2010; Dyckman et al., 2007; Jamadar et al., 2013).

The parietal cortex contributes largely to visual attention mechanisms, including saccade target selection, the suppression of unwanted saccades, and the maintenance of spatial information in working memory (Nikolov, 2020). Both the FEF (Sato & Schall, 2003) and the LIP (Zhang & Barash,

2000, 2004) areas participate in the vector inversion process crucial for anti-saccade execution. LIP receives inputs from the visual cortex via the dorsal stream, as described in Chapter 1, and further sends outputs to frontal structures, including the FEF, the SEF, and the DLPFC (Munoz, 2002) and its stimulation can directly trigger saccades (Johnston & Everling, 2008). The human homolog of the LIP is still debated; indeed, in the human PPC, distinct functional subregions characterized by specific activities have been found to contribute to reactive saccades (superior and lateral regions of the superior parietal cortex), voluntary saccades (inferior and medial regions of the superior parietal cortex), or both types of saccades (intraparietal sulcus, inferior parietal lobule and the supramarginal gyrus) (Ford et al., 2005; Jamadar et al., 2013; Krafft et al., 2012).

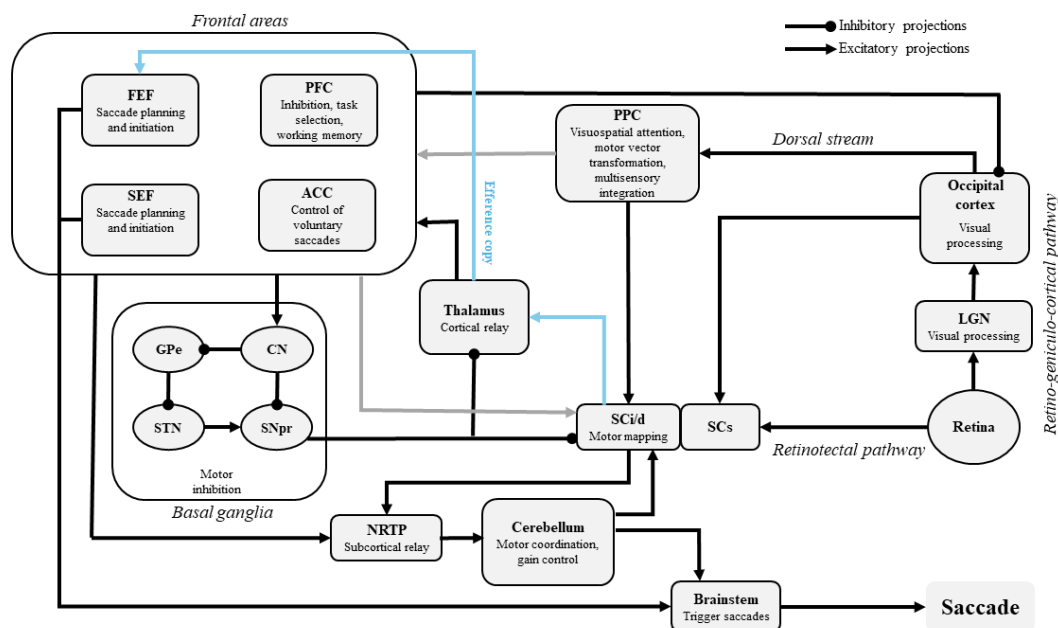


Figure 9: Saccadic eye movements network. Summary diagram of the different cortical and subcortical areas involved in saccadic eye movements. FEF: Frontal eye field, PFC: Prefrontal cortex, ACC: Anterior cingulate cortex, SEF: Supplementary eye field, PPC: Posterior parietal cortex, LGN: Lateral geniculate nucleus, SCs: Superior colliculus superficial layers, SCi/d: Superior colliculus intermediate and deep layers, NRTP: Nucleus reticularis tegmenti pontis, CN: Caudate nucleus, SNpr: Substantia nigra pars reticularata, STN: Subthalamic nucleus, GPe: external segment of the globus pallidus.

2.9. Saccades to non-visual targets

In a rich and vivid world, our sensory system is bombarded with infinite information originating from objects and individuals around us. This information can be encoded by visual, somatosensory, auditory, or olfactory systems, but it frequently results from a combination of at least two sensory modalities. Such multisensory processing is critical to gather and refine knowledge about the external world but also to adequately interact with it. Concerning eye movements, saccades can be performed

both toward visual and non-visual targets, like auditory stimuli (for example, the sound of a car brake nearby) or somatosensory stimuli (the sensation of a mosquito that landed on my hand).

Somatosensory and auditory saccades are less accurate than visual saccades but are nonetheless functionally important (e.g., preparing to visually process a zone of space where we anticipate the presence of an object of interest); in addition, they offer an interesting experimental tool to investigate multisensory integration, sensory-motor transformation, and coordinates transformation. In this section, we will review the literature examining the characteristics of somatosensory and auditory saccades.

2.9.1. Tactile saccades

Somatosensory saccades are aimed at somatosensory targets, which can be proprioceptive (sensory signals about static limb position), kinesthetic (sensory signals about limb movement), and tactile signals (sensory signals about touch on the skin). They are characterized by long latency and low peak velocity in comparison to visual saccades (Groh & Sparks, 1996a; Sullivan et al., 2004). The accuracy of somatosensory saccades is also lower and further decreases with increasing target eccentricity. In addition somatosensory saccades show a high within and well as between subjects variability. Blanke and Grüsser tested eccentricities ranging between 10 and 80 degrees of visual angle and showed that somatosensory saccades accuracy was minimal for saccades in a 40–50 degrees range and increased for larger stimulus eccentricities (Blanke & Grüsser, 2001). Furthermore, it was shown that the accuracy of somatosensory saccades does not change when varying the nature of somatosensory information or combining different types of somatosensory information (Goettker et al., 2020). Somatosensory saccades can also be classified as reactive or voluntary (Amlôt & Walker, 2006). Indeed, by comparing pro- and anti-saccades in the visual and somatosensory modality, Amlôt and Walker showed that the difference in latency seen for the visual modality (157 ms versus 229 ms) was present also for the somatosensory modality (222 ms versus 265 ms). Furthermore, erroneous pro-saccades in the somatosensory anti-saccades task occurred as often (11.04%) as in the visual anti-saccades task (13.13%) (Amlôt & Walker, 2006).

The difference in latency between somatosensory and visual pro-saccades is attributed to the time needed by the brain to change the representation of somatosensory information from a body-centered to an eye-centered frame of reference, as suggested by Neggers and Bekkering (1999). These authors compared the latencies of saccades and hand movements toward visual or tactile targets delivered on participants' knees. They found that for tactile targets, the latencies of hand and eye movements correlated more strongly with each other compared to visual targets. Their interpretation was that the tactile stimulation of the knee is represented in a leg-reference frame and thus needs to be translated into a trunk-reference frame to be used for arm movements and an eye-centered frame of reference to be used by the eyes, which increased at both the latency of those two movements and their temporal correlation whereas, the visual target is encoded in an eye-centered reference frame directly usable by

eye movements but requiring for arm movements to be translated into a trunk reference frame (Neggers & Bekkering, 1999).

Somatosensory saccades sometimes have curved trajectories, particularly in crossed-hand conditions where saccades start toward the non-stimulated hand and then curve away toward the stimulated hand (Groh & Sparks, 1996a; Overvliet et al., 2011). Such curved trajectories occur when participants have to initiate their saccades immediately after the tactile stimulation but not in conditions of delayed saccades. Furthermore, the latency of somatosensory saccades is higher toward crossed-hands than toward uncrossed hands as in the former condition, the conflict between the external and somatotopic representations is more demanding than in the uncrossed-hand condition and must be solved by spatial remapping of tactile inputs.

Groh and Sparks recorded neurons in monkeys' SC during a saccade task and found that among 86 cells exhibiting saccade-related activity, 85 discharged for both visual and somatosensory saccades. The discharge frequency for visual saccades was higher than that of somatosensory saccades, which might explain the lower velocity of the latter. Furthermore, the discharge of such bi-modal neurons did not depend solely on the location of the target nor the initial eye position but varied depending on the amplitude and the direction of the saccade, whether visual or somatosensory. This finding indicates that SC bimodal neurons have a movement field in relation to both visual and somatosensory saccades, encoding in both cases the saccade goal in an oculo-centric coordinate. This suggests, in turn, that the somatosensory signals were translated from their native body-centered reference frame into eye-centered motor coordinates prior to the SC recording site location. In addition, visual and somatosensory movement fields of individual cells were similar, letting the authors suggest that the inaccuracy of somatosensory saccades resulted from inaccurate signals reaching the SC rather than an error signal added downstream. Finally, the collicular motor activities started with the same delay following tactile and visual targets but reached their peak later for tactile saccades than for visual saccades, therefore indicating that the difference in latency between both saccades modalities might originate from the difference in collicular motor cell activity (Groh & Sparks, 1996b).

In a separate study, Groh & Sparks (1996c) investigated whether the coordinate transformation from a body-centered to an eye-centered frame of reference, which is necessary for the correct activation of SC motor responses, occurs at the level of the SC or upstream. They recorded the activity of 34 neurons exhibiting sensory responses to somatosensory targets in the intermediate and the deep layers of monkeys SC during a delayed saccade task and found that the somatosensory response of 25 of these cells was significantly affected by eye position, therefore indicating that coordinate transformation has taken place as least partly upstream the SC. During a somatosensory saccade task in humans, Buchholz and colleagues showed that a gamma-band response occurred in the posterior parietal cortex (PPC), contralateral to the gaze-centered location of the stimulus, even though the stimulus was not seen, simultaneously with a transient stimulus-induced gamma-band response in

somatosensory areas, contralateral to the stimulated hand in a body-centered frame. They suggested that a fast bottom-up sensory-induced remapping occurred in the PPC (Buchholz et al., 2011).

2.9.2. Auditory saccades

Spatial acoustic cues allowing the localization of a sound source rely on the sound's physical interaction with the head and the external ears and differ between the horizontal and the vertical plane. The detection of sound azimuth (in the horizontal plane) relies on comparing acoustic signals (interaural time difference and interaural intensity difference) between both ears. Sound elevation (in the vertical plane) is more complex to localize due to the lack of binaural discrepancies; it rather relies on the pinna geometry, which modifies the sound and creates spectral cues that the brain interprets to determine the elevation. Humans are faster at detecting auditory targets than visual ones as the sound reaches the cortex faster. However, when it comes to saccades, visual saccades are initiated faster than auditory saccades, as for the latter, the sensory signals need to be transformed from their native head-centered frame of reference into the oculocentric frame used by the saccadic system. Auditory saccades can be reflexive (for high-intensity stimuli) or voluntary (low-intensity stimuli), and differences in latency that can go up to 120 ms have been found when comparing auditory saccades in a step paradigm to those in an overlap paradigm (Hu & Vetter, 2024; Zambarbieri, 2002).

Like somatosensory saccades, auditory saccades are characterized by their higher latency (for saccades up to 30°) and lower peak velocity in comparison to visual saccades (Frens & Van Opstal, 1995; Yao & Peck, 1997). However, one unique feature of auditory saccades is that contrary to visual saccades (where the latency tends to increase with eccentricity, see section 2.2.), auditory saccades' latency decreases when the target eccentricity increases; this relationship does not depend either on auditory target frequency, intensity, or spatial location but rather depend on the eye initial position (Gabriel et al., 2010; Zambarbieri et al., 1995). When the sound is at or near the midline, the amplitude and the phase difference at the level of the ears are small, which makes the target location ambiguous. This can reflect that the latencies of auditory saccades to targets with small eccentricities are the highest. It also was shown that auditory saccades toward targets with narrowband noises have lower latency, which makes us better at localizing speech in space (Gabriel et al., 2010).

Auditory saccades sometimes have a curved trajectory, which increases with target eccentricity. Furthermore, they are often followed by secondary saccades with a latency varying in a wide range (0 to 500 ms). Both the curvature of primary saccades and the secondary saccades are thought to result from corrective processes that improve auditory saccades' accuracy. Both the peak velocity and saccade duration increase with the target eccentricity such that, as for visual saccades, auditory saccades follow the main sequence relationship (Zambarbieri et al., 1982). The accuracy of auditory saccades decreases with increasing target eccentricity. For example, while the gain of visual saccades toward targets at 10, 20, and 30 degrees of visual angle are 0.96, 0.94, and 0.9, respectively, the gain of auditory saccades toward targets at the same eccentricities are 0.91, 0.68, and 0.62 respectively

(Yao & Peck, 1997). It has also been shown that the accuracy of auditory saccades is not affected by the frequency of auditory targets (Gabriel et al., 2010). Furthermore, both the latency and the accuracy of auditory saccades depend on the location of the target relative to the eye rather than the target's spatial location (Yao & Peck, 1997). To decipher at which sensorimotor level auditory information is transformed into such eye-centered frame of reference, Jay and Sparks recorded the activity of visual-motor neurons and saccade-related burst neurons in the intermediate layer of monkeys' SC during a task involving delayed auditory and visual saccades. They found that 57 out of 59 visual-motor neurons had a sensory response to the visual target appearance but none to the auditory target presentation. Yet, 79% of the total number of recorded neurons (72) had a motor burst prior to saccades to both auditory and visual targets, with a burst strength related to the saccades' amplitude and direction. This indicates that auditory signals encoded originally in a head-centered reference frame have undergone a transformation that allows them to trigger saccadic eye movements using a common pathway with visually triggered saccades. The number of collicular cells discharging prior to auditory saccades was less than for visual saccades, which might explain the lower peak velocity of auditory saccades (Jay & Sparks, 1987a). A separate study suggested that the coordinate transformation of auditory signals occurs gradually (across time) within the SC (Jay & Sparks, 1987b). A more recent study (Lee & Groh, 2012) showed that in the deep layers of the SC, most recorded neurons (64%) exhibit a hybrid frame of reference, i.e., between the eye-centered and the head-centered ones, and that the percentage of neurons with an eye-centered frame of reference increases during saccade preparation and execution to reach 69% of the recorded population 20 ms after the saccade onset confirming and re-enforcing the previous suggestion of Jay and Sparks (Jay & Sparks, 1987b) on the gradual occurrence of coordinate transformation. Note that this maximal percentage was relatively close to the percentage of eye-centered neurons during the visual saccade task (89%), therefore showing that auditory signals are progressively translated into a reference frame roughly similar to that used for vision but only in the motor areas (Lee & Groh, 2012).

The inferior colliculus (IC) forms a fundamental structure in auditory perception where sound signals encoding both the horizontal and the vertical planes converge. Furthermore, the IC also receives somatosensory and visual information from cortical and subcortical areas and is reciprocally connected with the SC. It is suggested to be the main source of auditory signals used to trigger auditory saccades in the SC. Information in the IC is encoded in a hybrid frame of reference (Hu & Vetter, 2024).

The FEF contains, in addition to neurons responsive to visual stimulation, neurons responsive to auditory stimulation. It was shown that the activity of those auditory neurons was indistinguishable from visual neurons at the time of saccade onset, revealing a near-complete transformation of auditory signals to an eye-centered frame of reference in FEF (Caruso et al., 2016). The FEF has reciprocal connections with the superior temporal gyrus (STG), which belongs to the auditory system. STG is also part of the attentional network, whereby the auditory system could possibly enhance oculomotor

responses (probably to compensate for the reduced visual sensitivity due to the suppression mechanism during saccade) and reciprocally; the FEF could modulate the excitability of the auditory system and/or it might trigger saccades toward auditory targets directly through the FEF connections with the SC and the brainstem (Hu & Vetter, 2024; Leszczynski et al., 2023). Furthermore, it has also been suggested that the DLPFC and the basal ganglia play a role in auditory saccade suppression (Hu & Vetter, 2024). Last but not least, neurons responsive to auditory stimulations and active during saccades were also found in monkeys' LIP, a well-known cortical site of multisensory integration (Grunewald et al., 1999; Linden et al., 1999). It was shown that contrary to previous belief, LIP neurons exert a hybrid frame of reference rather than a shift to an eye-centered frame of reference slightly before and during saccades to both visual and auditory targets (Mulette-Gillman et al., 2009).

2.10. Conclusion

Saccadic eye movements are oculomotor actions that bring the fovea toward an object of interest either reflexively or voluntarily. They require the activation of a large set of cortical and subcortical areas, which eventually leads to the generation of a burst by motor neurons in the brainstem, which innervates the agonist and antagonist extraocular muscles. Saccades can also be triggered toward somatosensory or auditory targets, a process involving the translation of signals encoded in a body-centered or a head-centered frame of reference into an eye-centered frame of reference such that all saccade types share a common motor pathway. In the next chapter, we will discuss how our brain maintains the precision of saccades throughout life.

Chapter 3: Saccadic adaptation

The ability of the brain to change and adapt throughout our lives is referred to as brain plasticity. It represents a fundamental property of the nervous system and is involved in various pathological or physiological situations, including injuries, experiences, memory, and learning. The brain structures can strengthen or weaken neural connections, form new ones, and even create new neurons in certain areas. Sensorimotor plasticity is a specific form of brain plasticity that involves changes in the sensorimotor system to ensure optimal perception and motor control in response to changes occurring in our body and our environment.

Due to their short duration, saccades, especially the short ones, lack an online mechanism that allows their trajectory to be modified in flight. When saccades repeatedly miss their goal, two compensatory responses are observed. First, a secondary, corrective saccade takes place about 100 to 300 ms after completion of the primary saccade, and second, a gradual modification of the primary saccade takes place. This second compensatory response, involving an adaptation of the saccade motor commands, re-installs primary saccade precision and thus reduces the costly generation of two consecutive saccades to acquire one particular target. This gradual modification of saccade trajectory, so-called saccadic adaptation, is a plasticity-based mechanism that allows us to maintain saccade precision throughout life, overcoming the detrimental effects of fatigue that we are subject to in our daily life, of the age-related decline of cognitive and physical capabilities, as well as of cerebral and neuromuscular lesions.

In this chapter, we will review the key features of saccadic adaptation with an emphasis on those relevant to this thesis's purpose. We will describe how saccadic adaptation is studied in the laboratory, the different adaptation types, the specificities of adaptation related to the different types of saccadic eye movement (reactive vs. voluntary), the nature of the error signal driving saccadic adaptation as well as the neural correlates of the various components of saccadic adaptation.

3.1. Studying saccadic adaptation

Saccadic adaptation can be studied in monkeys via invasive techniques, such as weakening the extraocular muscles to produce saccade inaccuracy. When the horizontal recti muscles of one eye are weakened by tenectomy, saccades of the weakened eye are hypometric. When the normal eye is patched, the amplitude of the weakened eye saccades gradually increases and becomes normometric after a few days. Furthermore, hypermetric saccades are performed with the normal eye when the patch is removed. Repatching the weakened eye after normalization of its gain produced a return of deficits in that eye over a few days. Indeed, saccadic adaptation increases both the step and the pulse discharges of motor nuclei in the brainstem in order to restore normometric saccades (Optican & Robinson, 1980; Snow et al., 1985).

The results seen in monkeys after tenectomy can also be seen in humans with extraocular muscle innervation damage. For example, Kommerell et al. (Kommerell et al., 1976) studied a patient with abducens palsy, affecting the lateral rectus muscle that rotates the eye laterally, and Abel et al. (Abel et al., 1978) studied a patient with a medial rectus paresis secondary to a partial third nerve palsy. In the first study, the patient had normometric saccades for the weak eye compared to hypermetric saccades for the normal eye. When the weak eye was patched, the normometric saccades were restored in the normal eye. In the second study, the patient had hypometric saccades in the weak eye. When the good eye was patched, a gradual increase toward normal amplitudes took place for the saccades of the weak eye in parallel with an increasing hypermetria for the normal eye saccades.

In those lesion studies, patching the normal eye forces the participants to rely on the weakened

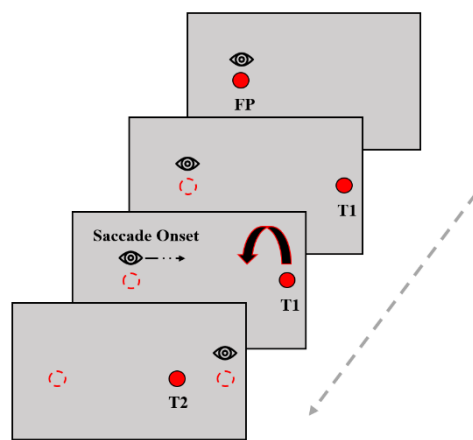


Figure 10: McLaughlin's paradigm. Eliciting backward adaptation of reactive saccades by the McLaughlin's double-step target paradigm. After a random fixation interval a visual target appears in the periphery (T1), simultaneously with the disappearance of the fixation point (FP). The participant is required to perform a saccade toward T1. Once the onset of the saccade is detected the target undergoes a backward shift (T2) which results in a mismatch between the eye landing position and the location of the visual target.

eye for vision and, therefore, increases the detection of the saccadic errors made due to the weakening. Thus, saccadic adaptation modifies the saccade motor command to overcome the consequences of the lesions. Those modifications take place apparently at a locus common for both eyes, which explains the gain change in the normal eye when the patch is removed.

Fortunately, non-invasive techniques are available to study saccadic adaptation in human volunteers. First, the double-step target paradigm also referred to as the constant target step, introduced by McLaughlin (McLaughlin, 1967), consists of stepping the visual target while the saccade is in flight in order to introduce a mismatch between the eye landing position at the end of the primary saccade and the visual target, as represented in Figure 10. The participants usually do not perceive the second target step thanks to saccadic suppression (described in the next paragraph), but

the mismatch related to the saccade landing position is monitored by the brain and interpreted as a saccade error. The repetition of this type of trial with a systematic target perturbation (constant target step paradigm) induces a progressive modification of the saccade amplitude in order to reduce the experienced inaccuracy of saccades. An inward (toward the initial eye position) second step of the visual target induces an adaptive decrease in saccade amplitude, so-called backward or inward adaptation, whereas an outward (in the direction of the saccade) second step induces an adaptive increase in saccade amplitude (forward or outward adaptation). Furthermore, saccadic adaptation can be triggered by shifting the visual target orthogonally relative to the saccade direction, up or down, yielding an adaptation of the saccade direction. During the course of such directional adaptation, saccades usually show a curved trajectory that might describe a late-arriving motor correction, suggesting a possible online correction for this adaptation type (Chen-Harris et al., 2008).

In the McLaughlin paradigm, the visual error decreases over time as saccadic adaptation develops, reaching an asymptote after over 100 trials in humans (several hundred trials in monkeys), as represented in Figure 11. While most studies investigate saccadic adaptation in a head-restrained condition, little is known about the adaptation of saccadic gaze shifts performed with the head free to move. Nonetheless, it is known that the double-step target paradigm effectively induces gaze adaptation in both humans and monkeys (Cecala & Freedman, 2008, 2009).

Initial reports comparing saccadic adaptation induced by the double-step paradigm and adaptation induced by extraocular muscle tenectomy in monkeys point to a slower adaptation rate in the latter procedure, suggesting two different adaptation mechanisms. However, Scudder et al. (Scudder et al., 1998) compared both techniques and showed that this difference results from the number of saccade targets that the monkeys were exposed to in each method. While in the double-step paradigm, only a few targets are used to induce adaptation, extraocular muscle tenectomy is a chronic intervention such that a wide range of saccade targets are experienced by monkeys with their severed muscles. Indeed, the authors report that when the number of visual targets is equalized, saccadic adaptation occurs at similar rates for both techniques.

Second, saccadic adaptation can also be induced via the so-called constant error paradigm (Robinson et al., 2003). This paradigm is a variation of the double-step target paradigm, but here, the visual error relative to the saccade endpoint, rather than the target step, is maintained constant throughout the adaptation exposure, irrespective of the ongoing change of the saccade amplitude. Therefore, this requires waiting until the saccade offset to measure the eye landing position before stepping the visual target. Note that this post-saccadic target step might thus be consciously perceived, constituting a second difference with the original, constant target step, McLaughlin's paradigm. It has been suggested that forward adaptation with constant error is less effective than forward adaptation with the constant target step, while backward adaptation has the opposite pattern (F. R. Robinson et al., 2003; Straube et al., 1997). In a recent study, forward and backward adaptation were both elicited more effectively with the constant error than with the constant target shift paradigm (Zimmermann &

Lappe, 2010), which might be caused by a stronger cumulative effect of the post-saccadic error during the entire experiment. This study also led to the proposal that constant error adaptation relies partially on the remapping of the visual target representation (Masselink & Lappe, 2021; Zimmermann & Lappe, 2010).

Saccadic adaptation can be induced via a third method based on reinforcement learning (Madelain et al., 2011). Contrary to the previous two methods, adaptation by reinforcement does not rely on a post-saccadic visual error. Instead, the experimenter selects a goal amplitude to which saccades' amplitude will be decreased (backward adaptation) or increased (forward adaptation). During the experiment, when the participant's saccade lands close to the goal amplitude, a reinforcement signal is provided to the participant by presenting either a tone or a visual target at the location of the fovea or both. The adaptation induced by this method shows the following common features with the constant target step paradigm: 1) a similar rate of adaptation, 2) a similar recovery, and 3) a similar transfer pattern to non-adapted locations.

In the different studies of this thesis, we will be using the constant target step in order to induce either backward or forward adaptation.

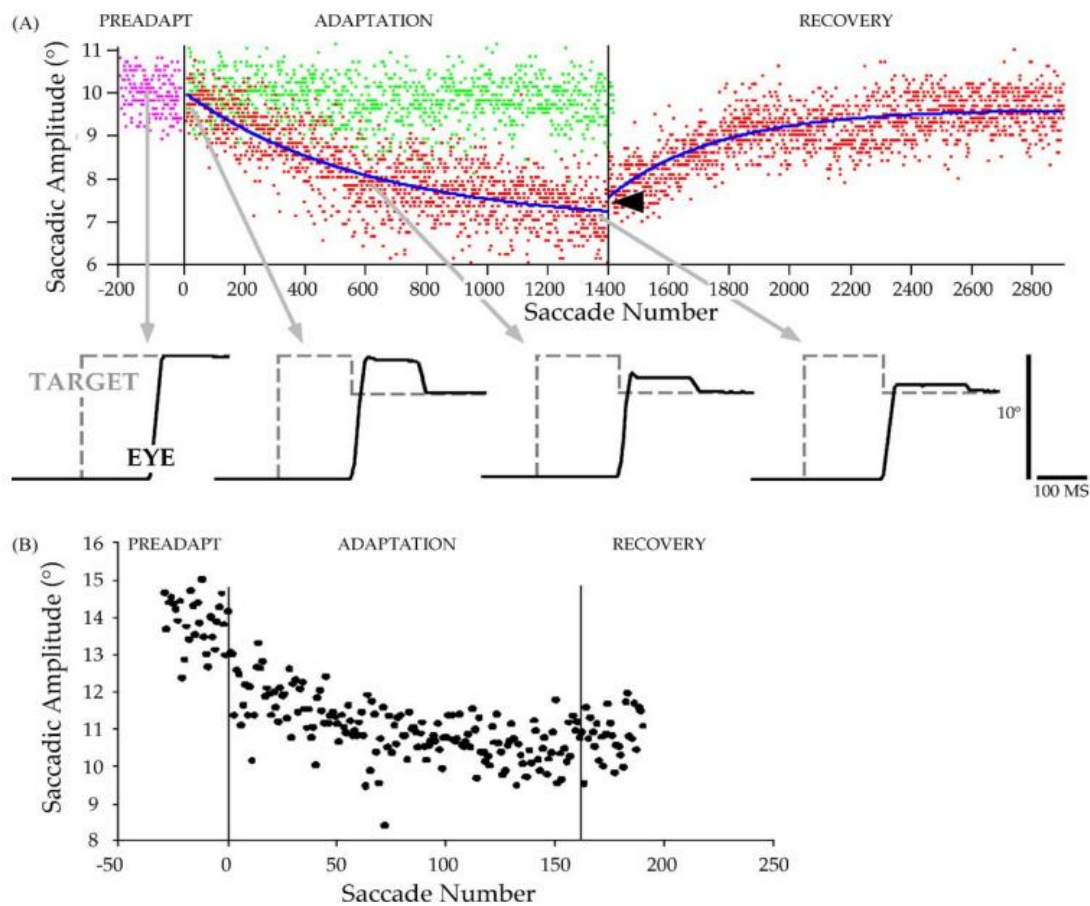


Figure 11 : The course of saccadic adaptations in monkeys (A) and humans (B). (A) Top: Backward adaptation and recovery of saccades made to 10° horizontal target steps with a 30% constant target step. Saccadic amplitude is plotted as a function of the number of the trial in each direction. The violet points correspond to the pre-adaptation trials. The red points correspond to the adapted saccade direction while the green points correspond to saccades in the non-adapted direction. Adaptation and recovery data are fit by exponential functions (blue curves). Bottom: examples of target (gray dashed lines) and eye (black lines) positions for different trials during the course of the experiment. (B) Adaptation and recovery time-courses of 15° horizontal saccades in humans. The backward adaptation was induced via 33% constant target steps. Modified from Hopp & Fuchs, 2004 (Figure 3)

3.2. Saccadic suppression

During saccades, the image shifts on the retina. However, we always perceive a stable visual world around us. One mechanism responsible for such perceived stability is saccadic suppression, which consists of a loss of visual sensitivity that takes place around 70 ms prior to saccade onset and lasts until saccade landing (Krock & Moore, 2014). The source, as well as the mechanism of saccadic suppression, is still debated. The inhibition of the magnocellular pathway of the LGN (which is color-

insensitive) was suggested to be the source of saccadic suppression, as the latter occurs for luminance-modulated stimuli but not equiluminant chromatic ones (Binda & Morrone, 2018). One mechanism has been proposed to play a role in saccadic suppression is the corollary discharge (described further in this chapter), hypothesized to suppress visual representations through the projection from the SC either to the FEF via the mediodorsal thalamus or to the middle temporal area via the inferior pulvinar (Anand & Bridgeman, 2002; Krock & Moore, 2014).

Saccadic suppression is affected by the saccade parameters (amplitude and velocity) as well as by the parameters of the stimulus to be suppressed (time of occurrence during the saccade, eccentricity, contrast, and spatial frequency). For instance, saccadic suppression has been found to 1) increase with increasing saccade amplitude (Bridgeman et al., 1975; Mitrani et al., 1970), 2) be maximal at the saccade onset and decrease progressively until nullifying at the saccade offset (Krock & Moore, 2014; Mitrani et al., 1970) 3) decrease when the stimuli are more peripheral relative to the saccade's trajectory (Osaka, 1987) and 4) increase when the stimuli are close to the saccade target (Bridgeman et al., 1975).

A particular type of saccadic suppression called saccadic suppression of displacement (SSD), is likely contributing to the participants' unawareness of the second target step in McLaughlin's double-step paradigm. Whether this failure to consciously detect this target perturbation is crucial for saccadic adaptation is still unclear. In their study, Fujita et al. (Fujita et al., 2002) varied the presentation time of the displaced target relative to the end of memory-guided and reactive saccades during a backward adaptation session. The second step of the saccade target could appear at 0, 100, 200, 400, and 600 ms after the saccade offset. They reported that their participants were aware of the target displacement when delayed by 100 ms or more. Concerning the induced adaptation, the amount of gain reduction decreased with increasing delays but was still significant for a 400 ms delay. More recently, Heins et al. (Heins et al., 2019) investigated whether participants can exert some voluntary control over saccadic adaptation. They compared backward and forward adaptation between two conditions in which they either asked the subjects to follow the intrasaccadic step when it occurs (adaptation condition) or to ignore it (inhibition condition). In both conditions, the participants were aware of the intrasaccadic step due to the instructions provided by the experimenter (they either had to look at the target location after the second step or ignore it and remain on the initial saccade target). Still, they showed a significant change in saccadic gain for both conditions (for both forward and backward adaptation in the adaptation condition, but only in backward adaptation in the inhibition condition). Therefore, even when the participants perceive the intrasaccadic step, saccadic adaptation still occurs, and this later is less important (however, always present) when the participants adopt a strategy to ignore the second step.

3.3. Effects of the properties of the intrasaccadic target step

The effects of several characteristics of the intrasaccadic target step have been examined in saccadic adaptation studies, including duration and timing, size, frequency, and consistency.

Duration and timing: In order to obtain an optimal gain change during saccadic adaptation, studies showed that the intrasaccadically stepped target must remain visible for at least 80 ms (Shafer et al., 2000) after saccade offset. In another study, even shorter presentation times were found to induce optimal adaptation with differences between reactive (15 ms) and voluntary saccades (50 ms) (M. Panouillères et al., 2011). This study also showed that optimal presentation time increases to 50 ms for reactive saccades and 100 ms for voluntary saccades if the displaced target is not just extinguished after the presentation duration but replaced by a visual mask.

Delaying the presentation of the second target step relative to the saccade offset was shown to reduce the amount of the resulting gain change. An optimal saccadic adaptation is obtained when the second target step is presented between 60 to 100 ms following the saccade offset (Fujita et al., 2002; Shafer et al., 2000). Nevertheless, significant adaptation still occurs for delays of up to 750 ms (Shafer et al., 2000). Beyond that, no significant gain change can be induced, and even some studies use delays of 1000 ms as a control to which saccadic adaptation conditions are compared (M. Panouillères et al., 2009b). It was also shown that saccadic adaptation can occur when the intrasaccadic target step is presented (for 30 ms) during the saccade, revealing the capability of the brain to extract information during the saccade (M. Panouillères, Gaveau, et al., 2013). Further tests from this study showed that saccadic adaptation still occurs when the intrasaccadic step takes place for 10 ms during the deceleration phase of the saccade (where saccadic suppression is weaker) but not during the acceleration phase. Note finally that an intra-saccadic step of only 2 ms occurring during saccade deceleration (but not at the time of peak velocity) was enough to induce a significant backward (but not forward) adaptation (M. T. N. Panouillères et al., 2016).

Size: The percentage of gain change obtained in saccadic adaptation studies depends on the relative, rather than the absolute, size of the intrasaccadic target step compared to the size of the first target step eliciting the primary saccade (Herman et al., 2013; F. R. Robinson et al., 2003). In addition, saccadic adaptation is more sensitive to small relative target step sizes compared to large ones. For example, in humans, a 30% intrasaccadic target step induces adaptation that reaches an asymptote at around 50% gain change (Alahyane et al., 2007; Shafer et al., 2000), while target step sizes of 10% or less induce adaptation that reaches asymptotes after 70% of gain change (Herman et al., 2013). In monkeys, intrasaccadic steps of 15, 30, and 50% induced 81, 77, and 72% of adaptation completeness (Straube et al., 1997).

Frequency: Mixing intrasaccadic step trials with trials where the saccade target extinguishes at saccade onset during the adaptation exposure phase led to a reduced gain change as compared to a

control exposure containing only intrasaccadic step trials, despite the number of intrasaccadic step trials matched in both cases (Noto & Robinson, 2001).

Consistency: Havermann and Lappe (Havermann & Lappe, 2010) showed that increasing the inconsistency of the error by varying the size of the intrasaccadic step across trials during the experiment reduces the amount of both backward and forward adaptation. These results contradict with those of Srimal et al. (Srimal et al., 2008) who showed that saccadic learning occurs on a trial-by-trial basis and is unaffected by error inconsistency. Recently, Eggert et al. (Eggert et al., 2022) re-investigated this matter, but in contrast to the two previous studies, they investigated the effect of consistency on the recovery from a previously induced adaptation. The authors found that the mean error size is the main factor determining the total adaptive change independently of the error inconsistency.

One other thing that can be noted in this section is that visual errors can be attributed to external factors. In the study conducted by Heins and Lappe (Heins & Lappe, 2024), participants were shown a fixation point surrounded by multiple objects arranged in a circular pattern. They were instructed to focus on the fixation point, select a specific object, and then, when the fixation point vanished, indicate their choice by making a saccadic movement toward it. After completing the saccade, participants received feedback on the computer's interpretation of their chosen target. Participants were informed that some errors might be introduced into the saccade endpoint data used to decode their selected target, and they were advised to account for these potential errors to help the machine accurately identify their choices. The authors reported that participants' saccade trajectories gradually adjusted during the task when the feedback was biased and that these adjustments were maintained after the task ended. These results revealed the operation of genuine adaptive mechanisms while the participants consciously employed strategies to enhance the machine's decoding accuracy.

3.4. Effects of the properties of the saccade target and visual background

While most of studies present in the literature use a point target to induce saccades and investigate saccadic adaptation, it was shown that adaptation can also be induced using various shapes like circles (Bahcall & Kowler, 2000), two open-ended contours (Collins & Doré-Mazars, 2006a), bars (adaptation can be induced by increasing or decreasing the size of the bar) (Bosco et al., 2015) as well as a string of letters (Collins, Vergilino-Perez, et al., 2007). Under such circumstances, the visuo-saccadic system uses the center of gravity of the visual configuration to define the location used as a saccade target and to compute the post-saccadic error signal for saccadic adaptation.

The presence of a background (random shapes in monkeys (F. Robinson et al., 2000), or natural image in humans (Madelain et al., 2013)) was shown to have no effect on saccadic adaptation, whether it remains static or moves with the adapted target. Saccadic adaptation was shown to occur as a result of a shift of the background only in the case where the saccade target extinguished at saccade

onset and reappears after the occurrence of the background shift (Madelain et al., 2013). Madelain et al. (Madelain et al., 2010) investigated the effect of presenting a distractor simultaneously with the displaced saccade target (the target and the distractor had different colors and shapes) during exposure to forward or backward adaptation as well as during recovery. They showed that when the distractor was added at the primary target location, while this target stepped backward or forward, subjects ignored the distractor and adapted to an extent comparable to the adaptation driven by conventional adaptation. In contrast, when the target and distractor locations were reversed so that the distractor was at the back-stepped or the forward-stepped location and the target remained at its primary location, saccadic adaptation did not occur. Similar effects were also seen during recovery, where saccade gain returns to its initial value when the saccade target remains at its primary location, even when the distractor is present at the stepped position. These results indicate that target selection in saccadic adaptation is unharmed by distractors. Ditterich et al. (Ditterich et al., 2000b) also found no effect of the background on saccadic adaptation when the visual target was a foveal point of 0.3° . However, when they used an empty circle of 4.8° as a saccade target, they showed that the background shifts did influence the saccadic adaptation mechanism, likely through an enlarged attentional focus around the target.

Based on these findings, it was concluded that target selection within different backgrounds, as well as in the presence of distractors, is critical to induce effective saccadic adaptation (Collins, Vergilino-Perez, et al., 2007; Madelain et al., 2010, 2013).

3.5. Spatial generalization of saccadic adaptation

It was previously thought that saccadic adaptation is parametric, meaning that once a certain saccade is adapted, the gain change resulting from adaptation would be observed for all other saccades performed in different amplitudes and directions (Abel et al., 1978; Deubel et al., 1986; McLaughlin, 1967). However, with time, it became clear that the generalization (transfer) of saccadic adaptation is non-parametric, as it occurs depending on how close the non-adapted saccade vector (amplitude and direction) is to the adapted one. The adaptation field represents the spatial window surrounding the adapted saccade, inside which the adaptation generalizes to saccades with different vectors (Collins, Doré-Mazars, et al., 2007; Deubel et al., 1986), and it seems to have similar characteristics for both backward and forward adaptation of both voluntary and reactive saccades, as we will see in the following.

Saccadic adaptation generalizes to saccades of the same vector performed from different initial eye positions. Conversely, the transfer of backward adaptation declines as a function of the increasing directional difference of the tested saccades and was shown for voluntary saccades to remain significant up to a 60° directional difference and to nullify for a 90° difference (orthogonal adapted and tested saccades) and larger angles (Alahyane, Devauchelle, et al., 2008).

The transfer of adaptation also decreases as a function of the increasing amplitude difference of the tested saccades. Collins et al. (Collins, Doré-Mazars, et al., 2007) investigated the field of a backward adaptation of voluntary horizontal saccades performed toward a 12° eccentric target. They examined the generalization of adaptation to saccades performed toward 38 targets around the adapted one, ranging between 4 and 24 degrees horizontally and between -8 to 8 degrees vertically. They showed an asymmetric transfer along the horizontal axis versus a symmetric transfer along the vertical one, as represented in Figure 12. In the horizontal axis, there was a steeper drop in generalization for saccades smaller than 12° than for saccades larger than 12°. Similar results (with a slightly stronger generalization along the vertical axis) were found by (Schnier et al., 2010), who investigated the adaptive field induced by forward adaptation of voluntary saccades toward two targets (14 and 20 degrees). Similar adaptation fields were also found in monkeys for both forward and backward adaptation of reactive horizontal saccades (Noto et al., 1999; Straube et al., 1997). Testing directional adaptation induced by a 5° vertical second step occurring during a 10° horizontal saccade, Noto et al. found that more than 88% of the change in the vertical saccade component produced in 10° saccades transferred to 20° saccades, but only 12% transferred to 4° saccades. Contrasting with such asymmetry along the amplitude dimension, the adaptation field was symmetrical along the vertical dimension, as the transfer to the vertical component was similar for saccades performed to targets located 10° above or 10° below the adapted target (Noto et al., 1999).

It has also been shown that it is possible to induce backward adaptation for saccade of a certain amplitude and simultaneously perform forward adaptation of a saccade with different amplitude but in the same direction (Semmlow et al., 1987). Therefore, it has been suggested that the effect of adaptation to saccades with intermediate amplitudes reflects a linear summation of the effects produced by both the forward and the backward adaptations at the intermediate location.

Neurons in both the FEF and SC have been found to have a “preferred saccade vector” for which they produce their most vigorous discharge, and their discharge rate decreases with increasing saccade deviations from this optimal vector. These characteristics define the movement fields of individual neurons, as described in the previous chapter. The rate of the discharge of some neurons along the SC movement field has been found to fall quickly for amplitudes smaller than the preferred one, while this rate decreases slowly for saccade’s amplitudes larger than the preferred one (Hopp & Fuchs, 2004). The similarities in the characteristics of both the movement field and the adaptation fields argue for the notion that saccadic adaptation modifies the oculomotor command at a level where it is still encoded as vectorial eye displacement rather than further downstream at the level of the brainstem where the vertical and the horizontal saccade components are separately encoded (Alahyane, Devauchelle, et al., 2008; Noto et al., 1999; Pélisson et al., 2010).

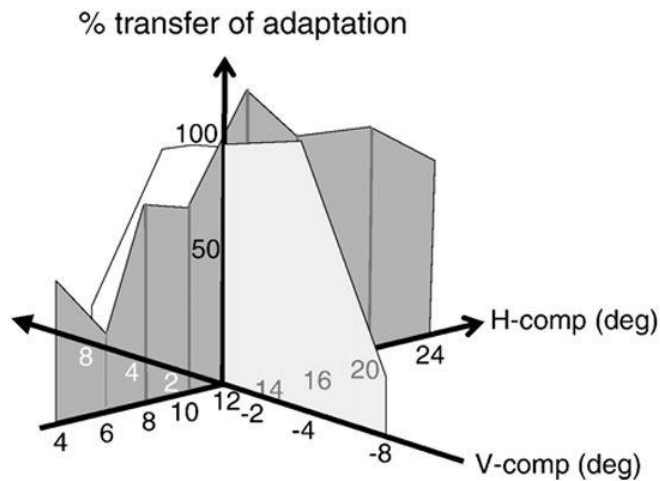


Figure 12 : Adaptation field, represented as the percentage of adaptation transfer from a 12° horizontal saccade to saccades of varying amplitudes sharing the same horizontal direction (gray) -and to oblique saccades sharing the same vertical 12° component- as the trained saccade. Modified from Collins, Doré-Mazars, et al., 2007 (figure 2).

3.6. Effects of contexts on saccadic adaptation

The brain can adapt saccades differently depending on the context in which saccades are performed. The effect of various contextual factors has been tested over the years, and in this section, we review some of those studies.

The adaptation field defined in a previous paragraph means that the amount of saccadic adaptation is tuned around the target location relative to the start location (2-D vector) of the trained saccade, which can thus be considered as a contextual cue. It was shown that, in fact, the 3-D saccade vector can act as a contextual factor for saccadic adaptation (Chaturvedi & van Gisbergen, 1997). These authors simultaneously induced both forward and backward adaptations of two saccades with similar 2-D vectors but directed to targets, respectively, either farther or nearer than the fixation point. They showed that forward adaptation to a far target and backward adaptation to a near target (and vice versa) can take place simultaneously, demonstrating that adaptation mechanisms are capable of calibrating different gains for saccades with similar 2-D vectors but ending in different depth planes. Target depth was thus considered as a contextual factor.

Herman et al. (Herman et al., 2009) tested backward adaptation of saccades directed either to a flickering target or a steady one and tested the transfer of adaptation to the un-adapted target modality. Their experiment reveals only a partial transfer of adaptation to the non-adapted target, whether steady or flickering, therefore suggesting that the frequency of the target can be, at least partially, considered as a contextual factor that affects adaptation.

Using a concurrent adaptation strategy similar to (Chaturvedi & van Gisbergen, 1997)), Shelhamer and Clendaniel (Shelhamer & Clendaniel, 2002) showed that forward and backward adaptation of the same 2-D saccade vector can be elicited simultaneously when the head position or the initial eye position is varied. Concerning the latter, a forward adaptation of saccades initiated from a downward eye deviation could develop concurrently with a backward adaptation of saccades initiated from an upward gaze (and vice versa), demonstrating the vertical starting position of the saccade as a contextual factor (note that even stronger effects were shown when varying the horizontal eye position). The effect of vertical eye position was also reported in two other studies in humans (Aboukhalil et al., 2004; Alahyane & Pélisson, 2004) and in monkeys (Tian & Zee, 2010). Aboukhalil et al. (Aboukhalil et al., 2004) further showed that a one-minute break between the adaptation blocks associated with different vertical eye positions induces a consolidation of oculomotor learning, further strengthening the contextual effect of vertical eye position. Zimmermann and Lappe (Zimmermann & Lappe, 2011) adapted either reactive or scanning saccades of a certain vector starting at one corner of their display screen and tested the transfer of adaptation to saccades of the same category and the same vector but initiated from the other three corners. They found only a partial transfer of adaptation to the non-adapted locations, suggesting the presence of a somewhat weak contextual factor of initial (horizontal and vertical) eye positions. Havermann et al. (Havermann et al., 2011) investigated the transfer of backward adaptation to non-adapted saccades of the same vector but starting from different horizontal eye positions. The initial eye position of the adapted saccade vector was varied across sessions. They found that in the sessions where adaptation was induced for saccades from the central position, a full transfer to saccades initiated from eccentric positions was observed; however when the adaptation of ‘saccades from eccentric positions’ was induced, the transfer decreased with increasing differences of saccade start position. This study thus confirms the contextual factor of horizontal initial eye position but also suggests that it is more complex than initially described.

Recently, Azadi et al. (Azadi & McPeck, 2022) found an even more complex context related to the rank of the adapted saccade in a sequence of saccades. Indeed, saccadic adaptation depended on the properties of both the preceding and the following saccades in the sequence. These properties include the direction of the preceding saccade, the direction and the amplitude of the following saccade, and the order of a given saccade within the saccade sequence.

Finally, while the color of the visual target (Cecala et al., 2015) are not taken as contextual factors when the saccadic system encounters competing training, the 3-D location and flickering of the visual target (but not its color), the rank of the adapted saccade in a sequence of saccades, as well as the initial eye/head positions play as contextual factors which significantly impact saccadic adaptation.

3.7. Differences between Forward and Backward adaptation

As described previously, whether McLaughlin's or the constant error paradigm is used, stepping the saccade target forward or backward results in an adaptive increase or decrease of saccadic gain, respectively. Accumulating evidence in humans and monkeys shows that forward and backward adaptation relies, at least partially, on different mechanisms.

Forward adaptation is less prevalent, slower to develop over time, and results in lower adaptation aftereffects (for the same number of trials and the same target's second step size) compared to backward adaptation. Using the constant error paradigm in monkeys, Robinson et al. (F. R. Robinson et al., 2003) showed that constant negative errors (backward) of 25–35% elicit an average reduction of 35% in the gain of 12° reactive saccade; in contrast, only an 8% gain increase was achieved with positive errors of the same size. Differences between both adaptation types were also seen in monkeys using the McLaughlin paradigm to adapt reactive saccades. While a 30% positive error resulted in around 23% gain increase after an average of 1178 trials, a 30% negative error resulted in a similar-sized gain decrease, but only after an average of 368 trials (Straube et al., 1997). Furthermore, the same study showed that recovery following forward adaptation is much faster (gain decreasing recovery required two-thirds the number of trials as gain increasing adaptation) than the recovery following backward adaptation (gain increasing recovery required the same number of trials as gain decreasing adaptation). In addition, studies have shown that in head-unrestrained conditions (gaze adaptation), backward adaptation was larger than forward adaptation in response to the same post-saccadic visual error in monkeys but not in humans (where nearly similar gaze changes were found for backward and forward adaptation) (Cecala & Freedman, 2008, 2009).

In humans, a slower time course and a lower adaptation aftereffect were also seen for forward adaptation compared to backward adaptation of both reactive and voluntary saccades (M. Panouillères, Gaveau, et al., 2013; M. T. N. Panouillères et al., 2012). Panouillères et al. (M. Panouillères et al., 2009b) also compared the two types of reactive saccades adaptation by testing their transfer to anti-saccades. In their experiment, all their subjects (fourteen) were significantly adapted in the backward condition, while only 74% (14 out of 19) showed significant change in the forward condition. They showed that backward adaptation transfers to the anti-saccades performed in the adapted direction but not to oppositely-directed anti-saccades. In contrast, forward adaptation did not transfer to anti-saccades in either direction. As explained in the previous chapter, the sensory and motor vectors are spatially dissociated in anti-saccade tasks. The rationale is that, on the one hand, if saccadic adaptation occurs before (upstream) vector inversion, then the adaptation-related changes in amplitude will be evident only in anti-saccades performed in the non-adapted direction. Indeed, these anti-saccades are produced by inverting a target vector that originally points towards the adapted field and which, according to the upstream hypothesis, has been altered by the adaptation process. Note that according

to this hypothesis, anti-saccades in the adapted direction will remain unaffected as their target vector pointing toward the non-adapted hemifield engages neural structures that are not subject to adaptive changes. On the other hand, if saccadic adaptation takes place downstream of the vector inversion process, anti-saccades performed in the non-adapted direction will remain unchanged, while anti-saccades in the adapted direction will be altered. Therefore, based on their results, the authors (M. Panouillères et al., 2009b) suggested that backward adaptation of reactive saccades occurs downstream from the vector inversion process (which possibly occurs at the PPC level and/or FEF). At the same time, for forward adaptation, the complete lack of transfer to anti-saccades did not allow them to discuss any possible adaptation locus, but the comparison with backward adaptation nonetheless provided additional evidence for different adaptation mechanisms.

Furthermore, Hernandez et al. (Hernandez et al., 2008) found that a transfer of reactive saccades adaptation to hand pointing occurs only in forward but not backward adaptation, suggesting that the latter occurs downstream the visual representation of the stimuli, at the level of oculomotor command while forward adaptation occurs partly at the level of the oculomotor command but also results in a remapping of the stimuli location.

In addition to the previous arguments, Ethier et al. (Ethier et al., 2008a) tested the difference between forward and backward adaptation of reactive saccades based on their kinematics. Using as a reference non-adapted saccades of the same amplitude performed in a control session a few days later, they found that backward-adapted saccades had reduced peak velocities, reduced accelerations, shallower decelerations, and increased durations; in contrast, the forward-adapted saccades did not differ from control saccades of the same size for any of the above kinematic variables. The authors also reported a decrease in saccade latency for both adaptation types (forward and backward), which is more pronounced for backward adaptation. (Ethier et al., 2008a) concluded that forward adaptation mechanism relies on a change of target sensory representation (target remapping) while backward adaptation relies on the modification of saccade trajectory (motor correction). The reduced deceleration due to backward adaptation was also reported by Collins et al. (Collins, Semroud, et al., 2008), whereas the decrease in peak velocities was reported by (Golla et al., 2008; Zimmermann & Lappe, 2010). However, the increase in saccade duration due to backward adaptation observed in (Ethier et al., 2008) seems odd and contradicts the results of other studies (Golla et al., 2008; Masselink et al., 2023). This might result from the experimental protocol used by (Ethier et al., 2008a), who compared their adapted saccades with the so-called mimic saccades used as control (in the control session, the saccade target at a certain trial n was set to be at the same location as the saccade endpoint obtained at the same trial during the adaptation session). Indeed, the increase in saccade duration that they observed in backward adaptation might be due to the comparison of saccades performed toward two different targets, even though their amplitudes are the same.

Another piece of evidence for different mechanisms between forward and backward adaptation relies on the comparison of the so-called savings phenomenon (Kojima et al., 2004).

Savings is the effect of a preceding adaptation on the speed of an adaptation of similar movements induced shortly after, during the same experimental session. In one of the conditions of this study, monkeys were first adapted (backward or forward adaptation phase), then de-adapted, and following a 30-minute pause in darkness, the monkeys were re-adapted (backward or forward adaptation phase, respectively). While the authors found a faster backward adaptation during the readaptation phase than in the initial adaptation phase, revealing savings, they found for the forward readaptation condition a step increase in gain relative to the initial phase, suggesting that the memory of forward adaptation was not merely retained but processed further during the period of darkness.

More evidence on the differences between backward and forward adaptation can be seen in studies related to perception as both adaptation types display different effects on the localization of flashed targets. Indeed, a flashed target that appears near the location of adapted reactive saccades is mislocalized after forward but not backward adaptation when tested in a gaze fixation condition (Zimmermann & Lappe, 2010). Performing a perceptual task under gaze fixation is advantageous compared to a perceptual task where a saccade target is present, whether a saccade execution is required or not, as participants have no landmarks to rely on in order to report the position of the flashed target. Therefore, the localization changes are thought to be a consequence of the saccade adaptation procedure and cannot be explained by motor performance changes or mismatches between the saccade and its related efference copy signals. The results of Zimmermann and Lappe's study argue for the existence of a target remapping mechanism during forward adaptation and suggest the involvement of a lower-level mechanism for backward adaptation. However, it is important to note that in their study, the author also observed mislocalizations when backward adaptation was induced in the constant error paradigm with a relatively large second target step, leading them to suggest that backward adaptation induced by a persisting post-saccadic error might be achieved by a mixture of motor changes (low-level mechanism) and of changes in the saccade target representation. In their study, Cheviet et al. (Cheviet et al., 2022) found a significant shift in trans-saccadic localization of flashed stimuli due to forward adaptation but not backward adaptation. However, they also found no significant localization effect of either adaptation type when tested under the fixation condition. Nevertheless, the changes in both localization tasks correlated significantly with the change in saccadic gain seen in all experimental conditions (backward, forward, and control).

Catz et al. (Catz et al., 2008) recorded Purkinje cell's simple spikes discharge in the oculomotor vermis (lobules VI and VIIA of the cerebellum) during forward and backward adaptation of reactive saccades in two monkeys. They showed that the collective simple spikes discharge of a large group of Purkinje cells in relation to a saccade, the so-called saccadic population burst, ends simultaneously with the end of saccades. In forward adaptation trials, this population burst increases in duration to maintain this timing with the saccade end. In contrast, during backward adaptation, the population burst did not end in synchrony with the saccades but rather well before, and the strength of this burst was progressively reduced. Based on their findings and previous literature, the authors

argued that the major variable controlled by Purkinje cell's population burst is saccade duration and, therefore, that these neurons contribute to forward adaptation by increasing their population burst duration. In contrast, for backward adaptation, the reduced discharge strength could contribute to the decrease in saccade peak velocity, while the early end of Purkinje cell's burst contributes to releasing the saccade earlier in order to be modified further by other structures.

It has been hypothesized that short-term (forward) saccadic adaptation reflects the work of a cerebellar mechanism needed to avoid cognitive fatigue. Golla et al. (Golla et al., 2008) tested this hypothesis by comparing backward and forward adaptation sessions in cerebellar patients to sessions performed with healthy volunteers as well as to a resilience session (in which patients had a long series of saccades toward a target that disappeared at the saccade's onset). Healthy participants showed an increase in saccade duration in the face of constant peak velocity during the forward adaptation session and a decrease in both saccade duration and peak velocities in the backward session. Whereas patients with intact vermis did not differ from healthy volunteers, those with vermal pathology lacked forward adaptation: they showed no changes in saccades amplitudes, durations, and peak velocities. In contrast, vermal patients demonstrated a significant decrease in saccade amplitudes, accompanied by a decrease in peak velocities but mostly unaltered saccade duration in the backward adaptation experiment as well as in the resilience test. Therefore, based on these results, they suggested that forward adaptation reflects an active mechanism for the compensation of fatigue residing in the cerebellum, while backward adaptation is at least partially based on uncompensated fatigue.

Finally, differences between backward and forward adaptation can also be revealed in fMRI studies. For example, Métais et al. (Métais et al., 2022) adapted rightward reactive saccades and found activation of right MT/MTS and right occipital for backward jump and the left MT/MST and left occipital for forward jump, which seems to be contralateral to the direction of intrasaccadic steps and could be related to these error signals. Liem et al. (Liem et al., 2013) found that forward adaptation results in more activity in the cerebellum than backward adaptation, which argues with the notion that the cerebellum is more involved in the processing of forward than backward adaptation.

To sum up, behavioral, electrophysiological, and imaging studies provide evidence that forward and backward adaptation relies, at least partially, on different mechanisms, with backward adaptation of reactive saccades acting at the motor level of the saccadic command while forward adaptation relies at least partially on the remapping of the visual target's representation.

3.8. Differences between Reactive and Voluntary saccadic adaptation

As described in the previous chapter, reactive saccades are performed toward the sudden appearance of stimuli in our environment, whereas voluntary saccades are performed based on our goals and motivations. As detailed in the following, adaptation of both saccade types share some similarities but

also entails differences, suggesting that reactive and voluntary saccade adaptations are at least partially different mechanisms. Alahyane et al. (Alahyane et al., 2007) compared reactive and voluntary saccades backward adaptation and showed that both adaptations 1) are incomplete and reach an asymptote associated with an adaptation after-effect of 48% and 39%, respectively, 2) show an incomplete recovery (65%) after a similar de-adaptation phase where the target remains at its primary position (no intrasaccadic step), 3) have similar adaptation fields, therefore, both adaptations involve neural structures where saccades are encoded as vectors, 4) do not lead to significant changes in the saccade main sequence relationships (duration vs amplitude and peak velocity vs amplitude). Furthermore, it has been demonstrated for both reactive and voluntary saccades that their adaptation induces a boost in spatial attention in the adapted hemifield (Nicolas, Bidet-Caulet, et al., 2019; Nicolas et al., 2020) and influences the pre-saccadic shifts of attention (Collins & Doré-Mazars, 2006a).

Nevertheless, the pattern of transfer of adaptation between voluntary and reactive saccades is asymmetric. Although varying in size between studies, the direction of asymmetry consistently corresponded to a stronger transfer from voluntary to reactive saccades than the transfer from reactive to voluntary saccades (37% vs. 11%, 84% vs. 15%, 74% vs. 56%, 79% vs. 22%, 43% vs. 36%) in (Deubel, 1995), (Collins & Doré-Mazars, 2006a), (Cotti et al., 2007), (Alahyane et al., 2007), and (Zimmermann & Lappe, 2009) respectively.

In addition to the asymmetric transfer between both adaptation types, it has been shown that backward adaptation of voluntary, but not of reactive saccades, significantly transfers to hand-pointing movements (46% transfer of voluntary saccades adaptation to hand-pointing (Cotti et al., 2007)). Another study found an even larger transfer amount (74%) for voluntary saccades (Bekkering et al., 1995). However, this large value might be due to the fact that they allowed eye movements during the pointing task, which was not the case in Cotti et al.'s study. Still, another study revealed this time a weak but significant transfer of adaptation of reactive saccades to hand pointing (17%) (Kröllner et al., 1999), but in this study, adaptation was induced in a head-unrestrained condition, which has been suggested to differ from saccadic adaptation elicited with the head restrained (Cecala & Freedman, 2008, 2009).

Reactive and voluntary saccade adaptations have also been compared by testing their transfer to bilateral anti-saccades (performed in the adapted and non-adapted directions). As detailed in the previous section, if saccadic adaptation occurs before (upstream) vector inversion, then the adaptation-related reduction in amplitude will be expected to affect anti-saccades performed in the non-adapted direction. In contrast, if saccadic adaptation takes place downstream of the vector inversion process, anti-saccades performed in the adapted but not the non-adapted direction will be altered. Cotti et al. (Cotti et al., 2009) found that while backward adaptation of reactive saccades transferred only to anti-saccades performed in the adapted direction, backward adaptation of voluntary saccades transferred to both types of anti-saccades. Therefore, the authors concluded that reactive saccade adaptation acts

downstream of the inversion site(s), whereas voluntary saccade adaptation involves two loci, acting upstream and downstream of the vector inversion location(s). In a similar study, Collins et al. (Collins, Vergilino-Perez, et al., 2008) found that backward adaptation of voluntary saccades transfers only to anti-saccades performed in the adapted direction, suggesting an adaptation acting downstream of the vector inversion. However, it is important to note that the latencies of their “voluntary” adapted saccades (187 ms on average) elicited via an overlap paradigm were closer to those of reactive saccades, which might explain why their results differed from those of Cotti et al. (Cotti et al., 2009). Adaptation of antisaccades themselves was shown to transfer to reactive saccades performed in the adapted direction but not the other direction, pointing toward a motor level of antisaccades adaptation and of a visual level of antisaccades vector inversion (Lévy-Bencheton et al., 2013).

Reactive and voluntary saccades adaptations differences have also been revealed regarding the temporal integration of visual information used for error signals processing. Indeed, as already reported above (section 3.3), Panouillères et al. (M. Panouillères et al., 2011) has found that an optimal adaptation required the displaced post-saccadic visual target to remain for at least 15ms after saccade offset in the case of reactive saccades or 50 msec for voluntary saccades, suggesting again, different adaptation mechanisms.

Another difference between reactive and voluntary saccades adaptations was found by Zimmerman and Lappe (Zimmermann & Lappe, 2009) by measuring their effect on visual mislocalization. Whereas mislocalization of a flashed target (50 ms after the presentation of the saccade target) was found after voluntary and reactive saccade adaptation, mislocalization of a stationary target (presented from the beginning of the trial until saccade onset) occurred only after voluntary saccade adaptation, pointing toward an origin of mislocalization confined to the voluntary saccade pathway.

Finally, an fMRI study (Gerardin et al., 2012) showed differences in cortical activation between the backward adaptation of reactive saccades (contralateral TPJ and hMT+/V5) and voluntary saccades (contralateral medial and posterior IPS). Differences between both saccade types also emerged in cortical activations related to recovery (contralateral DLPFC for voluntary saccade recovery and ipsilateral cerebellar areas VIIb and VIIIa for reactive saccade recovery).

To sum up, while reactive and voluntary saccade adaptations share similarities, they also entail differences, as evidenced by a significant number of studies. The adaptation of reactive saccades is hypothesized to act on the saccade’s motor command, while voluntary saccade adaptation acts on both the sensory and motor levels of the saccade circuitry.

3.9. Short vs long-term adaptation

Lesions of monkeys oculomotor vermis reduce saccades accuracy (dysmetria and increased variability) and abolish the capabilities of the monkey to adapt using the double-step target paradigm (Barash et al., 1999; Takagi et al., 1998). Nevertheless, by testing the monkeys for several days after

surgery, Barash et al. (Barash et al., 1999) revealed that the dysmetria slowly resumed due to a gain recovery toward unity. These findings point to the presence of two different adaptation mechanisms acting on different time scales: a short-term adaptation (minutes to hours) depending on the oculomotor vermis and a long-term adaptation (days) responsible for the previously reported recovery. Long-term saccadic adaptation can be induced by exposing the subjects to error using the double-step target paradigm repeatedly for sessions extending for several consecutive days (F. R. Robinson et al., 2006). Robinson et al. (F. R. Robinson et al., 2006) induced backward adaptation in three monkeys on 19 consecutive days. At the end of each adaptation session, and when the saccadic gain reached an asymptote, the monkeys were blindfolded until the next session. Monkeys showed for the first couple of days a rapid adaptation within each individual session, with poor retention across days; then, in the following days, the rate of individual session adaptation progressively decreased, and the retention between sessions increased. At the end of the 19 days, it took the monkeys around five days to recover from the gain decrease adaptation with a pattern of recovery similar to that of the adaptation. To further investigate the interaction between short-term and long-term adaptations, the monkeys were additionally exposed, at the end of day 1 and day 19, to target steps larger than those used to induce adaptation. Results showed that at the end of day 1, the increased intrasaccadic steps did not result in significant additional gain change, indicating that the short-term saccadic adaptation mechanism was saturated, whereas, at the end of the 19th day, the larger intrasaccadic steps led to a further reduction of saccade gain. This suggested that after some time, the long-term saccadic adaptation took over the short-term adaptation, releasing the latter adaptation mechanism from saturation and allowing it to cope again with new intrasaccadic target steps. Mueller et al. (Mueller et al., 2012) replicated the results of Robinson et al. (F. R. Robinson et al., 2006) and further investigated forward long-term saccadic adaptation. They showed 1) that forward long-term adaptation is slower than backward long-term adaptation (see figure 13) and 2) that forward short-term adaptation does not impair subsequent size increase (forward adaptation with larger intrasaccadic step performed at the end of the adaptation session), pointing to difference between forward and backward adaptation mechanisms which can be added to the arguments presented in the previous section discussion the differences between forward and backward adaptation.

A question one might ask is what adaptation mechanism (short- or long-term adaptation) is responsible for the gain change seen in a single session using the double-step-target paradigm? To test whether the adaptive gain changes obtained in such paradigms have long-lasting effects, Alahyane and Pélisson (Alahyane & Pélisson, 2005) induced a gain decrease adaptation of reactive saccades in one session (22% gain reduction, day 0) and measured saccades at 5-time points over a 19-day period. They found significant retention values, amounting to 36% and 19% of the initial gain change in the first and the fifth days, respectively, but no significant retention in the 11th and the 19th days. In another study, Wang et al. (Wang et al., 2012) tested retention of adaptation in total darkness (rather than in a dim-lighted room as Alahyane and Pélisson) and showed almost complete retention for up to

72 hours and even, in 3 subjects, for around two months. Therefore, in addition to the demonstration of the contributions of both short-term and long-term adaptations in the double-step paradigm (Alahyane & Pélisson, 2005; Wang et al., 2012) the study of Wang et al. shows that long-term retention of saccadic adaptation can be induced when the experimental sessions (both the exposure session and the session testing the retention) are performed in a dark environmental context.

Here, it is important to note in this section that studies have further suggested the existence of two adaptation processes taking place during a single adaptation session: a slow process that learns slowly from error but has strong retention and a fast process that learns rapidly from error but has poor retention. When a series of adaptation, reverse adaptation, and re-adaptation are performed in monkeys during the same session, saccadic adaptation in the re-adaptation phase occurs faster than the adaptation phase, even though the gain was brought to its initial value by the reverse adaptation phase. This suggests that the saccadic system did not return (in the re-adaptation phase) to its pre-learning state; instead, it relies on learning stored in memory (savings) in order to facilitate subsequent adaptation (Kojima et al., 2004). Those results were further extended to humans in the study of Ethier et al. (Ethier et al., 2008b) who estimated that the fast adaptation process is around 20-fold more sensitive to error than the slow adaptation process.

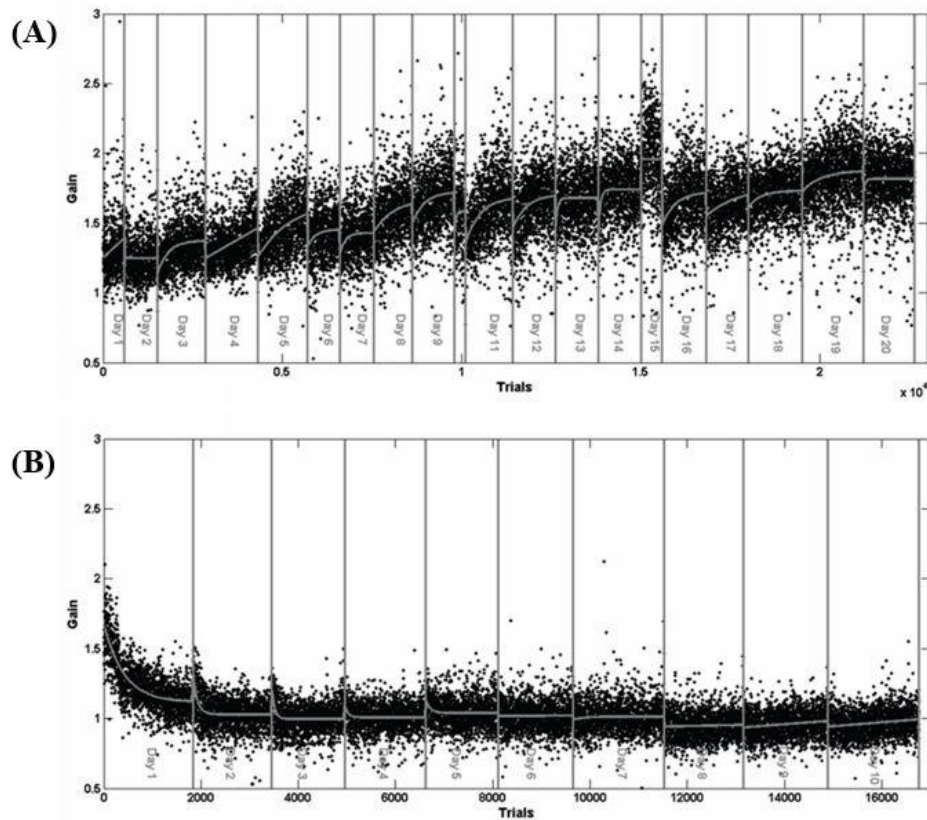


Figure 13 : Long term adaptation. Modified from Mueller et al., 2012 (figures 1 and 2). Results obtained from Monkey 3. (A) Forward adaption time course. Gains of leftward saccades as the monkey tracked targets that moved from 8° leftward to 16° leftward during each saccade, plotted as a function of trial number and over several sessions performed on different consecutive days. (B) Recovery from adaption.

3.10. Corollary discharge

Our visual perception of our environment represents a reconstruction based on the various neural activities taking place along the visual circuitry. The main role of the retina is to break down the image it receives into multiple features (like colors, contrasts, motion, spatial frequencies ...) and send them to the brain. At this level, mainly in the visual cortex, pieces of information consisting of visual snapshots taken during gaze fixation periods are rearranged in order to create our perception of the world. Every day, we perform hundreds of thousands of saccades, during which visual perception is suppressed because images shift at a too high speed on the retina. Therefore, useful visual information is mostly collected during the periods of fixation, which separate two consecutive saccades.

Nevertheless, despite this saccadic suppression of visual inputs, and despite the fact that the brisk position changes of the retinal image between two consecutive fixations cause a discontinuity in visual input, we always perceive a stable representation of the environment. One important component that

contributes to visual stability is the corollary discharge (CD), also referred to as the efference copy. This copy of the motor command of the saccade encodes its size and direction and is sent to the visual areas in order to inform them about the ongoing or impending movement, allowing them to predict the resulting retinal displacement and compensate for it (Wurtz, 2018). For instance, when we perform a double saccade task in which we are required to perform two successive saccades toward two simultaneously flashed targets, the second saccade is performed, in complete darkness, toward the memorized position of the now-absent target and initiated from the landing position of the first saccade. Despite being executed without direct visual target information, this second saccade has been shown to be accurate in several studies (Hallett & Lightstone, 1976; Walker & McSorley, 2006). This double saccade task reveals the capabilities of our saccadic system to program two consecutive saccades in parallel and also that information concerning the outcome of the first saccade, provided by the corollary discharge, is used in order to accurately acquire the second target; indeed, in order to make an accurate second saccade, the memory of the second target location must be adjusted to account for the displacement the eyes have made since this target vanished, i.e. the vector of the first saccade (Hallett & Lightstone, 1976; Sommer & Wurtz, 2008; Walker & McSorley, 2006).

The corollary discharge is first represented in motor coordinates (CD_M); however, in order for the visual areas to use such information, it needs to be translated via a forward dynamic model into visual coordinates referred to as CD_V (Masselink & Lappe, 2021). The CD is hypothesized to originate from the SC and the cerebellum, and several circuitries carrying the CD to cortical brain areas have been identified. The first pathway extends from the intermediate layers of the SC to the FEF through the medial dorsal thalamic nucleus (MD), and is suggested to contribute to the stability of visual perception as well as to target remapping in the FEF and the LIP (this later receiving projections from the FEF) (Cavanaugh et al., 2016, 2020; Wurtz, 2018). The second pathway extends from the SC superficial layers to the middle temporal cortex (MT) through the inferior pulvinar thalamic nucleus (PI) (Wurtz, 2018). This second pathway is hypothesized to carry suppressive effects onto the MT, mediating the saccade suppression phenomenon. The third pathway extends from the cerebellum to the FEF through the ventrolateral nucleus (VL) of the thalamus and is suggested to carry a prediction of the visual error encountered at the end of the saccade (Zimmermann et al., 2015). Concerning saccadic adaptation, a long debate exists about whether the CD is informed about the changes of saccade parameters due to adaptation. A possible reason for such debate is that instead of one CD, multiple CDs have been suggested to be generated in different saccade-related structures; some reflecting the non-adapted saccade (transmitted via the SC-MD-FEF pathway), and others reflecting the adapted saccades therefore, the accurate estimate of the adapted saccade (transmitted via the cerebellum-VL-FEF pathway) (Zimmermann & Lappe, 2016). Note that CD_V originating in the cerebellum was suggested to be partially informed about the adaptation (Cheviet et al., 2022).

3.11. Error signals driving saccadic adaptation

The nature of the error signals that drive saccadic adaptation has been, and still is, a matter of debate since the late nineties. Several hypotheses were successively developed, starting with the proprioceptive hypothesis, followed by the motor hypothesis, the retinal (or sensory) hypothesis, then the sensory prediction error hypothesis, and recently, the postdictive motor error hypothesis. In this section, we will go through each of these hypotheses in order to describe what can possibly be the nature of saccadic adaptation error signal.

First, in order to determine if the eye had rotated the appropriate distance toward the saccade target, the brain could use non-visual signals from the saccade burst generator or extraocular muscle proprioceptors. Seeberger et al. (Seeberger et al., 2002) tested this idea by inducing backward adaptation in monkeys and testing the extent of saccade amplitude recovery from adaptation under different conditions: the saccade target remains visible at the end of the saccade (both visual and non-visual signals are available), the saccade target disappears at the saccade onset (only non-visual signals are available) or finally, the monkeys remain in darkness, with the rare presence of saccades toward the adapted location (neither visual nor non-visual signals are available). These authors found that recovery occurs only when the visual target remains visible but not in the other two conditions. Therefore, they concluded that non-visual signals provided by extraocular muscles proprioception do not drive recovery. However, as recovery and saccadic adaptation can be two different mechanisms, these results, as stated by the authors, may not generalize to adaptation. Nevertheless, the contribution of extraocular muscle signals was further refuted in the study of Lewis et al. (Lewis et al., 2001), who showed that saccadic adaptation in monkeys still takes place after bilateral deafferentation (by sectioning the ophthalmic division of the trigeminal nerve) of the proprioceptive inputs from extraocular muscles.

When a saccade lands inaccurately, a corrective saccade follows and brings the fovea to the target location. One possibility is that saccadic adaptation attempts to modify the primary saccade trajectory in order to reduce and limit the need for corrective saccades. Therefore, based on this logic, the error signal that drives adaptation might be a motor one, originating from the corrective saccade motor command. However, this motor hypothesis was rapidly refuted by several studies which reduced in various ways the occurrence of corrective saccades during a saccadic adaptation exposure. Indeed, it was demonstrated that in both humans and monkeys, backward adaptation occurs even though the occurrence of corrective saccades was strongly reduced by reducing the duration of the stepped target (Noto & Robinson, 2001; Shafer et al., 2000; Wallman & Fuchs, 1998). In addition, using as saccade targets large objects like circles, compared to point targets, was shown to reduce significantly the number of corrective saccades but neither forward nor backward adaptation (Bahcall & Kowler, 2000). Furthermore, when following an intra-saccadic step, the saccade target is re-illuminated at its initial position before the occurrence of corrective saccade (triple-step paradigm),

adaptation still occurs even though corrective saccades are produced in the direction opposite to that of the second-step (Wallman & Fuchs, 1998). Therefore, in summary, neither proprioceptive signals nor corrective saccades drive saccadic adaptation.

Alternatively, the retinal hypothesis states that as an error signal, the brain could use the retinal location of the target image at the end of the saccade relative to the fovea to determine the saccade accuracy. The retinal hypothesis has been tested and challenged in several studies. For instance, this hypothesis does not align with the fact that saccades are naturally hypometric (Wong & Shelhamer, 2011), which means that the visual error which is always present at the end of normal saccades does not effectively drive any adaptation. Along this line of thought, Bonnetblanc and Baraduc (Bonnetblanc & Baraduc, 2007) asked their participants to perform simple saccades toward visual targets at different eccentricities ranging between 10 and 34° and compared the saccade amplitude between two conditions where the saccade target either remained after the end of the primary saccade or disappeared at the saccade onset. They found that large saccades, which are hypometric in nature, progressively increase in amplitude over time specifically in the condition of transient visual target; therefore, saccadic adaptation did occur even though no post-saccadic visual information was present. This finding led the authors to suggest that internal signals, probably the efference copy of the motor command, might be sufficient to elicit adaptive changes. Herman et al. (Herman et al., 2013) varied in different blocks of trials the size of the intrasaccadic step (ISS: from 0.1 to 1 degree) during backward adaptation of 10° saccades and found that the gain change rate reaches 70% of completeness no matter the size of the intrasaccadic step. They argued that if a retinal error signal drives the adaptation, then the adaptation rate should instead be proportional to the ISS size. Bahcall and Kowler (Bahcall & Kowler, 2000) instructed their participants to make primary saccades falling short of their target by about 25% during 3 types of trial blocks: forward adaptation, backward adaptation, and no-jump trials. The retinal hypothesis predicted an increase of saccade gain in all 3 cases as the post-saccadic retinal error signaled hypometric primary saccades. In contrast, whereas saccadic gain did not significantly change in the no-jump condition, it increased and decreased significantly in the forward and backward conditions, respectively. Therefore, in place of the retinal hypothesis, the authors suggested that error signals used for adaptation might result from the comparison between the actual post-saccadic retinal image (visual error) and the predicted visual error. Two main studies tested this sensory prediction error hypothesis. First, Wong and Shelhamer (Wong & Shelhamer, 2011) measured their participants' baseline hypometria (8.2% in this experiment) in a pre-adaptation phase. During the adaptation phase, they used the following modified double-step paradigm. Within 40 ms after the primary saccade had landed, the saccade target stepped to a constant position 0.7 degrees ahead of the primary saccade endpoint, thus producing a hypermetric visual error different from the expected hypometric visual error. The results revealed that the repetition of such trials led to a progressive decrease in saccadic gain rather than the increase that should have resulted from the post-saccadic visual error. This decrease in saccadic gain correlated significantly with the

difference between the baseline hypometria (predicted visual error) and the actual visual error. Second, Collins and Wallman (Collins & Wallman, 2012) conducted a study in which, to induce adaptation (experiment 1), a post-saccadic retinal error was introduced on average across trials without shifting the target during the saccade. Instead, the target was turned off immediately after saccade execution whenever the saccade amplitude was less than (group 1) or greater than (group 2) the median saccade amplitude computed during the pre-exposure phase. In a follow-up experiment (experiment 2), targets were turned off at the onset of saccades and then reappeared at positions that matched the retinal error observed on a trial-by-trial basis from the first experiment. Interestingly, although the retinal errors were identical in both experiments for each of the two groups, the degree of adaptation was significantly higher in the second experiment, where the anticipated target position was modified. These findings suggest that the eyes are aware of both its landing position and the expected target location and that discrepancies from this expectation play a more substantial role in driving saccade adaptation than retinal error alone.

As represented in Figure 14, the prediction error hypothesis states that the brain compares the actual post-saccadic visual error (distance of the target from the fovea at the end of the saccade: V_2) to a predicted representation of this post-saccadic visual error elaborated prior to the saccade (\hat{V}_2), and uses the outcome of this comparison ($E_{pre} = V_2 - \hat{V}_2$) as the error to induce -and to be nullified by- saccadic adaptation. \hat{V}_2 here represents the difference between the perceived target location in visual space before saccade onset (referred to as V_1) and the saccade displacement also expressed in visual space and predicted from the forward dynamic model (that is, a visual representation of the corollary discharge CD_V) ($\hat{V}_2 = V_1 - CD_V$). As previously described, visual stability during saccades is ensured via different mechanisms, such as the saccadic suppression mechanism. Therefore, the brain works under the assumption that the world surrounding us is stable and that the image of the world on the retina is the one that shifts. Here, the prediction error hypothesis is based, however, on the assumption that changes took place during the saccade, resulting in a mismatch between the predicted representation of this post-saccadic visual error (V_2) and the actual error (\hat{V}_2), which opposes the assumption of a stable world. Masselink and Lappe (Masselink & Lappe, 2021) proposed a more sophisticated hypothesis, the postdictive motor error hypothesis. They propose that the error signal driving saccadic adaptation (E_{post}) represents the difference between a post-saccadic visual error (\hat{V}_1) postdicted back to pre-saccadic space and the motor command (CD_M) of the saccade ($E_{post} = \hat{V}_1 - CD_M$). \hat{V}_1 represents the sum of the actual post-saccadic location of the target (V_2) and the visual representation (CD_V) of the corollary discharge ($\hat{V}_1 = V_2 + CD_V$). In simpler words, postdictive motor error is a retrospective estimation of the pre-saccadic target position based on the post-saccadic image. Such postdiction-based learning requires the visuomotor system to assume trans-saccadic stability (meaning that V_2 was the actual location of the target before the saccade onset) and to attribute the errors to internal causes (for example, a deficient motor command or an inaccuracy in the visual target localization, which impact the motor command (CD_M)) in accordance with the saccadic suppression

mechanism. In the next section, we will describe in detail the results of Masselink and Lappe's study on the postdictive motor error hypothesis.

3.12. The postdictive motor error hypothesis

In their experiment, Masselink and Lappe (Masselink & Lappe, 2021) compared four different learning conditions (forward vs backward adaptation, using either the constant error paradigm or the constant target step paradigm (also referred to as the double-step target paradigm)), preceded and followed by a localization task under fixation. They also had trans-saccadic localization tasks before, after, and during saccadic adaptation. They found that saccadic motor learning relies on multiple visuomotor plasticity mechanisms, including the adaptation of the visual target position (that is, the visual remapping of the target location, found only in the constant target step paradigm for both forward and backward adaptation), the adaptation of the inverse model which represent the visual to motor transformation that gives us the motor command, and the adaptation of the forward dynamic model which is the motor-to-visual transformation of the corollary discharge that gives the CD_V . Indeed, the change in the motor gain (referred to as ω_m in Figure 14) was larger than the changes in the corollary discharge gain (ω_{cd}), which in turn was larger than the change in the visual gain (ω_v). In addition, they found, as suggested in earlier studies (Cheviet et al., 2022), that the CD_V is partially informed about adaptation as ω_{cd} underestimates the size of the saccade change, and therefore, CD_V dissociates from the saccade during learning. In this study, only the postdiction model (compared to the predictive model) fits the data well as the modeled error reduction was consistent with the changes in the saccade vector as well as the changes in the pre- and post-saccadic localizations tasks. They also found that when the prediction error was nullified, the actual position of the shifted post-saccadic target did not match its predicted location.

The postdiction model has the advantage over the prediction model as 1) it takes into consideration the different learning mechanisms occurring during saccadic adaptation, 2) it explains the visuomotor steady states in baseline and after the learning has converged, 3) it explains saccade's hypometria and attributes it to the hypometria of the CD_V observed in baseline, 4) it explain the incomplete saccade learning from artificial target steps as it attributes it to the dissociation between the saccade and the CD_V observed during learning, and finally 5) explain the difference seen usually between backward and forward adaptation as it refers it to a larger visual error in forward adaptation compared to the backward adaptation due to the hypometria of the CD_V in the baseline. Recently, Heins et al. (Heins et al., 2023) implemented a new paradigm in which backward and forward adaptation was performed in parallel with pre- and post-saccadic localization tasks without presenting a pre-saccadic visual target. They showed that oculomotor learning takes place (both saccades and localization judgments changed in accordance with the shifting target position) based on post-saccadic visual information alone, therefore arguing in favor of the postdictive motor error hypothesis. However, the postdiction model proposed by Masselink and Lappe does not consider the fast and the

slow processes of saccadic learning and furthermore, does not take into consideration the effect of attention on saccadic adaptation (which will be discussed in the next chapter), which means we can still expect a better model in the future.

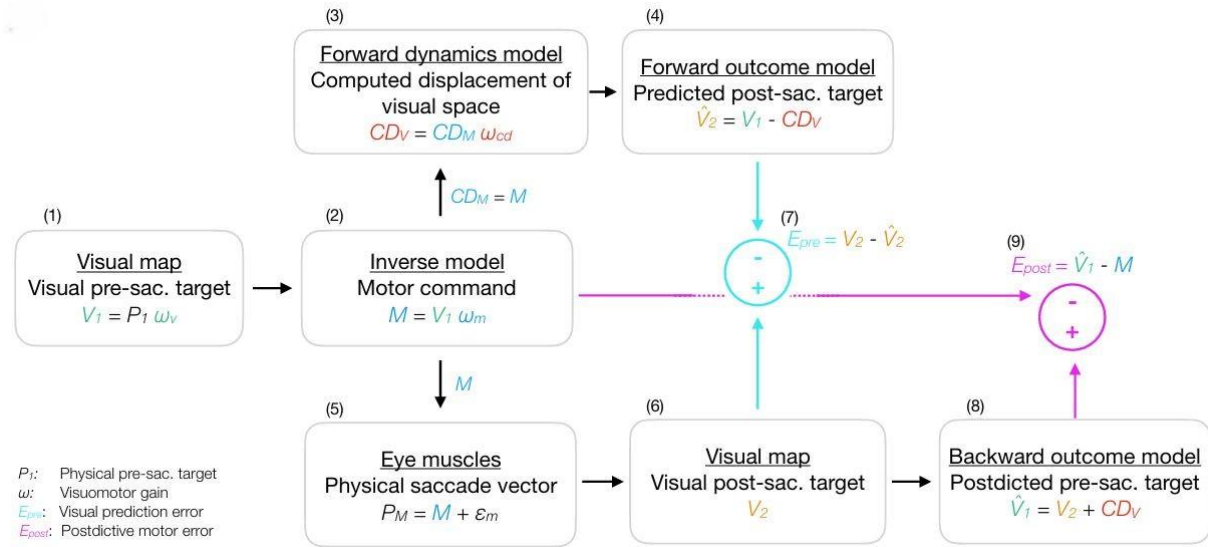


Figure 14: The visual prediction error model compared to the postdictive motor error model proposed by Masselink & Lappe, 2021. The visual pre-saccadic target V_1 is transformed into the motor command M . Before saccade execution, a forward dynamics model transforms a copy of the motor command CD_M into a computed displacement of visual space CD_V , a visual estimate of the saccade vector. Hence, the forward outcome model predicts the visual post-saccadic target to appear at position \hat{V}_2 . After saccade execution, the visual post-saccadic target appears at position V_2 . According to prediction-based learning, the visuomotor system detects an error if the visual post-saccadic target deviates from its prediction (E_{pre}). According to postdiction-based learning, a backward outcome model postdicts the visual post-saccadic target back to pre-saccadic space (\hat{V}_1) in order to retroactively evaluate the motor command (E_{post}). ϵ_m represent random motor noise in saccade execution. Modified from Masselink & Lappe, 2021 (figure 2).

3.13. The cerebellum

The cerebellum plays an important role in motor control and coordination, motor learning, and cognitive tasks such as attention, language processing, and problem-solving. It has a major role in the control of eye movements, including, in particular, saccadic adaptation. One of the earliest evidence is that total cerebellectomy in monkeys completely abolishes saccadic adaptation induced by the eye weakening procedure, with an adaptation failure of both the pulse and the step component of saccades motor command (Optican & Robinson, 1980). This study also showed that partial cerebellectomy targeting the vermis and the paravermis (lobes IV-IX) as well as the fastigial nuclei abolished only the

adaptive control of the pulse component of the saccadic command, while the drift resulting from impaired adaptation of the step component slowly recovered over time. The posterior vermis, including lobules VI and VII, also designated as the oculomotor vermis (OMV), plays an important role in the control of saccade accuracy and saccadic adaptation. For instance, microstimulations of the OMV evoke ipsiversive saccades organized topographically: stimulations in lobule V produces upward and horizontal saccades, while stimulations in lobules VI and VII elicit horizontal and downward saccades (Beh et al., 2017). Lesions of lobules VIc and VII result in the impairment of short-term but not long-term saccadic adaptation (Barash et al., 1999). Furthermore, significant activations of the OMV can be seen in human participants via PET measures during backward adaptation of reactive saccades (Desmurget et al., 2000). In addition, transcranial direct current stimulation applied to the OMV affects saccadic adaptation: cathodal stimulations tended to increase the extent of both forward and backward adaptations, while anodal stimulations strongly impaired forward adaptation and more lightly impacted backward adaptation (M. T. N. Panouillères et al., 2015).

The OMV inputs and outputs

The OMV receives mossy fibers afferents from a variety of cortical (FEF, SEF, and PEF) and subcortical regions (SC, vestibular nuclei, PPRF), via the contralateral dorsal, medial, and dorsolateral pontine nuclei (PN) as well as from the medial and dorsomedial regions of the contralateral nucleus reticularis tegmenti pontis (NRTP). Recording of neurons in NRTP shows that backward adaptation of reactive saccade affects the number of spikes in the burst of more than half of tested NRTP neurons, primarily by increasing burst duration but not frequency. These findings suggest that adaptive changes in saccade amplitude are already reflected at the level of a major input to the oculomotor cerebellum (Takeichi et al., 2005).

The OMV also receives climbing fiber afferent through the inferior olivary nucleus, serving as a relay between the intermediate and deep layers of the contralateral superior colliculus and the OMV (Voogd & Barmack, 2006; Yamada & Noda, 1987). In the clinical literature, Wallenberg's syndrome is considered a clinical model of OMV deafferentation, resulting from a lesion in the dorsolateral medulla disrupting the olivo-cerebellar pathways. Noteworthy, the impairment of both reactive and voluntary saccades backward adaptation reported in patients with Wallenberg's syndrome, therefore, highlighted the importance of this pathway in saccadic adaptation (M. Panouillères, Alahyane, et al., 2013; WAESPE & BAUMGARTNER, 1992).

The OMV sends ipsilateral inhibitory outputs to the caudal fastigial nucleus (cFN), also known as the fastigial oculomotor region (FOR), which in turn projects to brainstem centers such as the PPRF, riMLF, SC, and the vestibular nuclei that directly control eye movements as well as, via the ventrolateral thalamus to cortical areas, including the FEF known to participate in the planning and execution of voluntary eye movements. The cFN also receives innervation from mossy fibers originating from the NRTP (Voogd & Barmack, 2006; Yamada & Noda, 1987). Neurons in the cFN exhibit an early burst of spikes that is synchronized with the beginning of contraversive saccades and a

late burst of spikes that is synchronized with the end of ipsiversive saccades (Scudder & McGee, 2003). Unilateral inactivation of cFN through muscimol injections results in hypermetric ipsilateral horizontal saccades and hypometric contralateral ones. These dysmetria are accompanied by an increase in the acceleration of ipsilateral saccades and a decrease in the acceleration of contralateral saccades. Therefore, it has been suggested that the cerebellum plays a suppressive or a braking role in controlling ipsiversive saccades and helps accelerate contralateral saccades. The superior colliculus is thought to generate a raw command, which alone would result in hypermetric saccades. The cFN contributes to the adjustment of this collicular command at a downstream brainstem level via its excitatory connections to IBNs and EBNs (Fuchs et al., 1993; F. R. Robinson et al., 1993). Unit recordings at the single-neuron level during adaptive modification of saccade size provide consistent data with the above-mentioned role of the cFN. Indeed, cFN neuron activity is significantly increased during backward adaptation, while it is significantly reduced during forward adaptation (Inaba et al., 2003). Scudder and McGee (Scudder, 2002; Scudder & McGee, 2003) further showed that both the latency of cFN neurons' burst for ipsiversive saccades and the number of spikes of cFN neurons' burst associated with contraversive saccades positively correlate with saccade size during adaptation. The correlation seen for ipsiversive saccades was stronger with backward adaptation, while the correlation seen for contraversive saccades was more important with forward adaptation.

Bilateral inactivation of cFN in monkeys using muscimol injections results in small or very slow backward adaptation (F. R. Robinson et al., 2002). Nevertheless, when the monkeys were placed in darkness to eliminate post-saccadic visual feedback until the effect of muscimol vanished, they generated significantly adapted saccades when presented again with visual targets, an adaptation level comparable to the backward adaptation induced in control monkeys without cFN inactivation. These findings that cFN inactivation blocks the expression but not the induction of adaptation suggest that the cFN is located downstream of the adaptation site and serves as a relay of adapted signals toward the oculomotor system.

Examples of the effects of cerebellar lesions on adaptation

Straube et al. (Straube et al., 2001) investigated the impact of different cerebellar diseases on reactive saccades backward adaptation. They showed that, compared to healthy subjects, most patients with cerebellar lesions had impaired saccadic adaptation, including cases of cerebellar degeneration, cerebellar infarcts, and congenital malformation.

The disconnection of vermal Purkinje cells from their target cells in the cFN in patients with a unilateral infarction in the cortico-cerebellar territory of the right superior cerebellar artery involving vermal folia VI and VII results in the abolishment of backward reactive saccades adaptation (Waespe & Müller-Meisser, 1996).

The hypothesis of different neural substrates for adaptation of reactive versus voluntary saccades is consistent with the specific adaptation deficits related to cerebellar pathologies found in some studies. For example, Alahyane et al. (Alahyane, Fonteille, et al., 2008) showed that a medial

cerebellar lesion (infarct of antero-inferior cerebellar artery) impaired adaptation of ipsilateral reactive but not of voluntary saccades, whereas a lateral lesion (infarct of the medial branch of the postero-inferior cerebellar artery) affected adaptation of ipsilateral voluntary saccades, but not of reactive saccades. In another study investigating the effect of cerebellar lesions on saccadic adaptation, the supero-anterior cerebellum was shown to be implicated in the control of reactive saccades metrics, while the infero-posterior cerebellum was found to be implicated in the control of voluntary saccade metrics (M. Panouillères, Alahyane, et al., 2013).

Purkinje cells and recordings studies

The population response of large groups of Purkinje cells in the OMV gives a precise temporal signature of saccade onset and offset. Therefore, it was suggested that the response of the vermal population might help determine saccade duration. Accordingly, modifications of the duration of the vermal population response could be the neural underpinning of the adaptive changes in saccade amplitude (Thier et al., 2000). Indeed, in their study, Golla et al. (Golla et al., 2008) showed in a group of healthy participants, forward adaptation was associated with an increase in saccade duration, whereas backward adaptation was associated with a decrease in both the peak velocity and the duration of saccades. In contrast, patients with vermal pathology lacked forward adaptation and showed no change in saccade duration. These patients also showed during backward adaptation as well as during resilience testing (long repetition of simple saccades toward stationary targets) a significant decrease in saccade amplitude paralleled by a decrease in peak velocity with no marked saccade duration change. These findings support the notion that backward adaptation is at least partially based on uncompensated fatigue and that forward adaptation reflects an active mechanism for the compensation of fatigue residing in the cerebellum.

Cerebellar Purkinje cells generate both simple and complex spike activities, respectively characterized by their high firing rate (>100 Hz) and low discharge rate (1–2 Hz). According to the classical Marr-Albus hypothesis of the cerebellar role in learning (Albus, 1971; Marr, 1969), it is suggested that the complex spikes encode an error signal that drives changes in simple spike activity (through long-term depression LTD), the latter ultimately modulating motor behavior. This hypothesis, which predicts that complex spikes will discharge in relation to the error and at random once the error has been nulled by the adapted behavior, has been tested in the context of saccadic adaptation by the following studies. First, regarding simple spikes, some Purkinje cells in the oculomotor vermis exhibit changes in simple spikes activity specific to adapted saccades, which may therefore induce adaptation (Kojima et al., 2010). This postulated implication of Purkinje cells' simple spikes in saccadic adaptation is more clearly supported by analyses at the level of the population burst: for non-adapted saccades and saccades submitted to forward adaptation, the end of Purkinje cells' simple spikes population burst corresponds to saccades' termination whereas, in backward adaptation, the population burst ends well before the saccade offset (Catz et al., 2008).

Second, regarding complex spikes, conflicting results exist in the literature. Catz et al. (Catz et al., 2005) found that complex spikes activity was random before the adaptation onset when the error was maximal and increased progressively during the course of adaptation until it reached a peak of activity at the end of adaptation when the error was nullified. The authors suggested that complex spikes firing may underlie the stabilization of a learned motor behavior rather than the encoding of an error signal. In contrast, another team using similar recording approaches revealed that Purkinje cells complex spikes activities in the OMV during both backward and forward conditions either increase during the error interval (the fixation period between the primary saccade and the corrective saccade) for errors in one direction or decrease for errors in the other direction. As adaptation evolves and errors are reduced, no consistent change in the complex spikes activity can be seen. Furthermore, the complex spikes response associated with saccade adaptation was larger when associated with a decrease than an increase in saccade amplitude for the same visual error, suggesting that these responses do not simply reflect retinal error signals. In addition, Some Purkinje cells' complex spike discharges were not only direction-specific but also sensitive to the error size (Soetedjo et al., 2008; Soetedjo & Fuchs, 2006). Therefore, in summary, studies in the above literature argue with the implication of Purkinje cells' simple spikes in saccadic adaptation and the implication of complex spikes in both the error processing and the stabilization of motor learning.

The implication of areas outside the OMV in saccadic adaptation

In humans, TMS neurostimulation and fMRI have been used to decipher the role of the cerebellum in saccadic adaptation and/or error signals processing. TMS applied over Crus I (lateral cerebellum) during adaptation exposure depressed the after-effect of backward adaptation for ipsiversive saccades, whereas it potentiated the after-effect of forward adaptation for saccades in both directions (M. Panouillères et al., 2012). These findings provide the first evidence that the human cerebellar hemispheres are involved in saccadic adaptation, with possibly different neuronal populations implicated in adaptive lengthening and shortening.

An fMRI study showed activated neuronal clusters in vermis VIII, lobules VIII-X, and left lobule VIIb, which were observed with random saccadic errors at the end of rightward saccades compared to control saccades with no error, suggesting a possible role of areas within and outside the oculomotor vermis in the processing of saccadic errors (van Broekhoven et al., 2009). Four other fMRI studies showed activations of several cerebellar areas implicated in saccadic adaptation. First, Liem et al. (Liem et al., 2013) compared, for rightward reactive saccades, blocks of backward or forward adaptation trials to a block with random intrasaccadic steps trials and a block with stationary target trials (no intrasaccadic step). They showed that large saccadic errors (induced by large target steps) led to increased activity in cerebellar hemispheres, especially on the right side, whereas activation was found in the cerebellar vermis and paravermal areas in relation to small errors. They further showed that forward errors require, on average, a larger activity level than backward errors, revealing that the cerebellum is more involved in the processing of forward errors than backward

errors. Finally, a comparison between error and no error blocks of trials showed significant bilateral activation of lobules VI, VIII, and IX and unilateral activation in Crus 1 and 2 and lobule VIIb on the left. The results of Liem et al. study (Liem et al., 2013) are represented in Figure 15. Second, Gerardin et al. (Gerardin et al., 2012) showed activation of ipsilateral cerebellar area VIIb and VIIIa during reactive and voluntary saccade adaptation as well as in relation to reactive saccade de-adaptation. Third, Guillaume et al. (Guillaume et al., 2018) showed activations related to the adaptation process in the ipsilateral OMV (crus I and crus II of lobule VIIa) and the intermediate region in the contralateral cerebellum (crus II), as well as activation related to error processing in the ipsilateral cerebellum lobule V, contralateral cerebellum lobule VI, both being outside the OMV. Fourth, Métais et al. (Métais et al., 2022) showed activation related to error processing in the ipsilateral superior cerebellum (lobules VIII/IX and lobule VI) and the contralateral inferior cerebellum (lobules VIIb–VIIIa). To sum up, the OMV, through its Purkinje cells, is not the only structure in the cerebellum responsible for saccades adaptation. Instead, the studies presented above argue with the implication of several cerebellar regions in such a mechanism.

| Area | Error>no-error | Large>small | Small>large | Forward>backward |
|--------------|----------------|-------------|-------------|------------------|
| Vermis I | | | | |
| Vermis II | | | | |
| Vermis III | | | X | |
| Vermis IV, V | | | X | |
| Vermis VI | | | X | |
| Vermis VII | | | | |
| Vermis VIII | | | | |
| Vermis IX | | | X | X |
| Vermis X | | | X | X |
| Lobule I | | | | |
| Lobule II | | | | |
| Lobule III | | | | Right |
| Lobule IV, V | | | Both | Right |
| Lobule VI | Both | Right | Left | |
| Lobule VIIb | Left | | | Left |
| Lobule VIII | Both | Both | | Both |
| Lobule IX | Both | Left | | Both |
| Lobule X | | | | Right |
| Crus 1 | Left | Right | | Right |
| Crus 2 | Left | Right | | Left |

Figure 15: Cerebellar areas involved in saccadic adaptation. Summary of the areas of activation in the cerebellum for 4 different contrasts (the backward versus forward adaptations contrast is not reported as it did not reveal any significant activation in the cerebellum). Modified from Liem et al., 2013.

3.14. The superior colliculus

The superior colliculus, as described in the previous chapter, constitutes a major and essential relay between many cortical and subcortical areas, most of them being implicated in saccadic eye movements and some saccadic adaptation. Therefore, studies focusing on the role of the SC in saccadic adaptation must consider in their experimental designs the possible -and at least partially segregated- neuronal substrates of adaptation implicated in the different training directions (forward vs backward) or the different saccade types (reactive vs voluntary). Methodological differences between the existing studies resulted in different conclusions regarding the site of the adaptation loci in reference to the SC. In their study, Melis and van Gisbergen (Melis & van Gisbergen, 1996) found no transfer of voluntary saccade adaptation to saccade evoked via suprathreshold electrical stimulations of the SC, suggesting that such adaptation occurs in the SC or upstream structures. They also performed another experiment in which they investigated whether it is possible to adapt electrically evoked saccades. Saccades were elicited via suprathreshold electrical stimulations of the SC, and at the time of saccade termination, a visual target located either slightly forward or slightly backward from the saccade endpoint was presented. They showed that saccadic gain was modulated significantly as in a classical behavioral double-step paradigm, which suggests that this type of saccadic adaptation occurs at the level or downstream of the SC and, therefore, contradicts the previous conclusion. The adaptation of electrically evoked saccades was further found to transfer slightly but significantly to normal reactive saccades, bringing even more complication for someone to draw a certain conclusion. Here, two major points might act as limitations in Melis and van Gisbergen's study. First, many cortical areas contribute to the production of voluntary saccades, including the FEF, which is known to project directly on the brainstem, bypassing the SC. Second, the suprathreshold stimulations themselves may trigger saccades via different direct or indirect outputs to the brainstem burst generator. Edelman and Goldberg (Edelman & Goldberg, 2002) overcome the problem of suprathreshold stimulation by using low-threshold ones to evoke saccades. They showed in three monkeys that saccade evoked by low-threshold stimulation currents in the superior colliculi were modified after backward adaptation. In addition, the amplitude change of electrically evoked saccades was found to follow a similar time course and to be accompanied by a similar reduction in saccade velocity (with no decrease in duration) as the reactive saccades exposed to the adaptation procedure. Also, the more similar the velocity of electrically evoked and visually guided saccades prior to the start of saccadic adaptation, the greater the transfer of adaptation on electrically evoked saccades. These results suggest that the superior colliculus is upstream of the locus of adaptation (Edelman & Goldberg, 2002). The 'upstream' hypothesis from Edelman and Goldberg predicts no change in the SC neurons movement field (the effects of adaptation take place downstream of the SC), whereas the reverse is true for a 'downstream hypothesis' (modification of SC neurons movement field).

Recordings of the activity of saccade-related burst neurons in the SC in monkeys during both backward and forward adaptation of voluntary saccades (overlap paradigm) showed no evidence consistent with any related change in the locus of SC activity (Quessy et al., 2010). Similar results were also obtained for the backward adaptation of reactive saccades in a previous study by Frens and Opstal (Frens & Van Opstal, 1997) and therefore both studies argue with the hypothesis of Edelman and Goldberg (Edelman & Goldberg, 2002). In contrast, Takeichi et al. (Takeichi et al., 2007) showed that both backward and forward adaptation of reactive saccades were associated with significant changes in the number of spikes in the burst and/or changes in the shape of the movement field in 35 of 43 SC neurons tested. Changes in the number of spikes occurred gradually during adaptation and resulted from correlated changes in burst lead and duration without consistent changes in peak burst rate. These data indicate that the great majority of SC neurons show a change in discharge in association with saccade amplitude adaptation. The author suggested that the SC itself might be the site of adaptive plasticity or, at least, that plastic changes produced elsewhere are funneled through the SC. The conflicting results present in the literature point toward the need for additional future studies that might contribute to deciphering the enigma of the role of the SC in saccadic adaptation.

3.15. Contribution of other cortical and subcortical regions in saccadic adaptation

While it was originally thought that saccadic adaptation is a process restricted to the cerebellum, numerous studies have now provided data supporting the implication of the thalamus and of several cortical areas in saccadic adaptation. Gaymard et al. (Gaymard et al., 2001) compared backward adaptation of reactive saccades between a group of healthy participants and four patients with a thalamic lesion. Compared to healthy participants, saccadic adaptation was reduced in patients with associated cerebellar syndrome, but unaffected in patients without cerebellar syndrome. These results suggest that the thalamic nuclei lesioned in the former patients relays information between the cerebellum and cerebral cortical oculomotor areas, which is functionally important for saccadic adaptation.

TMS and fMRI approaches have been used to decipher the role of the cerebral cortex in saccade adaptation. Applying single-pulse TMS over the right posterior intraparietal sulcus (IPS), (M. Panouillères et al., 2014a) were able to reduce the amount of backward adaptation and the size of the after-effect of both leftward and rightward voluntary saccades. This was found when applying the TMS pulse over IPS 60 ms after the saccade onset when compared with the control session (application of TMS over the vertex). When applied 90 ms after the onset of rightward reactive saccades, TMS over the right (ipsilateral) IPS led to larger backward adaptation only at the end of the adaptation phase, with no persistent change in the after-effect. These results reveal the contribution of the IPS in backward adaptation of voluntary saccades or in error processing (M. Panouillères et al., 2014a). This conclusion is consistent with fMRI studies that showed an activation of the IPS

(contralateral medial and posterior IPS) attributed to the backward adaptation process of voluntary saccades (Gerardin et al., 2012) as well as an activation of the ipsilateral IPS attributed to the error processing component of backward adaptation of leftward reactive saccades (Guillaume et al., 2018). The contribution of the PPC in error processing was also supported by neuronal activity data in monkeys performing a delayed saccade task (Zhou et al., 2016). Finally, fMRI studies identified several areas of the PPC where significant activations were attributed to the error processing component of adaptation of reactive saccades (parietal eye field, the precuneus, the superior parietal lobule (Métais et al., 2022)), as well as the adaptation process (the precuneus and the anterior parietal lobule (Guillaume et al., 2018)).

In addition to the PPC, fMRI studies also show the implication of the TPJ in short-term reactive saccades adaptation (Gerardin et al., 2012) as well as in error processing (Guillaume et al., 2018). Inhibiting the activity of TPJ via TMS would imply a decrease in the adaptation of reactive saccades. Single pulse TMS over the right temporoparietal junction (TPJ) led to a 2–3.8-fold increase of the rate of leftward reactive saccades backward adaptation retention over approximately ten days compared to a condition where no stimulations were used and another TMS over the vertex. Even though these results are quite surprising, as one might expect a perturbation of the TPJ activities, they reveal the contribution of the TPJ in the long-term retention of saccadic adaptation. In contrast, this study did not show any significant differences between the different conditions in terms of short-term adaptation (Péllisson et al., 2018).

In addition to the PPC and the TPJ, several other cortical areas change their activity in relation to saccadic adaptation procedures, as revealed by fMRI studies. These areas include the medial temporal and medial superior temporal regions (for both backward and forward adaptation of reactive saccades: (Gerardin et al., 2012; Métais et al., 2022)), several occipital regions (again for both types of reactive saccades adaptation, supposedly in the adaptation process and the error processing : (Guillaume et al., 2018; Métais et al., 2022)) the insula (error processing: (Blurton et al., 2012; Guillaume et al., 2018)), the FEF (adaptation process: (Gerardin et al., 2012; Métais et al., 2022) , error processing : (Guillaume et al., 2018) during the adaptation of reactive saccades) as well as the supplementary eye field (error processing : (Blurton et al., 2012; Guillaume et al., 2018) the middle cingulate cortex (error processing: (Métais et al., 2022)) and inferior precentral sulcus (for voluntary saccades adaptation (Gerardin et al., 2012)).

3.16. Conclusion

Saccadic adaptation is a plasticity-based mechanism controlling the precision of saccadic eye movements. It can be studied via different techniques in the laboratory. Studies so far have suggested at least partially different adaptation mechanisms between backward and forward adaptations as well as between the adaptation of reactive and voluntary saccades. In both

cases, the error signal driving adaptation is hypothesized to result from the postdictive motor error. Saccadic adaptation was initially thought to occur mainly in the cerebellum, but accumulating evidence now highlights the implication of a vast cortical network, including the parietal regions, which are also implicated in the orienting of spatial attention. This overlap of parietal neural substrates points toward a possible interaction between spatial attention and saccadic adaptation, which will be discussed in the next chapter.

Chapter 4: Spatial attention

By simply typing the word “attention” into a search engine like PubMed and filtering the results in order to select the publication that appeared in the last 25 years, you will obtain “to this date” approximately 587,000 publications. If, on average, one may need 2 hours to read one publication, simple math shows that we need 134 years of 24/7 reading in order to go through all those “new” publications. What we can now agree on is that attention is indeed not a unitary mechanism; instead, it may be considered a characteristic and property of multiple perceptual and cognitive control mechanisms (Chun et al., 2011). Over the years, attention has been classified into different networks, classes, and subclasses, each having its own characteristics but also sharing certain similarities. Saccadic adaptation, which forms the main interest of this thesis, has been found to interact with attention. Nevertheless, the studies focusing on this interaction can be counted on the fingers. In this chapter, we will discuss the interaction between saccadic adaptation and attention; however, before we reach this point, we will describe certain key features in attention related to our subject of interest.

4.1. Definition and types of attention

Attention was defined by William James in 1890 as *“the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. ... It implies withdrawal from some things in order to deal effectively with others...”* (James, 1890).

Therefore, attention relies first on the selection of sensory inputs relevant to the ongoing task and requiring in-depth processing and second on the filtering of irrelevant signals. Attention can be divided into three networks according to Petersen and Posner (Petersen & Posner, 2012). First, the alerting network, which relies on the brainstem and certain frontal and parietal areas in the right hemisphere, prepares the brain for incoming tasks by increasing its sensitivity to new information, therefore maintaining an alert state and readiness to respond to those signals. Second, the executive control network, which relies on the anterior cingulate cortex, the dorsolateral prefrontal cortex, and the basal ganglia, exerts a top-down control on our behavior in order to regulate more complex cognitive functions, including managing conflicts, inhibiting inappropriate responses and controlling attention in tasks such as problem-solving and decision-making known to be highly demanding. Third, the orienting network, which will be our main area of focus in this chapter, directs attention to a specific area or stimulus in the environment in order to select relevant information among distractors. This network is responsible for orienting attention as a spotlight that moves within the sensory landscape. The orienting network is very close to the external attention class in the work of Chun et al. (Chun et al., 2011) where they attempt to draw a taxonomy of attention. This class was subdivided according to the focus of attention into 1) modality-specific attention, 2) temporal attention, 3) features and object-based attention, and finally, 4) spatial attention. As previously stated, in this chapter, as well as in this thesis in general, we will be more interested in the orienting of attention, more

specifically the spatial attention, how it is investigated experimentally, its different types and neuronal correlates, its cross-modal effects as well as its interaction with saccades generation and saccadic adaptation.

4.2. The cue-target paradigm to orient spatial attention

Due to our limited capacity to deal with all the information present in the environment, spatial attention prioritizes specific spatial locations in the environment in order to deal effectively with what those locations entail as information. Spatial attention has been investigated thoroughly using a variety of paradigms, among which is the cue-target paradigm proposed by Posner (Posner, 1980). This paradigm consists of orienting participants' spatial attention toward a certain location using a first stimulus, the cue, for example, the illumination of a particular placeholder as represented in Figure 16. After a certain delay (the stimulus onset asynchrony (SOA)), a second stimulation, the target, is delivered either at the cued (valid trial) or in another location, usually in the opposite hemifield (invalid trial). Generally, the participants have to either detect the target's appearance or discriminate its location or some characteristics of the target. The main behavioral result of this paradigm is that participants are faster and more accurate in performing these tasks in valid trials compared to invalid ones. This result is interpreted as the participants' attention being driven toward the cue location, allowing in-depth processing of the target when presented at the cued location, resulting in faster responses as compared to targets presented elsewhere. This is what is referred to as facilitation. When the target is delivered at the un-cued location, spatial attention needs to disengage from its current position and shift toward the target, which results in slower responses. In addition to valid and invalid trials, neutral trials can be used in which the attentional cue is central or global, not cueing any particular location and typically accompanied by instructions indicating that, in this case, the participant should orient their attention everywhere. Depending on the aim of the experiment, the cue type can be varied, as well as the duration of each stimulus, the inter-stimulus interval, and the proportion of valid, invalid, and neutral trials (for review, (Chica, Martín-Arévalo, et al., 2014)). One additional factor that can be varied in such a paradigm is whether the task involves a saccade toward the different stimuli (this is the case of the overt orienting of attention) or whether the participants are required to maintain fixation over a certain location during the trial (known as the covert orienting of attention). In this chapter, most of the studies reviewed are based on the covert orienting of spatial attention, as it will be our main interest in this work. Therefore, unless specified otherwise, we will be discussing *covert* spatial attention.

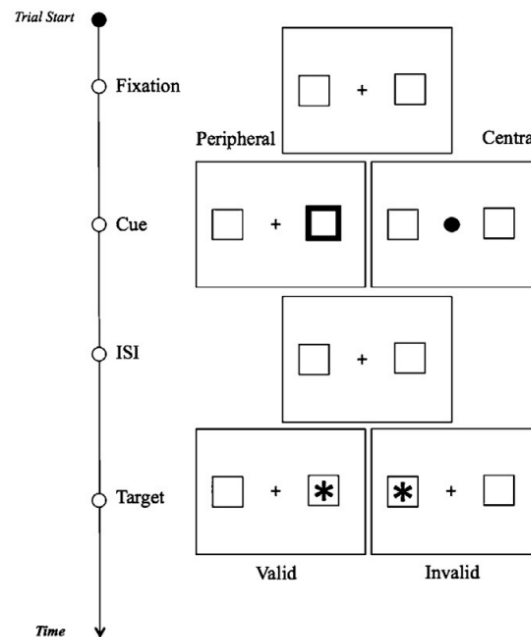


Figure 16: a cue-target paradigm used to study the orienting of spatial attention. Taken from (Chica, Martín-Arévalo, et al., 2014).

4.3. Endogenous vs exogenous orienting of attention

Similar to saccades, orienting spatial attention can be based on our internal goals and intentions; this is referred to as the endogenous orienting of attention (also called voluntary or top-down attention). Attention can also be oriented toward salient stimuli appearing or changing briskly in our environment; this is referred to as the exogenous orienting of attention (automatic or bottom-up) (Macaluso, 2010). The exogenous orienting of attention was suggested to be a phylogenetically older mechanism, allowing individuals to react quickly to stimuli in order to capture behaviorally relevant information. This orienting mechanism seems critical for survival, as it permits the locating of salient stimuli, which is particularly important when those stimuli present threats (Carrasco, 2011). However, creatures also need to search for sources of nutrients to survive. In such foraging tasks, endogenous orienting of attention is critical.

Endogenous attention can be experimentally oriented with the cue-target paradigm by using central, spatially predictive cues like arrows. Other non-spatial central symbolic cues like colors, instructing the participants to orient their attention to a certain location based on a specific color of the central cue was found to be less efficient, as it takes time to build this association between the color and the cued spatial location (Dodd & Wilson, 2009). When an arrow is used, it points toward the location to which the participants have to focus their attention and which predicts, in the majority of the trials, the actual location of the target to be discriminated. This, therefore, implies that participants voluntarily orient their focus of attention on the cued location (Chica, Martín-Arévalo, et al., 2014).

However, it is suggested that central arrows also rely on automatic symbolic orienting, a different form of attention that operates independent of, but in parallel with, exogenous and endogenous spatial attention (Ristic & Kingstone, 2012). The predictability of the cue can be varied, with the most commonly used frequency of occurrence for endogenous attention being 75% of valid vs. 25% of invalid trials. The facilitation effect of the central symbolic cues on target processing was shown to be effective for SOAs around 300 ms and can last for several seconds (Chica, Martín-Arévalo, et al., 2014; Remington & Pierce, 1984). The course of this facilitation effect depends, of course, on the time the participants need to interpret the cue (e.g., around 300 ms for arrows and 600 ms for colors).

Exogenous attention, on the other hand, is often oriented with the cue-target paradigm using peripheral cues. Those cues should be 1) non-predictive (50% valid vs. 50% invalid trials) so they will not entail strategic responses and 2) salient enough to engage exogenous attention. Cues for exogenous attention consist in the presentation of a peripheral stimulus but can also consist in the offset of a peripheral stimulus (i.e., the offset of a placeholder) (Riggio et al., 1998). Peripheral non-predictive cues were found to be effective for SOA ranging between 50 and 300 ms (Gabay & Henik, 2010; Lupiáñez et al., 1997; Milliken et al., 2003; C. Spence et al., 1998; C. Spence & McGlone, 2001). With larger intervals, this effect vanishes, and around 600 ms, it reverses, with participants' responses being faster in invalid than valid trials. This effect, known as inhibition of return (IOR), is caused by the fact that after orienting toward the cued location, spatial attention is disengaged from that location, and any potential return of attention to that location is temporarily penalized (Plax, 2021). The time course of the IOR depends on the task demand and can last for several seconds (Chica et al., 2006; Lupiáñez et al., 1997; Samuel & Kat, 2003).

Changing the frequency of occurrence of the peripheral cue to 75% valid vs. 25% invalid would render the cue spatially predictive and, therefore, would engage both exogenous and endogenous attention. Here, however, the exogenous attention component would disappear at large cue-target intervals (around 500 ms), and attention would be maintained endogenously (Chica et al., 2007; Chica, Martín-Arévalo, et al., 2014; C. Spence et al., 2000). The facilitation effects of endogenous attention are usually less affected by the IOR (Chica et al., 2006; Chica, Martín-Arévalo, et al., 2014; Klein, 2000) and can be seen in the first 100 ms following their onset and can last for up to 1000 ms (Chica et al., 2007; C. Spence et al., 2000).

Orienting spatial attention using the cue-target paradigm has been shown to be more effective when the participants have to discriminate the location or the characteristic of the target rather than simply detecting its presence. Nevertheless, detecting the target presence can be enhanced when the cue and target presentation times overlap (Collie et al., 2000; Klein, 2000; Lupiáñez et al., 1997). Finally, it is worth noting that giving instructions to participants prior to the experiment, especially when investigating the endogenous orienting of attention, can enhance their performances as instructions help make the required associations between the cue features and the cued location (Bartolomeo et al., 2007; Vaquero et al., 2010).

4.4. Neural correlates of spatial attention

It was previously thought that only the exogenous orienting of attention relies on the superior colliculus (SC), while endogenous attention relies instead on cortical structures (D. L. Robinson & Kertzman, 1995; Zackon et al., 1999). However, studies showed that both stimulus-driven and goal-directed orienting of attention are reflected within the activity of the SC neurons, irrespective of whether saccades are performed during the task (overt orienting) (Fecteau et al., 2004), or not (covert orienting) (Bell et al., 2004; Lovejoy & Krauzlis, 2010). Furthermore, endogenous orienting of attention was shown to modulate visual signals already along the retino-cortical pathway by increasing the responses of both the parvocellular and the magnocellular neurons of the thalamic lateral geniculate nucleus (LGN) and by inhibiting the activity of the adjacent thalamic reticular nucleus known to exert an inhibitory effect over the LGN (McAlonan et al., 2008). In addition, it was suggested that the pulvinar nucleus of the thalamus serves as a relay between the parietal cortex and the visual areas in the occipital cortex, whereby a top-down modulation is exerted by the parietal areas on the activity of the visual occipital cortex (Shipp, 2004).

In addition to subcortical structures, several cortical regions show activations during the cue-target interval of a task that involves discriminating covertly a visual target in the periphery, suggesting their involvement in shifting spatial attention. These areas include the frontal eye field (FEF), the middle frontal gyrus (MFG), the supplementary eye field (SEF), the superior parietal lobule (SPL), the intraparietal sulcus (IPS), and finally, the inferior parietal lobule (IPL). Only the IPS showed, in addition, activities related to the visual target presentation, which suggests that IPS is involved in both shifting spatial attention and target selection (Kastner et al., 1999). Corbetta et al. (Corbetta et al., 2000) used the cue-target paradigm to orient participants' endogenous attention. The cue consisted of a central arrow, which predicted the correct location of the target in 80% of trials. In the target phase, they found increased target-related activity in the temporo-parietal junction (TPJ), which was more pronounced in the right hemisphere than in the left hemisphere. They further showed that this target-related increase in TPJ activity was larger for invalid vs valid trials, pointing toward the role of this area in the re-orienting of spatial attention. Nevertheless, valid trials also showed significant activation of the TPJ. The cueing phase showed increased activity in the IPS, which was preserved even when the target never showed up in the trial, therefore indicating a role of this area in shifting attention.

In their review, Corbetta and Shulman (Corbetta & Shulman, 2002) showed that orienting is maintained in humans by two segregated but interacting frontoparietal networks, a dorsal network and a ventral one (see Figure 17). The segregation between both networks is nearly complete except for an overlap at the level of the MFG (Fox et al., 2006). The dorsal frontoparietal network includes the IPS, the SPL, and the dorsal frontal cortex along the precentral sulcus, near or including the FEF. It generates and maintains endogenous signals based on current goals and preexisting information about

the task at hand and sends top-down signals in order to modulate the processing of appropriate locations in the primary sensory cortex. The ventral frontoparietal network in contrast, is lateralized to the right hemisphere and includes the TPJ (the posterior sector of the superior temporal sulcus and gyrus and the ventral part of the supramarginal gyrus) and ventral frontal cortex (VFC), including parts of the MFG, the inferior frontal gyrus (IFG), frontal operculum, and anterior insula (Corbetta et al., 2008; Corbetta & Shulman, 2002). The right lateralization of the ventral frontoparietal network is supported by imaging studies. Also, behavioral studies in patients with neglect syndrome whose ventral frontoparietal network is damaged (see Figure 17) reveal problems mostly in the detection of stimuli compared to the top-down orienting of attention (Corbetta et al., 2008). It was suggested that the ventral network, notably the TPJ, does not modulate the occipital areas directly but interrupts the top-down effect of the dorsal network on visual areas when unexpected but relevant stimuli appear and, therefore, was frequently referred to as the “circuit breaker” (Corbetta et al., 2008; Corbetta & Shulman, 2002). However, many studies have misinterpreted Corbetta et al. work by attributing the endogenous orienting to the dorsal network and the exogenous orienting to the ventral one.

Accumulating evidence shows that the psychological distinction between the exogenous and the endogenous orienting of attention does not match the anatomical segregation between the ventral and the dorsal frontoparietal networks. For instance, Kincade et al. (Kincade et al., 2005) investigated the implication of the dorsal and ventral fronto-parietal networks in Posner-like tasks involving either predictive or non-predictive peripheral visual cues. They found that both the dorsal and the ventral frontoparietal networks are activated by both types of cues, with higher activity for predictive cues than non-predictive cues. While this is consistent with the implication of the dorsal network in the endogenous orienting of attention, it further shows that this network also contributes to the exogenous orienting. In addition, this indicates that non-predictive exogenous cues (salient and task-irrelevant stimuli) are not as pronounced as expected in activating the ventral networks if one thought that the segregation of the frontoparietal networks reflects the difference between the endogenous and the exogenous orienting of attention. Furthermore, Kincade et al. (Kincade et al., 2005) showed significant target-related activation of the ventral network after the presentation of an invalid target preceded by predictive cues, therefore pointing toward the implication of the ventral network in the re-orienting of spatial attention which, under such conditions, is generally considered as stimulus-driven. Natale et al. (Natale et al., 2009) obtained results consistent with those of Kincade et al. (Kincade et al., 2005). Further, they showed activations of the ventral network in the target phase of exogenous trials irrespective of the validity of the target (for both valid and invalid targets). Indovina and Macaluso (Indovina & Macaluso, 2007) compared the effect of presenting highly salient but task-irrelevant non-target stimuli to the effect of presenting low saliency task-relevant target stimuli on the frontoparietal areas activity in an experiment involving endogenous orienting of attention. They found that only invalid task-relevant targets activate the ventral frontoparietal network, which therefore demonstrates that task relevance is essential for the implication of the ventral network. In another study, it was also

shown that uninformative salient distractors activate the dorsal but not the ventral network (Fockert et al., 2004). Based on most of the previous findings, it appears that the orienting of both exogenous and endogenous attention depends on the dorsal frontoparietal network (Kincade et al., 2005; Natale et al., 2009), while stimulus-driven re-orienting of attention implicates both the ventral (Indovina & Macaluso, 2007) and the dorsal networks (Fockert et al., 2004). One potential implication of the dorsal network in the stimulus-driven re-orienting might be the retrieval and use of specific task-related instructions in order for the participants to detect or discriminate the target.

Nevertheless, and in contrast to the previous conclusion, studies showed that the ventral network is also implicated in the exogenous orienting of spatial attention. For instance, Downar et al. (Downar et al., 2002) showed the activation of the TPJ and the IFG in addition to the anterior cingulate cortex at the presentation of salient stimuli, whether they were relevant to the task at hand or not. Several TMS studies also showed the implication of the TPJ in the exogenous orienting of attention (Bourgeois et al., 2013b, 2013a; Chica et al., 2011) and the opposition to the previous conclusion was suggested to be the result of methodological differences between the different studies (Chica, Bourgeois, et al., 2014).

While the neural substrates (anatomically speaking) of the spatial orienting of attention are well determined, the interaction between the dorsal and the ventral frontoparietal network, as well as their role, have led to several hypotheses over time. For instance, the top-down effect of FEF on V4 has been investigated in the monkey. Neurons in the monkey occipital cortex area V4 are activated when certain visual stimuli fall in their receptive field (Moore & Armstrong, 2003). The FEF, belonging to the dorsal network, contains neurons organized in a retinotopic representation, which maps onto the retinotopic organization of neurons in area V4. Presenting a visual target to the monkey simultaneously with subthreshold electrical stimulation of FEF neurons that match the target location (their receptive field encompasses the target location) results in an increased activity within V4 compared to when the visual target is presented with no FEF stimulation, a boost of V4 activity observed for both efficient and inefficient visual targets. In contrast, the sole stimulation of FEF neurons in the absence of a visual target did not significantly affect V4 activity. Therefore, FEF contributes to the modulation of the occipital responses in the presence of visual stimuli. Furthermore, a more pronounced modulation was found, this time taking the form of a decrease of target-related V4 activity when in the presence of a distractor, the frontal subthreshold stimulation involved FEF neurons, which code the distractor but not the target. This last result indicates that attention suppresses the activity of neurons coding the non-selected location in addition to enhancing the activity of neurons associated with the target (Moore & Armstrong, 2003). In their fMRI study in humans, Vossel et al. (Vossel et al., 2012) showed an increase in the excitatory connectivity between the right IPS and the right occipital cortex during leftward orienting compared to rightward orienting. Therefore, the findings of these two studies (Moore & Armstrong, 2003; Vossel et al., 2012) are consistent with a top-down modulation of occipital areas coming from the dorsal frontoparietal network.

It has also been shown that the dorsal frontoparietal network exerts a suppressive role over the ventral network. For example, in their fMRI study, Shulman et al. (Shulman et al., 2003) found that while both the IPS and the FEF were activated during the search for a visual target among nontarget stimuli, the TPJ was deactivated. In addition, Todd et al. (Todd et al., 2005) showed that when the visual short-term memory load of a task increases, the activity of the TPJ is increasingly suppressed. The suppressive effect onto the TPJ was suggested to be mediated either 1) directly by the IPS (Corbetta et al., 2008) and/or the FEF (DiQuattro et al., 2014) via their connections to the TPJ, 2) or via the MFG, an area where the two networks overlap (Fox et al., 2006), or 3) indirectly via the locus coeruleus norepinephrine system (Corbetta et al., 2008). In their review, Vossel et al. (Vossel et al., 2014) suggested that depending on the task at hand, the ventral network may be more or less inhibited by the dorsal network.

It has been suggested that the sensory information of invalidity between the cue and the target location coming from the occipital cortex is not directly sent to the dorsal network but instead first engages the ventral network, which then modulates the dorsal network activity (Vossel et al., 2012). Indeed, these authors showed, using dynamic causal modeling, significant modulations of connectivity from the occipital cortex to the right TPJ and from the right TPJ to the right IFG and the right IPS, with all connections being more excitatory during invalid than during valid trials. Nevertheless, this hypothesis is still debated, as other studies suggest instead, a direct bottom-up influence of the visual areas on the IPS (Geng & Mangun, 2009; Ruff et al., 2008).

Finally, along the ventral network, the TPJ was found to be more sensitive to the mismatch between the cue and the target when it is more frequent, while the IFG and the MFG are more sensitive when such mismatch is unexpected. For instance, when comparing the activity of the ventral network related to the presentation of invalid trials between attention-orienting tasks involving either 10% or 40% of invalidity, Vossel et al. (Vossel et al., 2006) found greater activation of the IFG and the MFG when invalid trials are less frequent. In parallel, Doricchi et al. (Doricchi et al., 2010) found greater inactivation of the right TPJ following predictive (80% validity) compared to non-predictive (50% validity).

All of the studies mentioned above form only a sample of the vast literature on the interaction between the ventral and the dorsal frontoparietal networks and their role in the orienting of attention. With time, many hypotheses have been formulated in order to explain how the brain manages attention. Among those are the “salience map” and the “priority map” hypotheses. The former proposes that the brain generates topographical representations (maps) of the environment, which code the relative relevance of the different locations. Accordingly, the salience maps guide bottom-up attention by making certain stimuli “stand out” based on their inherent sensory characteristics. The stimuli selected by the salience map can, therefore, interrupt the ongoing top-down processing. On the other hand, based on the priority map hypothesis, the brain does not rely only on the saliency of

objects but also on the current behavioral goals and task demands, combining them into a unified representation of priorities.

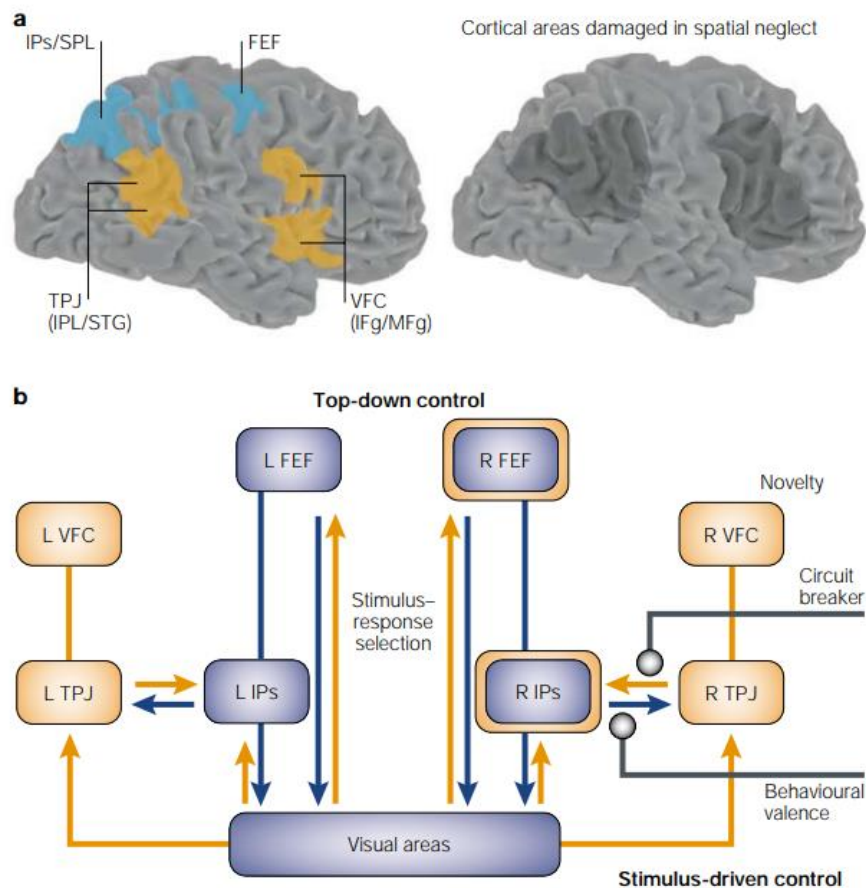


Figure 17: Neuroanatomical model of attentional control proposed by Corbetta and Shulman. (taken from Corbetta & Shulman, 2002). a) Dorsal and ventral frontoparietal networks and their anatomical relationship with regions of damage in patients with unilateral neglect. b) anatomical model of top-down and stimulus-driven control. L = Left, R= Right.

4.5. Cross-modal links in the orienting of attention

While research on spatial attention mostly focuses on the visual modality, a significant number of studies have explored the orienting of spatial attention in the tactile or auditory modalities. For example, Spence and McGlone (C. Spence & McGlone, 2001) investigated the exogenous orienting of tactile attention. In their experiment, participants held cubic foams with their hands in peripheral positions. Those cubes provided vibrotactile stimulations on the index and thumb fingers. The non-predictive cue, consisting of tactile stimulation on both the index and the thumb of one hand, was followed at different SOAs by a second tactile stimulation (the target), this time only on one finger, either at the cued or the uncued hand. Participants had to discriminate whether the target stimulation

occurred on the index or thumb finger (speeded elevation discrimination task) using a pair of pedals under their right foot. The authors observed faster reaction time in the valid compared to invalid trials for SOAs ranging between 200 and 400 ms, similar to what is usually seen for exogenous visuo-spatial attention (Chica, Martín-Arévalo, et al., 2014). Similar results were also obtained by Miles et al. (Miles et al., 2008) who further revealed the occurrence of IOR at SOA starting from 550 ms, which again is similar to what is usually observed in the visual modality. Other experiments have also revealed the effectiveness of both exogenous and endogenous tactile (Chica et al., 2007; Ho et al., 2005; Yates & Nicholls, 2009) as well as auditory (C. J. Spence & Driver, 1994) cues in orienting spatial attention.

Orienting spatial attention in one modality toward a particular location not only results in facilitation effects in this same modality but also enhances the processing of targets occurring at the same location but in other modalities. These cross-modal links in the orienting of spatial attention were explored mainly between the years 1990 and 2010. This research led to a significant contribution to the development of warning systems in automobiles, in addition to its basic research contribution to the understanding of attention. Spence et al. (C. Spence et al., 1998) investigated the cross-modal links of exogenous attention orienting between vision, touch, and audition. They performed a series of experiments in which they found that the presentation of a spatially uninformative auditory peripheral cue led to an advantage in the discrimination of tactile targets (continuous vs. pulsed) when those latter were presented at the cued position compared to a location contralateral to the cue. Participants also responded significantly faster to tactile targets presented at the position of a spatially uninformative visual cue, as compared to invalid trials. Furthermore, similar effects were seen in the discrimination of both visual and auditory targets after tactile cueing. Other studies (McDonald et al., 2000; Santangelo et al., 2008) further showed similar effects of exogenous auditory attention on visual target discrimination, while the literature lacks studies showing the inverse beneficial effect, i.e., of visual cueing on auditory target processing (Driver & Spence, 1998). This is thought to be a real lack of experimental evidence related to methodological issues rather than an asymmetry in the cross-modal effects between the different modalities (C. Spence, 2010). Further evidence of the cross-modal links in the exogenous orienting of attention was found in ERP studies between audition and vision (McDonald & Ward, 2000), as well as between vision and touch (Kennett et al., 2001, 2002). The cross-modal effect between touch and vision was also shown to take into account postural changes (crossed vs. uncrossed hands conditions) in a way that ensures directing spatial attention to the correct external location of the hand (Kennett et al., 2001, 2002; C. Spence et al., 2000).

Similarly, the cross-modal link was also evidenced in the endogenous orienting of attention, thanks to behavioral as well as event-related potentials (ERP) studies. It was demonstrated that orienting participants' endogenous visuo-spatial attention verbally or using central arrows boosts reaction time in the discrimination of tactile targets in the valid compared to the invalid trials (C. Spence et al., 2000). In ERPs, N1 and P1 are evoked potentials (named based on their polarity: N =

negative, P = positive) critically related to visual attention tasks. P1 (first positive component) is generated in the ventrolateral extrastriate occipital cortex and is associated with the initial stages of visual processing, while N1 is generated in the lateral occipito-temporal areas and is related to selective attention and the discrimination of relevant visual stimuli (Eimer & Driver, 2001). The cross-modal effect of touch on vision was demonstrated in the ERP study led by Eimer and van Velzen (Eimer & van Velzen, 2005). In their experiment, participants were presented with a cue consisting of an arrow pointing to the location toward which tactile attention should be allocated. The target was presented 600 ms after the central cue, and it can be either tactile (on the index of one hand) or visual (LEDs at 21° or 52° to the left and right). The hands were either positioned at the far location or the near location. The participants had to report verbally (yes) if there was tactile stimulation at the cued hand. Concerning first uni-modal tactile attention, they observed attentional modulations of the somatosensory N140 component (140 ms being the latency of this ERP) as well as of a subsequent sustained attentional negativity when ERPs to tactile stimuli presented to the cued versus uncued hand were compared. They found no interaction between hand posture and attention, which indicates that attentional modulations of somatosensory ERPs were unaffected by hand position. Second, concerning cross-modal attention, they showed enhanced visual N1 components that were elicited when visual stimuli were presented close to the somatosensorily cued hand relative to visual stimuli close to the other hand located on the opposite side. This observation, therefore, confirms the presence of cross-modal attentional links from touch to vision. A similar conclusion was also obtained in a previous ERP study which demonstrated a cross-modal effect in endogenous attention from touch to vision, as well as from touch to audition (Eimer et al., 2001). Furthermore, a PET study (Macaluso et al., 2002a) and an fMRI study (Macaluso et al., 2003) have both shown increased activity in visual occipital regions when participants attend to either vision or touch. In addition to all the previous findings, the cross-modal effects in endogenous attention were further seen between vision and audition (Eimer et al., 2004; Eimer & Schröger, 1998; Ho & Spence, 2005). It is important to note that in order to obtain a significant cross-modal effect, the cue and the target should be as close as possible, as separating them will gradually reduce the significance of the cueing effect. In summary, cross-modal links were found between vision, touch, and audition in both the endogenous and the exogenous orienting of attention.

Visual, tactile, and auditory spatial attention rely on the activity of modality-specific areas in the brain (Chambers et al., 2004; Macaluso et al., 2002a; Wu et al., 2007). Different studies have highlighted, in addition, the presence of brain areas where modalities overlap, which were further referred to as “supramodal” regions (Macaluso, 2010). For instance, in their fMRI study, Macaluso et al. (Macaluso et al., 2003) showed the activation of the dorsal pre-frontal cortex and the IPS irrespectively of whether the participants endogenously prepared to discriminate a tactile or a visual target. In another (ERP) study (Macaluso et al., 2002b), they presented their participants with a central auditory cue (80% valid vs. 20% invalid), instructing them to focus either on the right or the left of

fixation depending on the intensity of the tone. The participants had to discriminate the location of either a tactile (air puff on left or right hand) or a visual target (LED to the left or the right of fixation). On invalid trials, which require a stimulus-driven re-orienting of spatial attention, the authors found significant activation of the ventral fronto-parietal network (namely TPJ and IFG) irrespective of the target modality. A different study has also revealed the modulation of the activity of the ventral network following, this time, the presentation of a salient task-irrelevant auditory stimulus during a task involving an endogenous orienting of visual attention (Santangelo et al., 2009). Together, these studies highlight the role of several areas of the dorsal and ventral attentional networks (dorsal prefrontal cortex, IPS, IFG, and TPJ) in the integration of information from different sensory modalities.

4.6. The interactions between saccades and spatial attention

The Posner's cue-target paradigm (Posner, 1980) allow us to study the covert orienting of spatial attention (without eye movement), as described previously. Nevertheless, orienting spatial attention toward a certain location in the environment is usually accompanied by a saccade toward that location (i.e., attention is shifted 'overtly'). The relationship between saccadic eye movement and spatial attention has received a tremendous amount of interest over decades. Among the different hypotheses elaborated over time, the pre-motor theory of attention has been the most influential one. According to this theory, spatial attention and eye movement preparation are the same process, i.e., the covert orienting of spatial attention is a prepared but unexecuted eye movement, or in other words, attention results from a subthreshold activation of the cerebral circuits responsible for overt motor acts (Hunt et al., 2019). Other authors have suggested that a common attentional mechanism selects information for both object recognition and actions, therefore presenting attention as a fundamental mechanism critical to other cognitive processes. This hypothesis originates from the visual attention model proposed by Schneider (Schneider, 1995).

The FEF and the SC constitute two main structures implicated in both spatial attention, as described previously in this chapter, and the saccadic eye movement, as described in Chapter 2 of this thesis. Therefore, both the SC and the FEF constitute privileged targets of studies investigating the link between attention and saccades. However, these two structures are both multilayered and implicated in many cognitive processes due to their vast amount of projections. Establishing the demonstration of the premotor theory requires that, from a neurophysiological perspective, one must be able to compare the electrophysiological activity of individual neurons or the effects of electrical stimulation on individual neurons between an attentional task and a saccadic task. This is possible through single-unit electrophysiology in monkeys but not possible with fMRI or PET (due to spatial resolution limitations (Hunt et al., 2019)), nor possible with electrical microstimulations in monkeys (because of too much interference from connected structures being stimulated (Moore & Fallah, 2001,

2001; Müller et al., 2005)). Therefore, in the following, we will primarily describe 'single-unit in monkey' studies. Those studies were capable of dissociating between motor activities and visual selectivity. For instance, Ignashchenkova et al. (Ignashchenkova et al., 2004) recorded single-unit activities at the level of the SC's intermediate layer of two rhesus monkeys. The monkeys had to fixate on a central point while a C-letter target (more like the shape of a ring with a gap) appeared in one of two peripheral locations. The task was to determine the orientation of the gap in the C and respond by making a saccadic eye movement towards one of two green spots, indicating the perceived orientation. Spatial cues, either peripheral or central, were presented before the target presentation. The authors showed an enhancement of behavioral visual acuity, accompanied by enhanced responses of visual neurons, following the presentation of both cue types, therefore indicating that visual cells in the SC are enhanced by spatial attention. However, visuomotor neurons showed an enhanced and sustained firing rate during the cue-target interval with the peripheral but not the central cue. This result indicates that spatial attention is independent of motor responses at the level of the SC, at least in the case of the central cue, which was more likely to involve an endogenous orienting of attention. At the level of the FEF, Murthy et al. (Murthy et al., 2001) found visual neurons implicated in target selection but independent of saccade programming, therefore indicating that spatial attention and saccades can rely on different neuronal populations within the FEF.

Behavioral studies can also participate to this debate on the premotor theory by explicitly testing to what extent spatial attention and saccades can be independently manipulated. MacLean et al. (MacLean et al., 2015) performed two experiments in which participants' exogenous attention was oriented toward a certain location on a screen. They had to either discriminate covertly a digit target that follows the presentation of a peripheral cue or make a saccade toward the location designated by a central arrow cue appearing a few milliseconds after the peripheral target. In Experiment 1, the digit task was more likely (80% of the trials) than the saccade task (20% of the trials), whereas in Experiment 2, the probabilities of the two tasks were reversed. In Experiment 1, wherein participants were often required to attend to peripheral targets covertly, the authors found a facilitatory effect of the valid cueing on the discrimination task but no impact on the saccade latencies. In Experiment 2, wherein participants were often required to make eye movements in response to a central cue, they found the inverse effect, that is, a facilitatory effect of exogenous attention on saccades latency in parallel with no facilitation in the discrimination task. This study, therefore, indicates that it is possible to dissociate between exogenous orienting of attention and saccades preparation. This dissociation was also seen for the endogenous orienting of attention (Hunt & Kingstone, 2003).

Pre-saccadic shifts of attention can be considered as a specific type of spatial attention. They represent automatic shifts in covert attention that occur just before a saccade. Born et al. (Born et al., 2014) tested whether pre-saccadic shifts of attention are strictly dependent on voluntary saccade execution. In their experiment, the participants made voluntary saccades to a cued location while discriminating a stimulus either at the saccade target or at the opposite location. In a subset of trials, a stop signal was

presented, asking the participants to cancel their eye movements. The delay of the stop signal was set to cause inhibition of the saccades in 50% of the trials. The authors showed similar perceptual facilitation at the saccade target for saccades with or without a stop signal (in the case where the subject failed to inhibit their saccades), therefore indicating that the pre-saccadic shifts of attention are obligatory for all saccades. Nevertheless, this facilitation was seen only when saccades were actually performed, not when observers were able to inhibit them. Here, those results indicate that preparing an eye movement without subsequently executing it does not result in an attention shift. This further argues in favor of possible dissociation between endogenous attention and saccade preparation. In agreement with these previous findings, MacInnes et al. (MacInnes et al., 2015) found that saccade planning does not necessarily inhibit previously visited locations. In their experiment, participants made two consecutive saccades and responded with a third saccade to a visual probe appearing at a previously fixated or a control location. The saccade sequences were either independent, where each saccade was planned separately (the target of the second saccade was presented at the offset of the first saccade), or parallel, where both saccades were planned together (by presenting both of the saccade targets at the beginning of the trial while fixating). Saccadic IOR was observed for independently planned saccades, as revealed by an increased latency of the third saccade when the target was illuminated at the location of the first saccade target. However, no significant IOR was found in sequences of saccades planned in parallel. While the former result indicates that attention and saccade planning are tightly connected, the latter result shows that attention can be spread across multiple targets and doesn't always work directly with the motor system. Even more, it was found that while a reward speeds up the preparation of an eye movement, it does not facilitate the discrimination of the target at the rewarded location relative to the non-rewarded ones (McCoy & Theeuwes, 2018). Nevertheless, other studies have found that when an exogenous cue designates a location outside the oculomotor range, no significant shift of attention to that location is observed, whereas a significant shift was demonstrated when the same location was designated by an endogenous cue (Smith et al., 2010, 2012, 2014). These last results thus suggest that the premotor theory of attention can hold for exogenous –but not for endogenous- attention. In light of the arguments presented above and other studies existing in the literature (Hunt et al., 2019; Smith & Schenk, 2012), we can see that most of the evidence now refutes the general premotor theory of attention and rather favor a non-strict dependency of spatial attention on saccadic eye movements.

The other question that is worth considering in this debate is whether, conversely, saccadic eye movements depend on spatial attention. In agreement with the visual attention model (Schneider, 1995) that suggests an obligatory and selective coupling of saccade programming and visual attention to one common target object, Deubel and Schneider (Deubel & Schneider, 1996) found that it is not possible to direct attention to a certain location in order to discriminate a target while performing a saccade to a close but spatially distinct location and that discrimination is best when the discrimination stimulus and the saccade target represent the same object. While different studies agree with this

coupling (Born et al., 2014; Peterson et al., 2004), others do not (Stelmach et al., 1997; Van der Stigchel & de Vries, 2015). One reason for this difference could be that Deubel and Schneider (Deubel & Schneider, 1996) used a Posner-like paradigm to orient spatial attention, whereas Stelmach et al. (Stelmach et al., 1997) indexed attention using a temporal order judgment task, allowing them to report that it is possible to hold attention at one location in the visual field and perform a saccade to a different location without affecting the saccade latency. Van der Stigchel and de Vries (Van der Stigchel & de Vries, 2015) performed an experiment in which the participants were presented with a saccade target that was accompanied by a salient distractor. This resulted in the majority of eye movements landing in between the target and the distractor. Shortly before the execution of the saccade, participants had to discriminate a stimulus presented at the target or distractor location. The authors found strong attentional facilitation at both target and distractor locations but not in between these two locations, despite most saccades landing there. This suggests that attention did not follow the executed saccade, and therefore, some components of the saccade target selection process are independent of spatial attention. In real-life situations, some saccades are performed in order to accomplish specific goals, but a significant amount of saccades are not related to the task at hand, and even more, studies have shown that we are terrible at reporting our eye movements (Clarke et al., 2017; Morvan & Maloney, 2012; Nowakowska et al., 2017; Vö et al., 2016). Therefore, given the above considerations, it has been suggested that saccadic eye movement depends on spatial attention only in conditions that require target selection (Hunt et al., 2019).

4.7. The coupling between spatial attention and saccadic adaptation

The interaction discussed above between spatial attention and saccades can be further discussed by zooming into that between spatial attention and saccadic adaptation. Indeed, different fMRI and TMS studies investigating the neuronal substrates of saccadic adaptation and of spatial attention show overlaps in specific parietal regions. Indeed, the exogenous orienting of attention (Corbetta et al., 2008; Corbetta & Shulman, 2002) and the adaptation of reactive saccades (Gerardin et al., 2012; Guillaume et al., 2018; Péliisson et al., 2018) both yield significant activation of the TPJ and, on the other hand, the endogenous orienting of attention (Corbetta et al., 2008; Corbetta & Shulman, 2002) and the adaptation of voluntary saccades (Gerardin et al., 2012; Guillaume et al., 2018) both significantly activate the IPS. Note that these experimental approaches do not have the spatial resolution necessary to ascertain that these gross anatomical overlaps correspond to shared neuronal substrates. Nonetheless, this possibility might entail behaviorally detectable interactions between spatial attention and saccadic adaptation. In the following section, we will present several behavioral data available in the literature arguing in favor of such a coupling between attention and saccadic adaptation.

4.7.1. Saccadic adaptation and the pre-saccadic shift of attention

As mentioned previously, in the presence of a specific saccade target, spatial attention shifts to the target location prior to the saccade toward it. Doré-Mazars and Collins (Doré-Mazars & Collins, 2005) investigated whether this pre-saccadic attention follows the adaptive shift of saccadic endpoint or whether it remains anchored onto the saccade goal. Their participants were simultaneously presented with a fixation cross and five peripheral frames, and they had to perform a saccade toward the frames when the fixation cross disappeared (overlap paradigm). During the latency period, bars with different inclinations were presented, and the participants were asked to discriminate the bar inside one particular frame at the end of the saccade. Backward adaptation was induced by stepping the ensemble of the frames by 1° at the saccade onset. The participants' discrimination performance, which can be taken as an indicator of the locus of visual attention, was better at the locations nearest to the actual eye landing position than at locations close to the saccade visual target. Therefore, this indicates that the information about the change of saccade size resulting from the adaptation is available to the perceptual system. In a separate experiment, the authors (Collins & Doré-Mazars, 2006b) further extended their findings to the backward adaptation of reactive saccades. However, Ditterich et al. (Ditterich et al., 2000a) failed to demonstrate such effects for reactive saccades, which probably resulted from the low gain change induced in their experiment.

In light of the previous findings, as trans-saccadic feature integration relies on visuo-spatial attention (Stewart & Schütz, 2018), one might expect saccadic adaptation to affect trans-saccadic perception via its effects on the pre-saccadic shifts of attention. Van der Stigchel et al. (Van der Stigchel et al., 2020) tested this hypothesis by asking participants to report, before and after backward adaptation, the color of the saccade target, which could occasionally change slightly during a saccade to the target. Results indicated that after adaptation, trans-saccadic perception was found to have a stronger reliance on the post-saccadic color estimate than on the pre-saccadic color information, which supposedly became less precise. In turn, the inaccuracy of the pre-saccadic color information was suggested to be due to the modified pre-saccadic shift of attention following saccadic adaptation, therefore bringing additional arguments in favor of the findings of Doré-Mazars and Collins (Collins & Doré-Mazars, 2006b; Doré-Mazars & Collins, 2005).

When an irrelevant cue is presented shortly before the saccade target, it decreases the saccade latency (Corneil & Munoz, 1996) which is thought to be related to a facilitatory effect of exogenous attention on saccade preparation. Khan et al. (Aarlenne Z. Khan et al., 2010) used this approach to test again whether this attentional facilitatory effect changed after backward adaptation of reactive saccades. They found that the saccade latency was reduced after adaptation when the irrelevant cue was presented at the saccade landing position but not when presented at the saccade goal location. These results therefore suggest that rather than facilitating the visual processing of the target, attentional cueing facilitates saccade planning.

4.7.2. The effect of adaptation on attention

Several studies have investigated the effect of saccadic adaptation on covert attention. For instance, Habchi et al. (Habchi et al., 2015) induced backward adaptation (4° backstep) of voluntary and reactive saccades performed toward targets located at 11° either to the left or the right of a central fixation point. In their study, participants performed either a detection (experiment 1) or a discrimination task (experiment 2) prior to and after an adaptation phase. In experiment 1, they were required to fixate on a central point and then press a button whenever they detected the presentation of a peripheral target. In experiment 2, they were required to discriminate the hemifield of the visual target during fixation. These authors observed that, after the adaptation of leftward reactive saccades, but not rightward reactive saccades nor voluntary saccades, both the detection and the discrimination task reaction times decreased (relative to the pre-adaptation phase) for visual targets located in the adapted hemifield. These results point, therefore, to an effect of reactive but not of voluntary saccades backward adaptation on the exogenous orienting of attention, which might result from shared neuronal substrates at the level of the right TPJ, as suggested by the authors. They also suggest that, first, the absence of rightward reactive saccades effects on exogenous attention might probably originate from the fact that exogenous attention implicates regions lateralized in the right hemisphere, such as the right TPJ ipsilateral to the adapted hemifield, and second, the absence of voluntary saccades effects on exogenous attention was consistent with the absence of shared neuronal substrates, as inferred from neuroimaging studies (Corbetta et al., 2008; Corbetta & Shulman, 2002; Gerardin et al., 2012). Nicolas et al. (Nicolas, Bompas, et al., 2019) performed an experiment similar to the one of Habchi et al. in which they additionally recorded through MEG gamma band activities related to saccadic adaptation and spatial attention. Their behavioral data (discrimination performance) did not confirm the significant boost in exogenous spatial attention after adaptation. Nevertheless, they identified a sustained saccadic adaptation-specific increase of the gamma band activity (GBA) in the post-exposure saccadic task, spanning widely in the right hemisphere, including areas in the inferior parietal lobe, the superior temporal lobe, the supramarginal gyrus region, the insula, and the sensorimotor cortex. Furthermore, during the post-exposure attentional task, they showed a strong GBA increase in both hemispheres, overlapping with the areas activated after saccadic adaptation. One potential interpretation of such results is that saccadic adaptation affect spatial attention through a sustained boost in GBA that impact attentional areas. However, it is important to note that the detection and discrimination tasks used by Habchi et al. (Habchi et al., 2015) as well as by Nicolas et al. (Nicolas, Bompas, et al., 2019) do not really orient the exogenous attention like the different Posner-like paradigms: instead of being cued at a given location, participants react as fast as possible to the appearance of a salient target on the display screen. In a more recent behavioral study, Nicolas et al. (Nicolas et al., 2020) overcame this limitation by using a cueing paradigm to orient exogenous attention. They investigated the effects of forward and backward adaptation of leftward reactive saccades (performed toward targets at 11° from a central fixation point) on exogenous spatial

attention. They showed a boost in the exogenous orienting of spatial attention in the adapted hemifield after backward adaptation compared to a boost in the orienting of attention in the opposite, non-adapted hemifield after forward adaptation. Indeed, the first result agrees with Habchi et al. (Habchi et al., 2015) findings and further supports the idea of shared neuronal substrates (Corbetta & Shulman, 2002; Métais et al., 2022) at the level of the right PPC (PPC being involved in error processing during reactive saccades adaptation and in the orienting of exogenous attention); nevertheless, the second result would suggest that forward adaptation relies on a cortical region located in the left hemisphere. The authors (Nicolas et al., 2020), therefore, suggested that their results might be explained in the light of the error signal hypothesis (proposed in the prismatic adaptation studies (Martín-Arévalo et al., 2018; Pisella et al., 2005)), whereby the attention-boosting effect results from a cortical activation related to the encoding of error signals responsible for saccadic adaptation. Based on this hypothesis, the direction of the target step (or the error direction) would activate areas involved in error processing at the level of the ipsilateral cerebellum. The latter has an excitatory effect on the ipsilateral PPC, which in turn would inhibit the contralateral PPC through interhemispheric connections. In a separate study, Nicolas et al. (Nicolas, Bidet-Caulet, et al., 2019) further investigated the effect of voluntary saccades adaptation on the endogenous orienting of attention. They found that the adaptation of leftward - but not rightward - saccades boosts the orienting of endogenous attention in both the adapted and the non-adapted hemifield. They suggested that common neuronal substrates between voluntary saccade adaptation and the endogenous attention at the level of the right IPS might be the origin of the effects observed for leftward saccades. The right IPS has a bilateral connection with the visual areas in the occipital cortex (Capotosto et al., 2009, 2012), allowing the boosting of endogenous attention in both hemifields. Nevertheless, these findings are difficult to reconcile with the error signal hypothesis.

To our knowledge, one last and additional study can be described in this section. Wick et al. (Wick et al., 2016) investigated the effect of vertical reactive saccades adaptation on static attention (attention at fixation). Backward adaptation was performed for targets located at 4.6° and 6.9° while forward adaptation was performed for targets located at 6.9° and 9.2° . Spatial attention was measured at fixation using the flanker paradigm: participants had to discriminate the target (E or F) at the fixation while a distractor (F or E respectively) was presented at either 2.3° , 4.6° , or 9.2° . Their results showed that backward adaptation led to decreased interference from nearby distracters, suggesting that the static attentional map contracted after backward adaptation. Additionally, forward adaptation led to an increase in distractor interference at the largest eccentricity. Therefore, they suggested that the attentional field expands and shrinks with forward and backward adaptation, respectively. A shrinking of the attentional field could also be concluded from the study of Nicolas et al. (Nicolas, Bidet-Caulet, et al., 2019) in the case of backward adaptation of endogenous attention (saccades of 9°), as the participants were better at discriminating targets located at 3° from fixation after adaptation, but not at discriminating targets located at 7° of eccentricity.

In summary, the studies presented above argue in favor of modulatory effects of both reactive and voluntary saccade adaptation on the orienting of exogenous and endogenous attention, respectively.

4.7.3. The effect of attention on saccadic adaptation

Complementing the studies described above investigating the effect of saccadic adaptation on attention, other studies have provided evidence for a modulatory effect of attention on saccadic adaptation. To begin with, Connolly et al. (A. Connolly et al., 2016) observed that ADHD patients can adapt their saccades but to a reduced extent relative to control participants and that the amount of adaptation correlates with motor difficulties. The abnormally low level of adaptation observed in ADHD patients was suggested to be due to their altered attentional capabilities. Second, Bock et al. (Bock et al., 2017) investigated the effect of priming attentional focus via the scrambled sentence task on reactive saccades directional adaptation. Prior to the adaptation task, each group of -young or elderly- participants was given 20 lists of five words and had to select four words from each list to form a meaningful sentence (crossing out the non-fitting word). The lists either denoted a wide or a narrow focus of attention. Results showed that both young and elderly participants adapted more when primed toward wide than toward narrow attentional focus. In another study (Borisova & Grigорова, 2015), using Navon's stimuli, central capital letters (global letters) constituted of multiple sentence case letters (local letters) were presented to the participants prior to and during the directional adaptation of reactive saccades. Participants were instructed either to focus on the global letter (global attentional focus) or on the local letter (local attentional focus), which resulted in the global attentional focus being associated with more adaptation compared to the local attention focus. Note that these last two studies showed a speed-up in saccadic amplitude change during the double-step phase but no effect in the post-exposure phase, where no adaptation after-effect was seen. In still another study, Bock et al. (Bock et al., 2014) investigated the effect of spatial attention associated with a manual tracking task on saccadic adaptation. During directional adaptation of reactive saccades, their participants had to maintain, by using a joystick, a square that appeared on the screen at a central position, either close to the adaptation location or away from it. The results did not show any difference in saccadic adaptation between the close and the far conditions.

The effect of attention on adaptation was also investigated by making use of the attention-catching effect of distractors. In their study, Khan et al. (Khan et al., 2014) presented, at the time of reactive saccade onset, a visual distractor close to the saccade target (± 3 degrees), which could be either salient (birds, other animals, anime characters, recognizable objects, and popular cartoon characters) or not (a random noise pattern) compared to the saccade target. Despite the saccade target remaining stationary, the salient distractor was enough to induce backward saccadic adaptation when presented systematically less eccentric than the target, as revealed by both a progressive decrease of saccadic gain and a significant after-effect. The authors proposed the intriguing possibility that the locus of attention drawn toward the distractor can, on its own, act as an error signal for the saccadic

adaptation process. In contrast, another study (Madelain et al., 2010) contradicted those findings and concluded that adaptation is not affected by distractors but note that in this study, the distractor and the target were equally salient as both stimuli were identical in size and differed only in shape and color.

One particular study suggested that spatial attention itself can be adapted (McFadden et al., 2002). In this experiment, McFadden et al. presented a peripheral target to their participant while fixating on a central point. The subjects were instructed to remain on fixation; however, at the time their attention shifted toward the peripheral target (as measured by the so-called line-in-motion task), this latter stepped either backward or forward. The authors showed that the estimated shift of spatial attention significantly adapted (backward adaptation being stronger than forward adaptation) and further revealed, in the case of backward adaptation, a transfer to saccadic responses measured in the post-exposure phase. Therefore, they suggested that saccades are directed specifically to the locus of attention and that saccadic adaptation could result from either adaptation of attentional shifts or, from saccadic adaptation at the motoric level, or both. However, whether these findings, which have not been replicated yet, generalize to other situations is questionable, given the methodological differences between this experiment and experiments using the double-step target paradigm.

Finally, Gerardin et al. (Gerardin et al., 2015) tested the effect of the attentional load on reactive saccades adaptation. In their adaptation exposure trials, participants performed saccades toward a peripheral target consisting of Gabor stimuli that the subjects had to discriminate at the end of the saccade. This target systematically jumped at the saccade onset in order to elicit backward adaptation. The attentional load level was varied in separate sessions as ‘low’ or ‘high’ by varying the difficulty of the discrimination task. The results showed a stronger adaptation of reactive saccades in the high load condition (difficult discrimination) compared to the low load condition (easy discrimination). The authors suggested that the higher attentional load required by discriminating the saccadic target could boost either the processing of target error signals necessary to elicit adaptation and/or the plasticity processes underlying saccade adaptive modifications. However, this study does not allow us to disentangle whether this effect on oculomotor adaptation is due to spatial or sustained attention.

In summary, the studies presented above suggest an effect of attention on saccadic adaptation. Nevertheless, none of them directly examines the effect of “spatial” attention on saccadic adaptation.

4.8. Conclusion

In this chapter, we described some key features related to spatial attention. Similar to saccades, spatial attention can be oriented automatically toward salient stimuli or voluntarily based on our goals. In addition to subcortical regions, several cortical areas are implicated in the orienting of spatial attention and are further classified into two segregated but highly, and still mysteriously, interacting networks: the ventral and the dorsal fronto-parietal networks. Along those networks, studies have shown that the TPJ and IPS are activated in a supramodal manner, which means that they are activated no matter the

modality of the stimulus. Finally, in addition to the vast literature on the coupling between saccades and attention, increasing evidence suggests that saccadic adaptation and spatial attention interact, which might result from shared neural substrates.

B. EXPERIMENTAL CONTRIBUTIONS

In the introduction part of this thesis, after briefly describing the visual and the saccadic systems, we reviewed the pertinent studies investigating saccadic adaptation, which constitutes the mechanism responsible for maintaining saccade accuracy throughout life. Then, we introduced some of the concepts of spatial attention and described the studies investigating its interaction with saccades and saccadic adaptation. Indeed, our understanding of saccadic adaptation has increased significantly since the beginning of this century. Nevertheless, several questions remain unanswered.

Researchers have studied saccadic adaptation over decades thanks to the double-step target paradigm introduced by McLaughlin (McLaughlin, 1967), which creates a mismatch between the saccade landing position and the saccade target. The brain interprets this mismatch as a saccade programming error that the saccadic system needs to overcome. Here, an obvious point that emerges from the literature is that all saccadic adaptation studies, without exception, have focused on visual saccades. Thus, nothing is known about whether non-visual saccades are subject to adaptive modifications. Of course, the lack of such studies is related to the fact that we rely primarily on visual information to perform saccades, which in turn are generated to explore mainly the visual environment. Nevertheless, as our saccades are performed toward visual but also non-visual tactile and auditory targets, one might hypothesize that a similar adaptive process would contribute to the control of non-visual saccade accuracy. Therefore, we predict that exposing non-visual saccades to repeated aiming errors via the double-step target paradigm would also engage saccadic adaptation in order to enhance our performances.

In Chapter 2, we described that saccades can be performed to non-visual auditory or tactile targets. Before triggering saccades, auditory and tactile information undergo changes in their frames of reference in order to share, along with visual information, common neuronal structures dedicated to saccades execution. Indeed, different studies have shown that such translation occurs in various parts of the brain, like the SC, FEF, and PPC, thought to represent sites of convergence of information from different sensory systems (Buchholz et al., 2011; Caruso et al., 2016; Groh & Sparks, 1996b, 1996c; Jay & Sparks, 1987a, 1987b; Linden et al., 1999). In parallel, we discussed in Chapter 3 the differences between reactive and voluntary saccade adaptations and showed that they rely on, at least partially, different adaptation mechanisms. The adaptation of reactive saccades is thought to occur at the motor rather than the sensory level of saccade programming, which is supported by different studies investigating the transfer of adaptation to hand-pointing movements (Cotti et al., 2007) and antisaccades (Cotti et al., 2009) as well as the effect of adaptation on visual perception (Zimmermann & Lappe, 2009). If true, we can hypothesize that a transfer of visual reactive saccades adaptation would occur to auditory and tactile reactive saccades performed toward the adapted location. In

addition, we hypothesize that non-visual reactive saccade adaptation, if it exists, would transfer to visual saccades.

In this thesis, we performed two different studies (**Study 1** and **Study 2**) designed to test the hypothesis mentioned earlier. In the first study (**Study 1**), our participants performed rightward saccades toward targets located at 15, 20, 25, and 30 degrees of visual angle, identified either visually (LEDs) or tactually (electrical stimulation of the fingers). In the first part (Experiment 1), visual reactive saccades performed toward the LEDs located at 20° and 25° were subjected to backward adaptation by stepping the visual target 5° toward the fixation point. We hypothesized that backward adaptation of visual reactive saccades would transfer to non-adapted visual saccades performed toward the LEDs located at 15° and 30° as well as to tactile reactive saccades performed toward the adapted (20° and 25°) and the non-adapted locations (15° and 30°). In the second part (Experiment 2), while our participants performed tactile reactive saccades to an electrical stimulation occurring either at their middle (20°) or index (25°) fingers, they received a second electrical stimulation (on the ring (15°) or the middle (20°) fingers respectively), simulating a backward step of the tactile stimulation, therefore, creating a mismatch between the post-saccadic tactile target and the eye landing position. We hypothesized that tactile reactive saccades gain will adaptively decrease due to the backward step and that this gain decrease will transfer to non-adapted (15° (ring finger), and 30° (thumb finger)) tactile saccades as well as to visual saccades performed toward the adapted and the non-adapted locations. In **Study 2**, our participants performed either auditory or visual saccades toward targets located at 10, 15, and 20° to the left or the right of a central (visual) fixation point. In Experiment 1 of this study, we induced, in two different sessions and hemifields, both backward and forward adaptations of visual saccades to targets located at 15°. We hypothesized that both backward and forward adaptation of reactive visual saccades would transfer to the non-adapted visual saccades (10° and 20°), as well as to auditory saccades performed toward the adapted (15°) and the non-adapted locations (10° and 20°). In Experiment 2, we employed the same strategy used in Study 1 in order to investigate the adaptation of auditory saccades. While the participants performed a saccade toward an auditory target located at 15° from the fixation point, the sound was switched to another location in order to create either a backward (from 15° to 10°) or a forward (from 15° to 20°) step of the saccade target. We hypothesized that both forward and backward steps of the auditory target would result in adaptive changes in auditory saccades and that those modifications would transfer to non-adapted auditory saccades as well as to all the tested visual saccades.

The first two studies (**Study 1** and **Study 2**) allowed us to report novel compelling evidence supporting the existence of backward adaptation in tactile and auditory saccades in a dark environment without the presence of post-saccadic visual information regarding the stimulus location. As reviewed in Chapter 3, post-saccadic visual information is so far deemed critical for the processing of the error signal, according to the two most widely accepted hypotheses: predictive sensory error (Collins & Wallman, 2012) and postdictive motor error (Masselink & Lappe, 2021). One of the potential factors

that may play a role in error processing during non-visual saccades adaptation is spatial attention (Khan et al., 2014). Several studies have shown that saccadic adaptation enhances the orientation of spatial attention (Nicolas, Bidet-Caulet, et al., 2019; Nicolas et al., 2020). The inverse effect, that is, the effect of spatial attention on saccadic adaptation, remains uncertain as none of the available studies have directly examined the effect of the “spatial orienting” of attention on adaptation. Nevertheless, one might hypothesize that spatial attention affects saccadic adaptation. We, therefore, predicted that orienting spatial attention using a cue-target paradigm combined on a trial-by-trial basis with an adaptation double-step paradigm will impact the resulting adaptation.

We investigated this prediction **in Study 3**, comprising two experiments in which we tested the effect of exogenous spatial attention on the adaptation of reactive saccades (Experiment 1) as well as the effect of endogenous spatial attention on the adaptation of voluntary saccades (Experiment 2). Combining the Posner paradigm (Posner, 1980) with the double-step target paradigm leads to potential dual-task interference which we attempted to reduce as much as possible by tapping on different sensory modalities for the attention Posner task (tactile) and the saccadic adaptation double-step task (visual). Indeed, we took advantage of the cross-modal link in the orienting of spatial attention reviewed in Chapter 4 and specifically of the tactile-to-visual transfer of attention. In each experiment, saccades were preceded by a tactile cue that oriented participants' tactile attention either toward or away from the location of the adapted target (in two different sessions). We hypothesized that for both experiments, orienting tactile attention toward the adapted target would boost the amount and the speed of adaptation, and in contrast, orienting tactile attention away from the adapted target would decrease the amount and the speed of adaptation.

Study 1: Saccades to both vision and touch are modified following adaptation but cross-modal transfers are asymmetrical

Ali Batikh¹, Valérie Gaveau¹, Muriel T.N. Panouillères¹, Éric Koun¹, Roméo Salemmé¹, Alessandro Farnè^{1§}, Denis PéliSSon^{1§}

¹*IMPACT Team of Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University Claude Bernard Lyon 1, France.*

[§] *These authors contributed equally to this work.*

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Abstract

Adaptation of reactive saccades (RS), made toward the sudden appearance of stimuli in our environment, is a plastic mechanism thought to occur at the motor level of saccade generation. As saccadic oculomotor commands integrate multisensory information in the parietal cortex and superior colliculus, adaptation of RS should occur not only towards visual but also tactile targets. In addition, saccadic adaptation in one modality (vision or touch) should transfer cross-modally. To test these predictions, we used the double-step target paradigm to adapt rightward saccades made at two different eccentricities toward the participants' index and middle fingers, identified either visually (Experiment1) or tactually (Experiment2). In each experiment, the rate of adaptation induced for the adapted modality and the rate of adaptation transfer to the non-adapted modality were compared to that measured in a control (no adaptation) session. Results revealed that touch-triggered RS can be adapted as well as visually triggered ones. Moreover, the transfer pattern was asymmetric: visual saccadic adaptation transferred fully to tactile saccades, whereas tactile saccadic adaptation, despite full generalization to non-adapted fingers, transferred only partially to visual saccades. These findings disclose that in the case of tactile saccades, adaptation can be elicited in the absence of post-saccadic visual feedback. In addition, the asymmetric adaptation transfer across sensory modalities suggests that the adaptation locus for tactile saccades may occur in part upstream of the final motor pathway common to all saccades. These findings bring new insights both on the functional loci(us) and on the error signals of RS adaptation.

New & Noteworthy

The present study revealed that, as predicted from a large literature, adaptation of visual reactive saccades transfers to tactile saccades of the same as well as neighboring amplitudes. Furthermore, in a modified double-step target paradigm, tactile saccades exposed to repeated errors adapt with similar

rate and spatial generalization as visual saccades, but this adaptation only slightly transfers to visual saccades. These findings bring new information on saccadic adaptation processes.

Keywords: Saccadic adaptation; Touch; Vision; Cross-modal transfer.

Introduction

We perform over 100,000 saccades per day to bring the image of objects of interest onto the fovea, the highest acuity part of our retina. Saccadic eye movements triggered by the sudden appearance of an object are classified as reactive (or reflexive) (RS), whereas those produced based on our internal goals are defined as voluntary saccades (VS). The latter relies on the activation of a wider neural network in comparison with the former (Gaymard et al., 1998).

Not only visual but also auditory (i.e., the sound of car brakes nearby) as well as somatosensory stimuli (i.e., a bee landing on our hand), can trigger saccadic eye movements. Compared to visual saccades, auditory saccades are less accurate, their latency decreases with increasing amplitude and they display a lower peak velocity (Jay & Sparks, 1987). Similarly to auditory saccades, tactile (or somatosensory) saccades are less precise, less accurate, and display longer latency and lower velocity peak than visual saccades of the same amplitude (Blanke & Grüsser, 2001; Groh & Sparks, 1996a; Sullivan et al., 2004). Consequently, due to their lower speed and longer duration, saccades toward a non-visual target show a curved trajectory more often than visual saccades, reminiscent of feedback- or feedforward-based on-line correction (Overvliet et al., 2011).

Importantly, the categorization into reactive or voluntary also applies to tactile saccades. Amlôt and Walker (Amlôt & Walker, 2006) studied the latency of pro-saccades (RS directed toward a target) and anti-saccades (VS to the opposite direction of a target) in response to visual or tactile targets and found that, in both modalities, the latency of pro-saccades is shorter than the latency of anti-saccades. Also, an equivalent of the visual grasp reflex (the failure of the oculomotor system to inhibit an erroneous pro-saccade toward the visual target in anti-saccades trials) was observed for tactile anti-saccades, with a very similar erroneous pro-saccades rate in the tactile (11.04%) and visual modality (13.13%). Whether voluntary or reflexive, the increased latency of somatosensory saccades relative to visual saccades can be attributed in large part to the additional processing step of coordinate transformation, as evidenced by Neggers and Bekkering (Neggers & Bekkering, 1999). In their study of goal-directed eye and hand movements toward visual and tactile targets delivered on the participants' knee, these authors found that across subjects correlations between saccadic and hand reaction time (RT) were higher for somatosensory than visual targets. They argued that the information elicited by tactile stimulation of the knee, initially encoded in a leg-reference frame, had to be translated into an adequate reference frame for both the eye and arm motor responses, leading to correlated RT. In contrast, the information elicited by the visual target, initially encoded in an adequate reference frame for the saccadic system, thus needs to be translated into another reference frame only for the arm movement, yielding a weaker correlation between eye and hand RTs.

The additional cost of coordinate transformation on somatosensory saccades is further evidenced by the so-called crossed versus uncrossed hand paradigm (Heed & Azañón, 2014). The reaction time of saccades toward a tactile target on the hand is longer when hands are crossed over the midsagittal plane than in the uncrossed hands condition. This cost is thought to be related to a conflict between the somatotopic (anatomical) representation of the stimulated hand locus and its external (spatial) representation. In addition, in the crossed condition some tactile saccades follow a curved trajectory: these ‘turnaround’ saccades start in the direction dictated by the anatomical coding of the target and then are corrected in flight toward the actual, spatial location of the target. This phenomenon can be used to timestamp the underlying coordinate transformation between the anatomical and spatial representations of tactile targets. Indeed, firstly, the latency of the turnaround point relative to the tactile stimulation (332 ± 30 ms) was similar to the reaction time of straight saccades in the crossed hands posture (319 ± 25 ms); and secondly, the reaction time of turnaround saccades was similar to that of (straight) saccades executed when the arms are uncrossed (Overvliet et al., 2011).

The superior colliculus (SC) plays an important role in the convergence of somatosensory and visual signals. Groh and Sparks (Groh & Sparks, 1996b) found that among 86 neurons exhibiting saccade-related activity in the monkey SC, all but one additionally responded both to tactile and visual input. Interestingly, just like visuo-saccadic neurons, these multisensory saccadic neurons have a saccadic movement field, meaning their motor discharge is tuned to the amplitude and direction of the impending saccade and not to its endpoint relative to the body. Therefore, at the SC level, the somatosensory signals have already been transformed into saccadic signals encoded in an eye-centered coordinate reference frame. To test whether this transformation takes place within the SC, the researchers also recorded the target-related activity of 34 SC somatosensory neurons while monkeys performed saccades toward visual or tactile stimulations delivered to their hands. They found that the discharge of 74% of those cells varies with initial eye position and is therefore not solely encoded in a somatotopic reference frame, suggesting that somatosensory signals reaching the SC have already been remapped, at least in part, in upstream structures (Groh & Sparks, 1996c).

One critical feature of the oculomotor system is its plasticity. Saccades are the fastest movements that we can produce. Due to their high speed, and besides the exceptions already mentioned above, saccades usually cannot be modified in flight, but nonetheless, their precision is maintained throughout life. Sensorimotor adaptation mechanisms correct for saccade errors caused by fatigue, aging, or neurological diseases. Errors eliciting such so-called saccadic adaptation occur when the saccade landing position repeatedly overshoots (hyper-metria) or undershoots the target position (hypo-metria), leading respectively to an adaptive decrease or increase of saccade amplitude. In the laboratory, saccadic adaptation is most often elicited by the double-step target paradigm introduced by McLaughlin (McLaughlin, 1967). This method consists of stepping a visual target (1st step) to elicit the saccadic response and, when the eyes are in-flight, stepping it again either backward or forward

relative to the on-going saccade (2nd step) to elicit a post-saccadic error. Although the intrasaccadic step is usually not consciously perceived by subjects, the resulting post-saccadic error elicits, shortly after the primary saccade, a corrective saccade bringing the eye back to the stepped target. When repeated across identical double-step trials, the post-saccadic error is interpreted by the brain as a saccade programming error and leads adaptation mechanisms to reduce (for backward steps) or increase (for forward steps) the primary saccade amplitude, reaching a steady state level after some 10th to 100th of trials in humans (for review see, (Hopp & Fuchs, 2004; Iwamoto & Kaku, 2010; Pélisson et al., 2010)).

Saccadic adaptation has been initially thought to result from motoric changes unfolding at the level of the cerebellum and brainstem (for review see (Hopp & Fuchs, 2004; Iwamoto & Kaku, 2010)). However, further studies disclosed that this mechanism additionally affects visual perception and relies also on higher cerebral areas. Studies combining fMRI with the double-step target paradigm have identified several cerebral or/and cerebellar areas whose activation can be related to the different subprocesses of saccadic adaptation: the detection and the processing of the motor error, the learning process itself, the modifications in corrective saccades metrics (Blurton et al., 2012; Gerardin et al., 2012; Guillaume et al., 2018; Liem et al., 2013; Métais et al., 2022).

Behavioral studies have also mitigated the pure motoric hypothesis of adaptation, but mainly for VS. First, studies comparing the effect of RS adaptation onto non-adapted VS (RS-to-VS transfer) to the effect of VS adaptation onto non-adapted RS (VS-to-RS transfer) found an asymmetric pattern of transfer of adaptation with a stronger transfer from VS to RS than the other way around, suggesting the existence of partially segregated adaptation sites for these two types of saccades (Alahyane et al., 2007; Collins & Doré-Mazars, 2006). Second, RS and VS also show different patterns of adaptation transfer to hand-pointing movements and anti-saccades. Indeed, adaptation of VS, but not of RS, transfers to hand pointing movements performed under gaze fixation condition (Cotti et al., 2007), suggesting that only the former type of adaptation involves a sensory level. In addition, the adaptation of RS along a single horizontal direction transfers toward anti-saccades performed in the same (adapted) direction but not to those directed away (un-adapted direction) whereas in the case of VS, unidirectional adaptation transfers to both adapted and un-adapted directions. As in anti-saccades tasks the sensory and the motor vectors are dissociated, these results suggest that RS adaptation takes place at a motor level, whereas VS adaptation recruits both motor and sensory loci (Cotti et al., 2009). Altogether, these studies strongly suggest that backward adaptation of RS acts at an oculomotor level. In contrast, as forward adaptation (of both VS and RS) has been much less investigated, its corresponding neural substrates are still debated. Forward adaptation is generally harder to induce than backward adaptation and the underlying mechanisms were suggested to differ between these two types of adaptation (Ethier et al., 2008; Panouillères et al., 2009). For these reasons, we focused the present study on RS backward adaptation mechanisms.

This hypothesis that RS backward adaptation takes place at a motor level implies that backward adaptation of visually triggered RS should transfer toward RS triggered by stimuli in other sensory modalities. In agreement with this prediction, Frens and van Opstal (Frens & van Opstal, 1994) showed that adaptation of visually guided RS transferred to ‘auditory saccades’ of the same vector (see also (Collins et al., 2010)). However, no empirical evidence from tactile saccades is available to support the notion of a motor locus of adaptation for RS. Indeed, neither the possibility to induce adaptation of touch-triggered saccades, nor the cross-modal transfer of adaptation to and from tactile saccades, have ever been investigated so far.

Thus, the present study seeks to further characterize the mechanisms involved in RS adaptation by addressing these two questions. To this twofold aim, we performed two experiments where backward saccadic adaptation was induced by the double-step target paradigm. In Experiment 1, we adapted RS toward visual targets (LEDs placed on the fingers of the participants’ right hand) and tested the effect of such adaptation on RS toward both visual and tactile targets (electrocutaneous stimulations of the participant’s fingers). In Experiment 2, we exposed participants to adaptation of RS toward tactile stimuli thanks to a tactile double-step paradigm and tested the effect of such potential adaptation again on RS toward both visual and tactile targets. We predicted in both experiments, first a significant decrease of adapted RS amplitude due to the adaptation exposure and second, a significant generalization of this adaptation to non-adapted RS toward nearby targets as well as a significant transfer to RS in the non-adapted modality.

Experiment 1: Transfer Of Visual Saccades Adaptation To Tactile Saccades.

Materials And Methods

Participants

Sample size was calculated via the open access software G*Power 3.1.9.7 (effect size = 0.4, α = 0.05, Power = 0.8 and correlation among repeated measures = 0.6). There was no previous study investigating the transfer of adaptation from visual to tactile saccades, therefore we relied on the high visual to auditory transfer of adaptation reported in the literature (Collins et al., 2010) to select an effect size = 0.4. Twenty-one naïve volunteers (all right-handed, 8 males and 13 females, mean age 27.5 ± 4.2 ranging between 22 and 37 years old) participated in the first experiment. Fifteen participants were involved in a session where adaptation was elicited (ADAPT session), and fifteen participants were involved in another session where control saccades were performed (CTRL session) (nine of them had participated in the ADAPT session).

Participants’ vision was normal or corrected-to-normal. Exclusion criteria were simultaneous participation in other experiments involving sensorimotor adaptation, a history of neurological or psychiatric disorders, cognitive disorders preventing the comprehension of the instructions,

consumption of psychotropic drugs or alcohol, and severe sleep deprivation during the last 24 hours. Participants were asked not to wear makeup or to remove it before the experiment (to prevent any problem with the eye tracker).

Both experiments of this study were done in two separate phases. The initial sample sizes for Experiment 1 and 2 were 10 and 16 respectively. Around eight months later and following the reviewers suggestions on the first submitted version of the manuscript, sample sizes were increased to 15 participants in the first experiment and 30 participants in the second one.

Ethical Statement

Both Experiment 1 and Experiment 2 of the present study conformed with the Code of Ethics of the World Medical Association (Declaration of Helsinki 1964) and were approved by the ethics committee of INSERM (IRB00003888; decision n° 21-762 dated 19/01/2021). An informed consent was received from every participant prior to each experiment.

Experimental setup

Participants were sitting in total darkness with their head stabilized using a chinrest. They faced a vertical panel situated 30 cm from their eyes which maintained their right hand in a vertical position by a strap surrounding their wrist and rings surrounding the second phalanx of their fingers. In this position, the pinky, ring, middle, index, and thumb fingers were respectively at 5, 10, 15, 20, and 25 degrees of visual angle in the horizontal axis relative to the participant's midline (see Figure 1A). Six red light-emitting diodes (LED, diameter 2 mm) were positioned on the panel: one LED used as a fixation point (FP) was located at the participant's gaze level and 5 degrees to the left of the participant's midline; the five other LEDs were embedded in the rings maintaining the fingers. LEDs located on the index, middle, and ring fingers were horizontally aligned with the FP, the pinky and thumb LEDs were located below this line. The LEDs were attached on the front face of 5 wooden rings fixed on a vertical wooden board, allowing to maintain each finger aligned with its corresponding LED. In addition, rings and board were painted black and, before inserting their fingers in the rings, participants wore a black fabric glove. Finally, the LEDs' intensity was kept low enough to prevent any lightning of the black gloves or rings. Therefore, the participants could never see the location of their fingers or hand during the experiment. For tactile stimulation, two electro-dermal electrodes with opposite polarities (Neuroline 7000, Ambu, Denmark) were placed on each finger underneath each LED, at the level of the distal (anode) and middle (cathode) phalanxes. The supra-threshold (100% detection accuracy) electrocutaneous stimulus felt like tingling, resulting from a squared wave pulse delivered by constant-current stimulators (Iso-Flex, A.M.P.I.). A horizontal ruler was positioned on the top of the vertical panel (50 mm above the middle finger position), allowing to measure, at the beginning and end of each session, the participants' perceptual estimate of the middle finger position of their unseen hand (see below: section4/Procedures). Eye movements were recorded with an infrared eye tracker (EyeLink 1000, SR Research, Canada) at a frequency of 1000 Hz with an

accuracy of 0.1° . Eye velocity was calculated online using a two-point central difference algorithm (Terry Bahill & McDonald, 1983) and the time of saccade onset, used to trigger intra-saccadic target step or target extinction during rightward saccades, was based on a velocity threshold of $30^\circ/s$.

Each experimental session started with a calibration of the eye tracker, with participants being asked to fixate a central LED as well as four other LEDs placed on the panel (up, down, to the right, and the left of the central LED). A drift correction was performed after each experimental block and, whenever the eye drifted more than two degrees from the central LED, a calibration of the eye tracker was repeated.

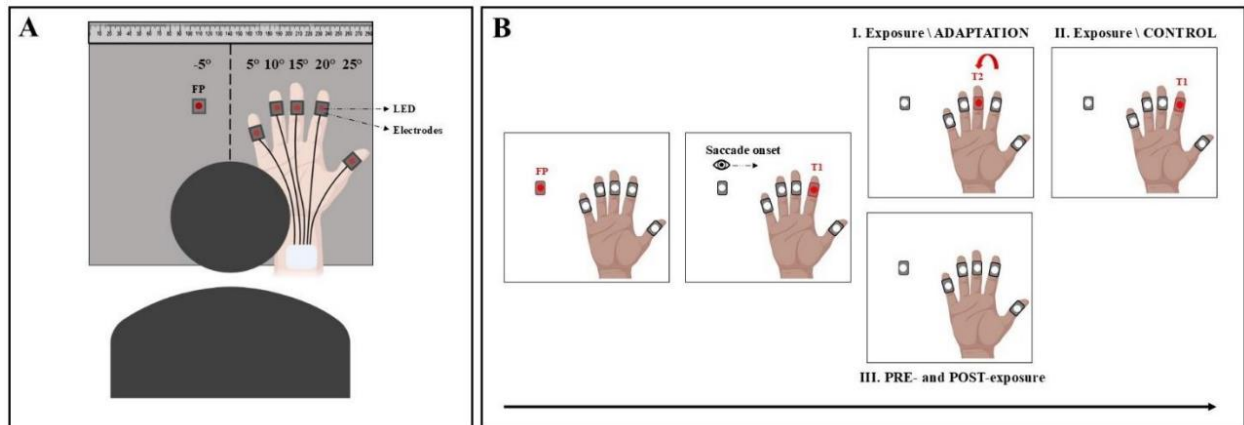


Figure 1: Experiment 1 setup and procedure. (A) A vertical board was placed in the frontal plane at 30 cm from the participants' eyes. The right hand was immobilized in a supine position on the board through rings located on the 5 fingers. The rings, separated from each other by five degrees, contained a red LED that served as visual target, and a pair of electrodes placed on each finger allowed to generate an electrocutaneous stimulation which served as tactile target. Another red LED serving as fixation point was placed on the board five degrees to the left of the participant's midline. At the top of the board, a ruler was made visible to participants during the proprioceptive location assessment. At any other time, the environment was completely dark and invisible (except a single lit LED in visual saccade trials), as the whole set-up was painted black, the participants' hand was covered by a black tissue glove and when lit, the LEDs' intensity was low. **(B)** Participants gazed at the FP which disappeared simultaneously with the presentation of a peripheral stimulus on one of their fingers in the visual or tactile modality, according to counterbalanced blocks of trials; once the saccade onset detected, the stimulus either stepped backward in the exposure phase of the ADAPT session (I), remained stationary until the end of the trial in the exposure phase of the CTRL session (II), or turned off in the PRE- and POST-exposure phases (III).

Procedures

As experiments were conducted in a completely dark room, we took into consideration the fact that our conscious perception of hand position drifts toward our body midline (so-called proprioceptive drift) (Wann & Ibrahim, 1992). We thus measured this drift before and after ADAPT and CTRL sessions, by asking participants to indicate which number on the visible ruler best matched

the position of their occluded middle finger (measured 9 times, randomly sliding the ruler each time to avoid response strategies (Tsakiris & Haggard, 2005)).

ADAPT and CTRL sessions each involved five steps: a PRE proprioceptive location assessment, a saccade PRE-exposure phase, a saccade Exposure phase, a saccade POST-exposure phase, and a POST proprioceptive location assessment. We detail the time course of the saccade trials below (see Figure 1B).

During PRE-exposure the baseline performance of visual saccades and tactile saccades was evaluated: participants performed one block of 75 rightward saccades directed toward visual targets (visual block) and one block of 75 rightward saccades directed toward tactile targets (tactile block). All trials were initiated with the participants staring at the FP for a random duration (2000 to 3000 ms). Then, the FP was turned off and one of the five (visual or tactile) peripheral stimuli was presented randomly. Participants were instructed to saccade toward the location of the target as rapidly and as precisely as possible. During the saccadic response, the (visual or tactile) stimuli were terminated, but participants nonetheless had to maintain fixation on the now-absent target until the reappearance of the FP. At the end of the trial, the Fixation LED was turned on again, indicating the participant to get prepared for the next trial. Participants were asked to blink on their way back to the fixation point to reduce the amount of blinking that can occur during the saccades.

In the Exposure phase, participants performed 120 visual saccades randomly directed toward the index or the middle finger. As in PRE-exposure, each trial started with a fixation period which ended with the simultaneous appearance of the visual stimulus and the disappearance of the FP. In the ADAPT session, saccade onset detection triggered a 5 deg leftward intra-saccadic displacement of the target (from the index to the middle finger or from the middle to the ring finger), this backward shift being aimed at inducing an adaptive shortening of saccade amplitude (McLaughlin, 1967). During the CTRL session, aimed at measuring any potential change of saccade metrics unrelated to adaptation mechanisms, the target remained at its initial location (index or middle finger) for the duration of the trial.

The POST-exposure was identical to the PRE-exposure phase. Comparisons of saccade gain between these 2 phases allowed evaluating the after-effect of visual saccades adaptation and the transfer of adaptation to tactile saccades.

The order of the two saccade blocks (visual and tactile) performed in each PRE- and POST-exposure phase was counterbalanced between participants: half of them performed the visual block followed by the tactile block in the PRE-exposure, then the tactile followed by the visual block in the POST-exposure (Vis-Tact/Tact-Vis) and the other half vice versa (Tact-Vis/Vis-Tact).

The nine participants who performed both experimental sessions (ADAPT and CTRL) were tested with at least one week washout delay in-between to avoid any cross-over effects related to the retention of adaptation (Alahyane & Pélisson, 2005).

Analysis

Horizontal and vertical eye positions were analyzed offline using software developed in MATLAB by our team. Saccades onset and offset were identified based on a velocity threshold of 15°/s. Saccade amplitude was measured as the difference between eye positions 50 ms before the saccade onset and 50 ms after the saccade offset. The following dependent variables were then extracted for each saccade: 1) gain: ratio between the saccade amplitude and the target initial eccentricity (difference between the target position and saccade starting position), this parameter was used to investigate the effect of the double-step adaptation exposure on saccade size as it presents the advantage, over saccade amplitude, of being expressed relative to the target distance, thus allowing to measure the mean accuracy of saccades toward targets of different eccentricities pooled together (see (Hopp & Fuchs, 2004), (Pélisson et al., 2010)); 2) latency: time between the appearance of the initial target (T1) and the saccade onset; 3) duration: time between saccade onset and saccade offset; 4) peak velocity: maximum eye velocity reached during the saccade. Trials where saccades were made toward the pinky were discarded from further analyses; indeed, this closest target from fixation (10°) was the most difficult for our participants to localize through tactile saccades, resulting in the highest saccade amplitude variability among all fingers; in addition, restricting our analyses to the ring and thumb allowed us to perform our generalization tests to the two symmetrical locations around the index and middle fingers used for adaptation. Trials where the saccadic gain fell outside the range defined by the mean gain $\pm 2 \times$ standard deviations (calculated and applied for each participant across each session, phase, modality and target location separately), trials where the saccade latency was lower than 80 ms or higher than 700 ms, and trials where a blink occurred during the primary saccade were excluded from the analysis (exclusion of 9.57% of the trials in total).

Two additional parameters were then calculated. First, in the exposure phase, the slope of the linear relationship between saccadic gain and trial number was calculated for visual saccades toward the middle and the index fingers, separately. Second, we calculated, for each finger and separately in the adapted and the non-adapted modality, the following ratio of saccadic gain change between the pre- and post-exposure phases: $\text{Gain change ratio} = (\text{Gain PRE} - \text{Gain POST}) / \text{Gain PRE}$. Therefore a positive gain change ratio indicates a decrease in saccadic gain in the POST-exposure phases compared to the PRE-exposure (compatible with backward adaptation) while a negative gain change ratio indicates an increase in saccadic gain (for example, a gain change ratio of +0.3 corresponds to a 30% decrease of gain in post-exposure relative to pre-exposure).

Statistical analysis

Statistical analyses were done using IBM SPSS statistics 29.0.0.0. First, to check if the double-step exposure successfully elicited adaptation of visual RS, the slope of the linear relationship between saccadic gain and trial number was submitted to a repeated measures ANOVA with the factor 'Target position' (middle finger vs index finger) as within-subjects factor and the factor 'Session' (ADAPT vs

CTRL) as between-subjects factor. In addition, the gain change ratio of RS in the visual (adapted) modality, used as a measure of adaptation after-effect, was also submitted to the same repeated measures ANOVA Target position (middle and index fingers) x Session (ADAPT vs CTRL). Second, to investigate whether adaptation of visual RS generalized to targets near the adapted locations, the gain change ratio of visual saccades toward non-adapted fingers was submitted to a repeated measures ANOVA with 'Target position' (ring and thumb fingers) as within-subjects factor and 'Session' (ADAPT vs CTRL) as between-subjects factor. A similar ANOVA was performed on the gain change ratio of tactile saccades toward all 4 fingers to investigate the transfer of adaptation to the other modality, except this time the within-subjects factor 'Target position' had 4 levels (ring, middle, index and thumb fingers). We included in this analysis of transfer only participants who showed a significant level of adaptation (14 subjects out of 15), i.e. showing a significant decrease of visual RS gain (independent-samples t-test comparisons between PRE and POST phases) at least for the index or the middle finger.

Third, we submitted the proprioceptive assessments to a repeated measures ANOVA with the factor 'Phase' (PRE vs POST) as within-subjects factor and 'Session' as between-subjects factor.

We also analyzed separately the latency, duration, and peak velocity, for both visual and tactile saccades in the 14 significantly adapted participants using a 3-way repeated measures ANOVA with 'Phase' (PRE vs POST), 'Modality' (Visual vs Tactile) and 'Target position' (index vs middle finger) as within-subjects factors and 'Session' (ADAPT vs CTRL) as between-subjects factor (see supplemental material for the results of this analysis).

Results

The adaptation of visual RS

As stated in the Methods, the existence of visual RS adaptation was addressed by two analyses of visual RS performed toward the index and the middle fingers, first, on the slope of the gain change during the exposure phase, then on the ratio of gain change between PRE and POST phases. Examples of gain values for individual saccades performed toward the index and the middle fingers in the PRE- and POST-exposure phases (visual and tactile saccades) as well as during the Exposure phase (visual saccades) are plotted in Figure 2.

Saccadic gain (Participant 15, Experiment 1)

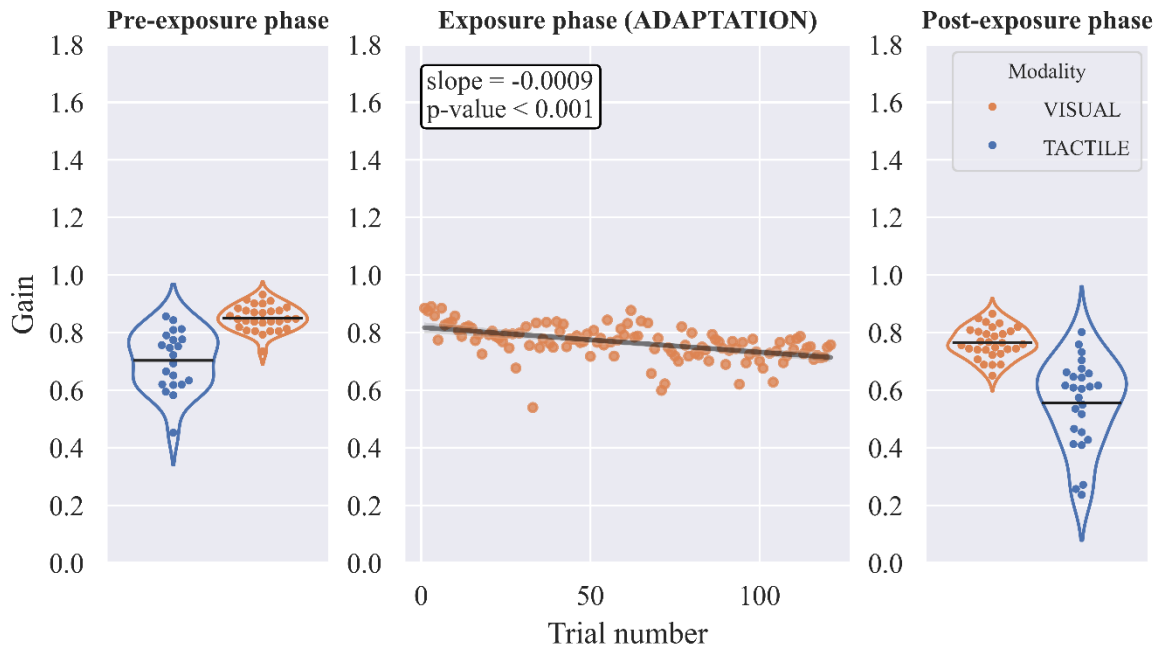


Figure 2: Experiment 1 individual data (participant 15, ADAPTATION session): the gain of tactile (blue) and visual (orange) saccades toward the middle and the index fingers in the PRE- and the POST-exposure phases (black lines represent the mean gain value) as well as the variation of gain across trials in the Exposure phase (slope value and statistical significance of the linear regression are presented in the central panel).

a. Gain slope during Exposure phase

The gain change during the Exposure phase of the ADAPT session can be seen in supplemental figure 1 for all significantly adapted participants (see Methods). The mean slopes of the gain change during the exposure block are illustrated in Figure 3A. The repeated measures ANOVA revealed a main effect of the factor Session ($F(1, 28) = 20.061$, $p < 0.001$) (mean slope \pm s.d.: ADAPT = -0.000549 ± 0.000528 , CTRL = 0.000164 ± 0.000319). No other significant effect or interactions were found (all $F \leq 3.212$, all $p \geq 0.084$). These results suggest that the double-step paradigm was successful in reducing the size of visual saccades similarly for both adapted locations and that this decrease was significantly larger than in the CTRL (no step) paradigm.

b. Gain change ratio between PRE and POST phases

As illustrated in Figure 3B, the mean gain change ratio for visual RS performed toward the index and the middle fingers was larger in the ADAPT session than in the CTRL session. Indeed, the 2-way ANOVA revealed a significant main effect of the factor Session ($F(1, 28) = 139.45$, $p\text{-value} < 0.001$) (mean gain change ratio \pm standard deviation: ADAPT = 0.1238 ± 0.04 , CTRL = -0.0207 ± 0.025) as well as a significant Session \times Target position interaction ($F(1, 28) = 5.05$, $p = 0.033$). There was no significant main effect of the factor Target position ($F(1, 28) = 0.569$, $p\text{-value} = 0.457$). Post hoc pairwise Bonferroni comparisons showed a significant difference between the ADAPT and CTRL

session for both middle fingers (p -value < 0.001) and index finger (p value < 0.001); it also revealed a significant difference between the index and the middle fingers (mean difference index - middle = -0.018 ± 0.008 , p value = 0.043) in the ADAPT session but not in the CTRL (mean difference index - middle = 0.009 ± 0.008 , p value = 0.300). These results indicate that visual RS gain after-effects were significantly larger in the ADAPT session than in the CTRL session, showing that exposure to the double-step paradigm successfully induced adaptation of visual saccades.

We next verified whether the order of visual and tactile blocks, despite their counterbalancing (see Procedures section), could affect the above results. To this aim, we submitted the gain change ratio to the same ANOVA but with the additional between-subjects factor ‘Block order’ (Tact-Vis/Vis-Tact vs Vis-Tact/Tact-Vis). This analysis showed that there was neither a main effect of Block order nor any interaction with the other factors (Session and Target position, all $F \leq 2.730$, all p values ≥ 0.111). In sum, these results strengthen our conclusion that exposure to the double step paradigm successfully induced adaptation of visual saccades.

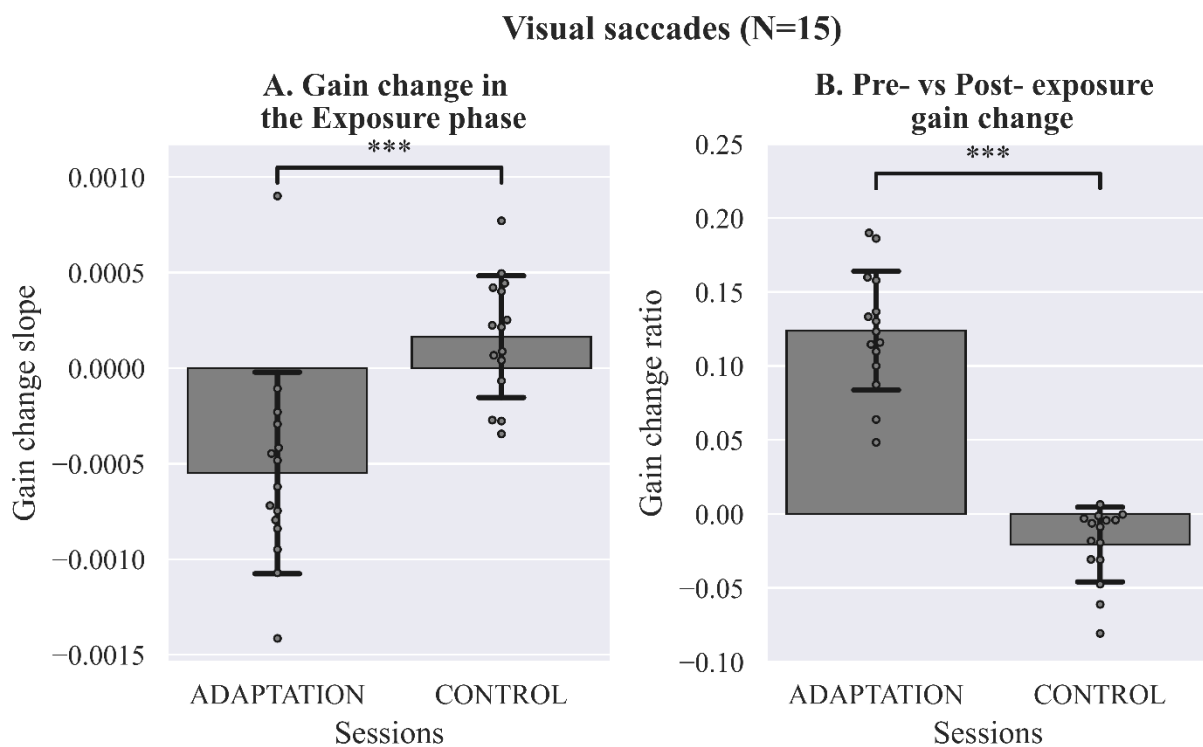


Figure 3: Experiment 1 adaptation results (all participants). Panel A: mean saccadic gain change in the exposure phase (slope of the linear regression between saccadic gain and trial number) in the ADAPTATION and CONTROL sessions. Panel B: mean saccadic gain change ratio between the PRE- and the POST-exposure phases in the ADAPTATION and CONTROL sessions. In both graphs, only visual saccades toward the index and the middle fingers were considered. Error bars represent standard deviations. * : t -tests ($p < .001$).**

Transfer analysis

This analysis includes only the 14 participants who were significantly adapted in the ADAPT session for at least one of the two ‘adapted’ fingers (middle and/or index finger) (see Methods).

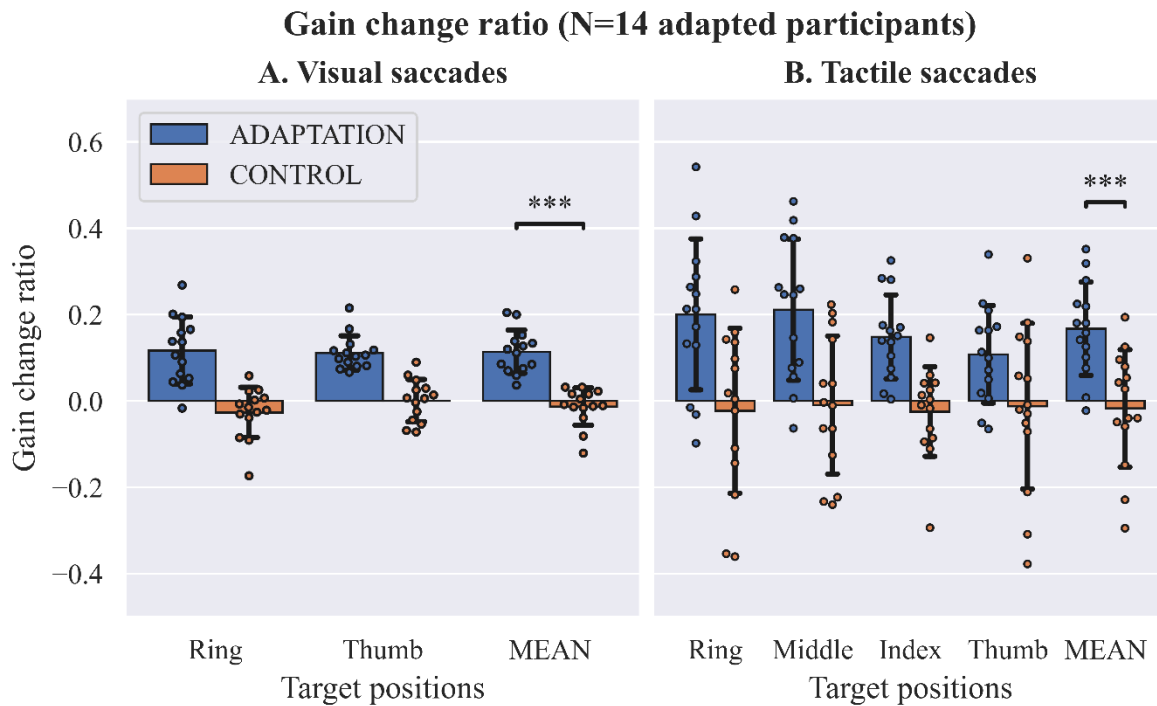
As shown in Figure 4A, visual RS adaptation generalized to nearby locations. Indeed, the repeated measure ANOVA performed on the gain change ratio of non-adapted visual RS showed a significant main effect of the Session factor ($F(1, 26) = 51.778$, $p\text{-value} < 0.001$) (mean gain change ratio \pm standard deviation: ADAPT = 0.114 ± 0.050 , CTRL = -0.013 ± 0.043) with no other significant main effect or interaction (all $F \leq 1.664$, all p values ≥ 0.208). This result indicates a significantly larger gain decrease for visual non-adapted saccades in the ADAPT in comparison to CTRL session, irrespective of the target location.

We tested a possible effect of the order of visual blocks in the experimental protocol, by submitting the gain change ratio to the above ANOVA with the additional ‘Block order’ factor (Tact-Vis/Vis-Tact vs Vis-Tact/Tact-Vis). Results showed neither significant main effect of Block order, nor significant interaction with the other factors of the ANOVA (all $F \leq 1.821$, all p values ≥ 0.190).

As shown in Figure 4B, the visual RS adaptation transferred to tactile RS. Indeed, the repeated measures ANOVA performed on the gain change ratio of non-adapted tactile RS showed a significant main effect of the Session factor ($F(1, 26) = 15.766$, $p\text{-value} < 0.001$) (mean gain change ratio \pm standard deviation: ADAPT = 0.167 ± 0.108 , CTRL = -0.017 ± 0.136) with no other significant main effect or interaction (all $F \leq 1.447$, all p values ≥ 0.243). This result indicates a significantly larger gain decrease for tactile non-adapted saccade in the ADAPT in comparison to CTRL session, irrespective of the target location.

As for the previous analysis, we tested a possible effect of the order of visual and tactile blocks, by submitting the gain change ratio to the above ANOVA with the additional ‘Block order’ factor (Tact-Vis/Vis-Tact vs Vis-Tact/Tact-Vis). Results showed neither significant main effect of Block order, nor significant interaction with the other factors of the ANOVA (all $F \leq 1.681$, all p values ≥ 0.192).

In summary, these results indicate that the gain of visual RS to non-adapted targets (ring and thumb fingers) as well as the gain of all non-adapted tactile RS decreased significantly more in the ADAPT session than in the CTRL session, therefore showing that visual RS adaptation generalized to nearby locations and transferred to tactile RS.

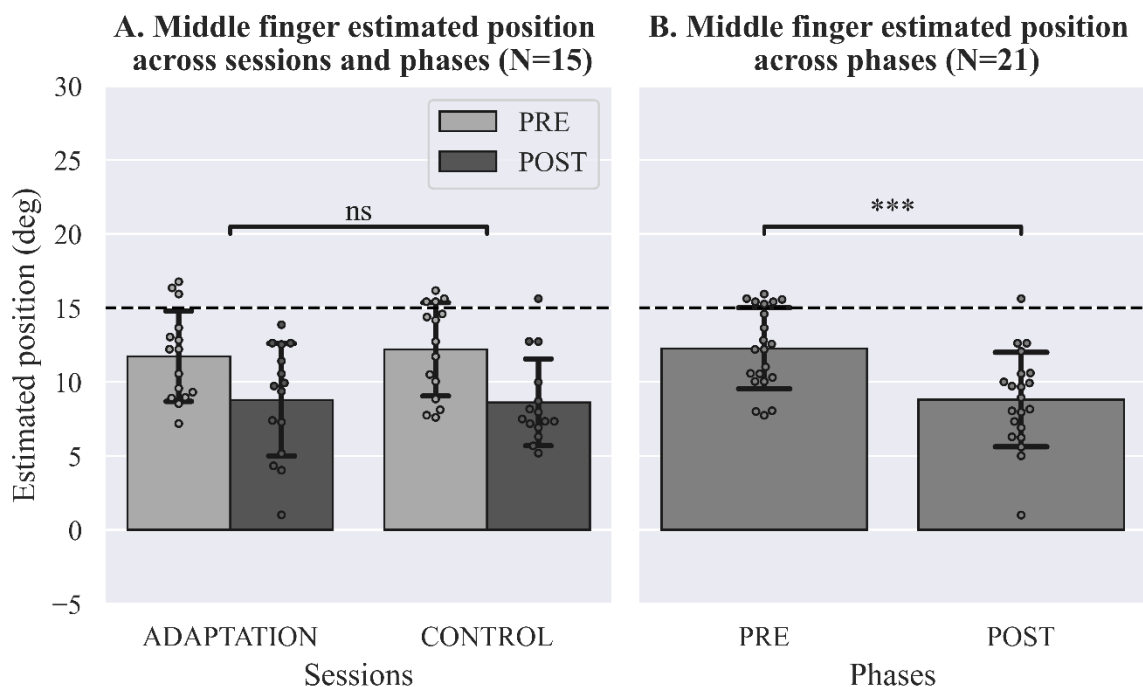


*Figure 4: Experiment 1 generalization and transfer results (only adapted participants). Mean saccadic gain change ratio in the ADAPTATION and the CONTROL sessions, plotted as a function of the target location separately for visual (Panel A) and tactile (Panel B) saccades, as well as the grand mean (MEAN) of gain change ratio across all locations plotted in each panel. Only non-adapted locations are plotted in this figure. Error bars represent standard deviations. *** : t-test ($p < .001$).*

Proprioceptive drift

As shown in Figures 5, participants underestimated their unseen middle finger location. This proprioceptive drift was larger in the POST phase in comparison to the PRE phase (Figure 5B) but importantly, this pattern of change did not differ between the CTRL and the ADAPT sessions (Figure 5A). Indeed, the repeated measure ANOVA disclosed a significant main effect of the factor Phase ($F(1, 28) = 24.78, p < 0.001$) (mean estimations (in degree) \pm s.d.: PRE = 11.96 ± 3.06 , POST = 8.7 ± 3.33), but no significant main effect of Session, and no significant Session \times Phase interaction (all $F \leq 0.237$, all $p \geq 0.630$). Therefore, the proprioceptive drift of the hand increased to a comparable extent during the ADAPT and CTRL exposures. Thus, changes in proprioceptive drift differ from, and hence are not likely responsible for, the changes in tactile RS gain reported above.

Proprioceptive drift



*Figure 5: Experiment 1 proprioceptive drift results (all participants). Mean estimated position of the middle finger location in the PRE- and POST- proprioceptive location assessment phases of the ADAPTATION and CONTROL sessions are plotted separately (Panel A) and as a grand mean pooled over both sessions (Panel B). The dotted line represents the actual middle finger location. Error bars represent the standard deviation. ns : t-test ($p > .05$), *** : t-test ($p < .001$).*

Experiment 2: Investigating The Adaptation Of Tactile Saccades And Its Transfer To Visual Saccades.

Results from Experiment 1 indicate that the adaptation of visual RS transfers fully to non-adapted saccades in the same modality. Most notably, they additionally reveal that visual RS adaptation also transfers to tactile RS, irrespective of whether they were directed toward adapted or non-adapted finger locations. Importantly, this transfer across modalities is independent of the proprioceptive drift, as the latter was equally present in the CTRL condition where neither adaptation nor transfer were observed.

In keeping with the previously reported visual-to-auditory adaptation transfer (Frens & van Opstal, 1994), this visual-to-tactile adaptation transfer is consistent with the hypothesis that RS adaptation modifies the saccade motor command, thus acting downstream, at a level of the final common pathway where multisensory information about the target has already been transformed into a motor, oculocentric, reference frame. To further support this hypothesis, we designed Experiment 2 to determine, first, whether saccades to tactile targets can be adapted and, second, whether saccadic adaptation transfer is bidirectional, i.e., also from tactile to visual saccades. To this twofold aim, we

adapted the double-step paradigm to electrocutaneous stimulation of the fingers during the tactile saccade execution, to repeatedly expose tactilely triggered saccades to a backward aiming error. Then, similarly to Experiment 1, we assessed the effectiveness of this tactile saccade adaptation and measured its effect on both visual and tactile saccades performed toward different target eccentricities.

Materials And Methods

Participants

Sample size was estimated via G*Power 3.1.9.7 (effect size = 0.25, α = 0.05, Power = 0.8, correlation among repeated measures = 0.6). As in Experiment 1, previous studies investigating tactile saccades adaptation were lacking, therefore we based our choice of a moderate effect (effect size = 0.25) on the well-established low precision (high standard deviation of the gain) of tactile saccades (Sullivan et al., 2004). Thirty volunteers (3 left-handed, 22 females and 8 males, mean age = 26.8 ± 4.7 , ranging between 19 and 37 years old) participated in Experiment 2 (all but one, the experimenter, were naïve to the objectives of this study). Inclusion and exclusion criteria were the same as in Experiment 1. All participants performed an ADAPT and a CTRL session separated by at least 7 days, in a counterbalanced order (15 participants started with the CTRL session, and the other 15 started with the ADAPT session).

Experimental setup

The experimental setup was the same as for Experiment 1. Eye movements were recorded at a 1000 Hz frequency using the remote configuration of the EyeLink® 1000 plus infrared Eye Tracker (SR Research, Canada).

Procedures

The design was the same as in Experiment 1, except that all subjects performed both ADAPT and CTRL sessions (within-subject design). Each session consisted of the same 5 steps as in Experiment 1: a PRE proprioceptive location assessment, a saccade PRE-exposure phase, a saccade exposure phase, a saccade POST-exposure phase, and a POST proprioceptive location assessment. The testing order of tactile and visual saccades blocks in the PRE-exposure and POST-exposure phases were counter-balanced between participants: half of them performed visual saccades before tactile saccades in the PRE-exposure then tactile saccades before the visual ones in the POST-exposure (Vis-Tact/Tact-Vis), the other half were assigned the reverse order (Tact-Vis/Vis-Tact).

The PRE- and POST- exposure blocks differed from those of Experiment 1 only by the duration of the visual and tactile targets, here 100 ms, to make the tactile stimulations more comfortable for participants, and by a slightly reduced intensity of the LED to provide a more comfortable contrast.

For the exposure phase in the ADAPT session, a tactile target double-step paradigm was implemented, as follows. Participants first fixated on the FP for a random duration similar to

Experiment 1, then a tactile stimulation was applied for 100 ms to their index or middle finger. Participants had to look as rapidly and as precisely as possible toward their stimulated finger and as soon as their saccadic eye movement was detected, a second tactile stimulation of 100 ms was delivered on the middle finger or the ring finger, respectively (inducing in every trial a 5° tactile backward step). Participants were asked to fixate on the last felt position of the tactile stimulation until the FP reappeared. In the CTRL session, the sequence of events was identical except that the second tactile stimulation was applied to the same, initially stimulated, finger (no target step).

Analyses

As in Experiment 1 saccades performed toward the pinky finger were discarded from the analysis. The same exclusion criteria were used as in Experiment 1, which resulted in the exclusion of 12.9% of trials. As in Experiment 1, we calculated the following parameters for all visual and tactile saccades: latency, amplitude, gain, duration, and peak velocity; then, the slope of the relationship between tactile saccade gain and trial number of the exposure phase was computed separately for the ADAPT and CTRL sessions and for the middle and the index fingers. We finally computed the gain change ratio.

Statistical analysis

A data quality check showed that some participants systematically performed very hypometric tactile saccades in the PRE-exposure phase of both the ADAPT and CTRL sessions. Thus, using K-Means clustering methods, we checked if we could detect significantly different sub-groups in our sample of 30 participants based on their mean tactile saccades gain in the PRE-exposure phase. The number of sub-groups was determined using the elbow method (3 sub-groups) then fed to the K-Means clustering revealing that all three subgroups differ statistically from each other's according to their mean tactile RS gain: group 1 (5 subjects, mean gain = 0.374, range 0.342 to 0.471), group 2 (11 participants, mean gain = 0.676, range 0.623 to 0.752) and group 3 (14 participants, mean gain = 0.9915, range 0.847 to 1.205). As this study focused on the adaptive amplitude reduction of saccades, we decided to exclude group 1, resulting in a final sample size of 25 participants. This decision was based on the fact that the strong hypo-metricity of tactile saccades in group 1 would have led 1) to a biased and underestimated adaptation capacity (amplitude reduction adaptation is limited when baseline saccade gain is already low), and 2) even if those participants would nonetheless be adapted, to a biased and underestimated transfer of such adaptation to the visual modality because the adapted tactile saccades vectors would differ too much from the non-adapted visual saccades vectors.

Using the same method we checked if we could identify participants with very hypometric saccades in Experiment 1. We were able to identify 2 best fitted subgroups of participants according to their mean tactile RS gain, however, none of them qualified to have very hypometric saccades (mean gain \pm standard deviation: Group 1 (7 participants) = 0.589 ± 0.116 , Group 2 (8 participants) = 0.9392 ± 0.093) which might be related to the smaller sample size in Experiment 1 compared to Experiment 2.

We then followed the same analysis strategy as in Experiment 1. First, the slope of the linear relationship between saccadic gain and trial number during exposure was submitted to a two-way repeated measures ANOVA with the within-subjects factors ‘Session’ (ADAPT vs CTRL) and Target position (middle vs index fingers). Then, the gain change ratio of tactile (adapted modality) RS, used as a measure of adaptation after-effect, was submitted to the same repeated measures Target position (index and the middle fingers) x Session (ADAPT vs CTRL) ANOVA. Second, we investigated a possible generalization and/or transfer of adaptation. To this aim, we submitted the gain change ratio of non-adapted tactile and visual RS to two separate 2-way repeated measures ANOVA with ‘Target position’ and ‘Session’ (ADAPT vs CTRL) as within-subjects factors. The ‘Target position’ factor had 2 levels in the first ANOVA (ring vs thumb fingers) and 4 in the second ANOVA (ring, middle, index and thumb fingers). We included in this last analysis only participants who showed a significant level of adaptation (13 subjects out of 25), i.e. showing a significant decrease of tactile RS gain (independent-samples t-test comparisons between PRE and POST phases) at least for the index or the middle finger. Third, we submitted the proprioceptive assessments to a two-way repeated measures ANOVA with the within-subjects factors ‘Session’ (ADAPT vs CTRL) and ‘Phase’ (PRE vs POST).

As in Experiment 1, we also analyzed separately the latency, duration, and peak velocity, for both visual and tactile saccades in adapted participants only (see supplemental material for the results of this analysis).

Results

The adaptation of tactile RS

As in Experiment 1, we present below examples of gain values for individual saccades performed toward the index and the middle fingers in the PRE- and POST-exposure phases (tactile and visual saccades), as well as during the Exposure phase (tactile saccades), plotted in Figure 6.

Saccadic gain (Participant 16, Experiment 2)

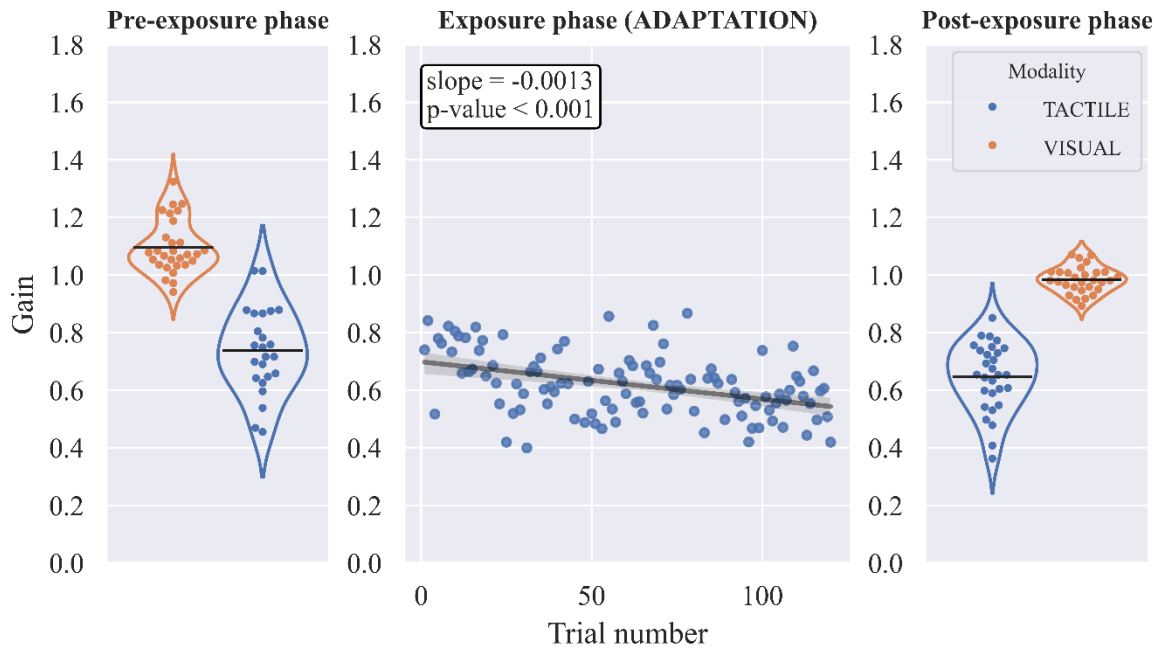


Figure 6: Experiment 2 individual data (participant 16, ADAPTATION session): the gain of tactile (blue) and visual (orange) saccades toward the middle and the index fingers in the PRE- and the POST-exposure phases (black lines represent the mean gain value) as well as the variation of gain across trials in the Exposure phase (slope value and statistical significance of the linear regression are presented in the central panel).

a. Gain Slope during exposure phase

The gain change during the Exposure phase of the ADAPT session can be seen in supplemental figure 2 for all significantly adapted participants (see Methods). The mean slopes of gain change during the exposure phase are illustrated in Figure 7A. The repeated measures ANOVA revealed a significant main effect of the factor Session ($F(1, 24) = 4.971$, $p = 0.035$) (ADAPT = -0.000942 ± 0.001145 , CTRL = -0.000154 ± 0.001196). No other significant main effect or interaction was found (all $F \leq 0.772$, all $p \geq 0.388$). These results suggest that the target double step paradigm was successful in reducing the size of tactile saccades similarly for both adapted locations and that this decrease was significantly larger than in the CTRL (no-step) paradigm.

b. Gain change ratio between PRE and POST phases

The results of this analysis, illustrated in Figure 7B, revealed that the gain change ratios of tactile RS performed toward the two trained targets (index and middle fingers) were larger in the ADAPT session than in the CTRL session. Indeed, the two-way repeated measures ANOVA showed a significant main effect of the factor Session ($F(1,24) = 10.614$, $p\text{-value} = 0.003$) (mean gain change ratio \pm standard deviation: ADAPT = 0.0877 ± 0.1594 , CTRL = -0.0272 ± 0.2102). No further main effects or interactions were found (all $F \leq 1.758$, all p values ≥ 0.197). Thus, the significantly larger

after-effect in the ADAPT session than in the CTRL session suggests that the double step paradigm exposure successfully induced adaptation of tactile saccades.

We then tested the effects of block order and of session order by adding to the previous repeated measures ANOVA the following two between-subjects factors: ‘Block order’ (Tact-Vis-Vis-Tact vs Vis-Tact-Tact-Vis) and ‘First session’ (ADAPT vs CTRL). This analysis showed neither main effect of these two additional factors, nor significant interactions between them or with the other factors (Session and Target) (all $F \leq 3.163$, all p values ≥ 0.09). These results show that the blocks order did not affect our previous conclusion.

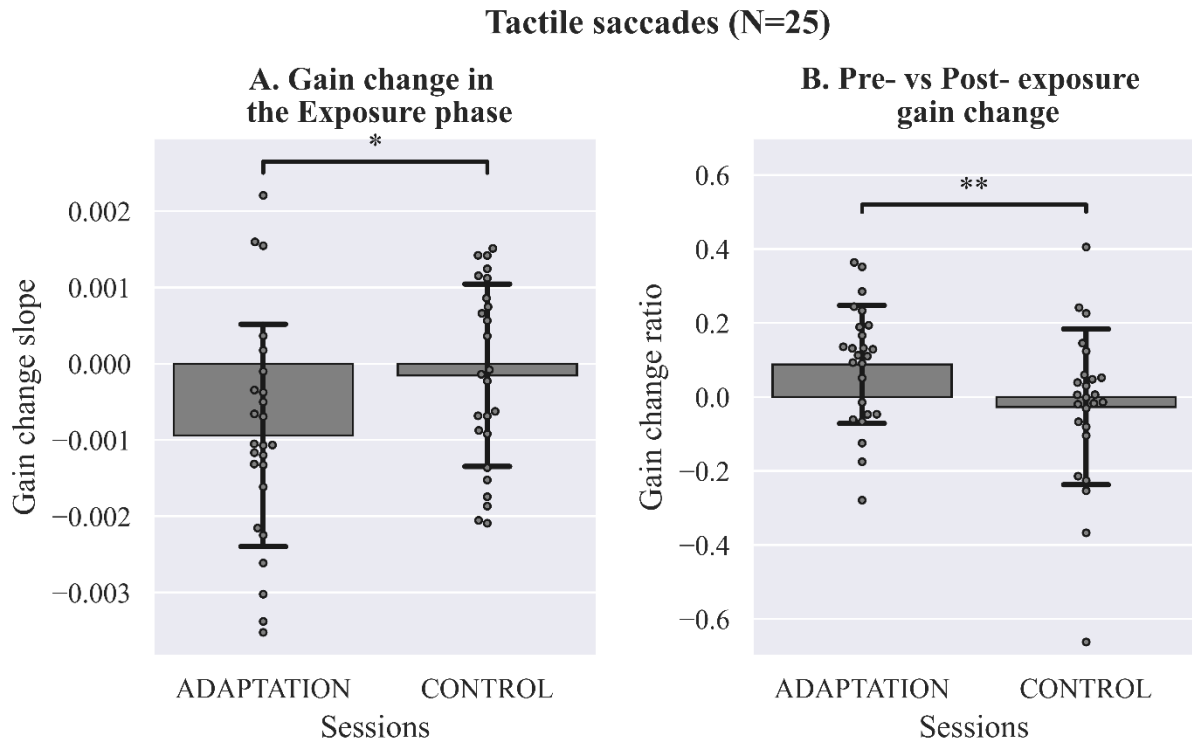


Figure 7: Experiment 2 adaptation results (all participants). Panel A: mean saccadic gain change in the exposure phase (slope of the linear regression between saccadic gain and trial number) in the ADAPTATION and CONTROL sessions. Panel B: mean saccadic gain change ratio between the PRE- and the POST-exposure phases in the ADAPTATION and CONTROL sessions. In both graphs only tactile saccades toward the index and the middle fingers were considered. Error bars represent standard deviations. *: t-test ($p < .05$), **: t-test ($p < .01$).

Transfer analysis.

As in Experiment 1, this analysis includes only the 13 participants who were significantly adapted in the ADAPT session for at least one of the two ‘adapted’ fingers (middle and/or index finger)(see Methods).

The 2-way repeated measures ANOVA performed on the gain change ratio of tactile non-adapted RS showed significant main effect of the factor Session ($F(1, 12) = 8.198$, p -value = 0.014) as well as a significant Session \times Target location interaction ($F(1, 12) = 6.127$, p -value = 0.029). Post hoc

pairwise Bonferroni comparisons performed to assess this interaction showed significant differences between sessions for both the ring (p-value = 0.014) and thumb (p-value = 0.031) fingers (mean \pm standard deviation for ring finger: ADAPT = 0.222 ± 0.202 , CTRL = 0.016 ± 0.221 , Thumb finger: ADAPT = 0.186 ± 0.087 , CTRL = 0.106 ± 0.116). It revealed neither significant difference between Target locations in the ADAPT session (p-value = 0.473) nor in the CTRL session (p-value = 0.086). There was no significant main effect for the factor Target location ($F(1, 12) = 0.436$, p-value = 0.521). These results (plotted in Figure 8A) suggest that the adaptation of tactile RS generalized to tactile RS toward nearby non-adapted locations.

We then tested the potential effects of block order and session order by an ANOVA with two additional between-subjects factor 'Block order' (Tact-Vis-Vis-Tact vs Vis-Tact-Tact-Vis) and 'First session' (ADAPT vs CTRL). This analysis showed neither significant main effect of Block order and First session, nor significant interaction between these two factors or with the other within-subjects factors (all $F \leq 3.018$, all p-values ≥ 0.116 .)"

The 2-way repeated measures ANOVA performed on the gain change ratio for visual non-adapted RS showed a significant main effect of the factor Session ($F(1, 12) = 13.462$, p-value = 0.003) (mean \pm standard deviation: ADAPT = 0.034 ± 0.062 , CTRL = -0.008 ± 0.048). No other main effects or interaction were found in this ANOVA (all $F \leq 2.444$, all p-values ≥ 0.113). These results (plotted in Figure 8B) suggest that the adaptation of tactile RS transferred to visual RS performed toward all tested locations.

We also tested the potential effects of block order and session order by a similar ANOVA with two additional between-subjects factor 'Block order' (Tact-Vis-Vis-Tact vs Vis-Tact-Tact-Vis) and 'First session' (ADAPT vs CTRL). This analysis showed neither significant main effect of Block order and First session, nor significant interaction between these two factors or with the other within-subjects factors (all $F \leq 1.606$, all p-values ≥ 0.237).

In summary, the current analysis indicates that the gain of tactile RS to non-adapted targets (ring and thumb fingers) as well as the gain of all non-adapted visual RS decrease specifically in the ADAPT session, therefore showing that tactile RS adaptation generalized to nearby locations and transferred to visual RS.

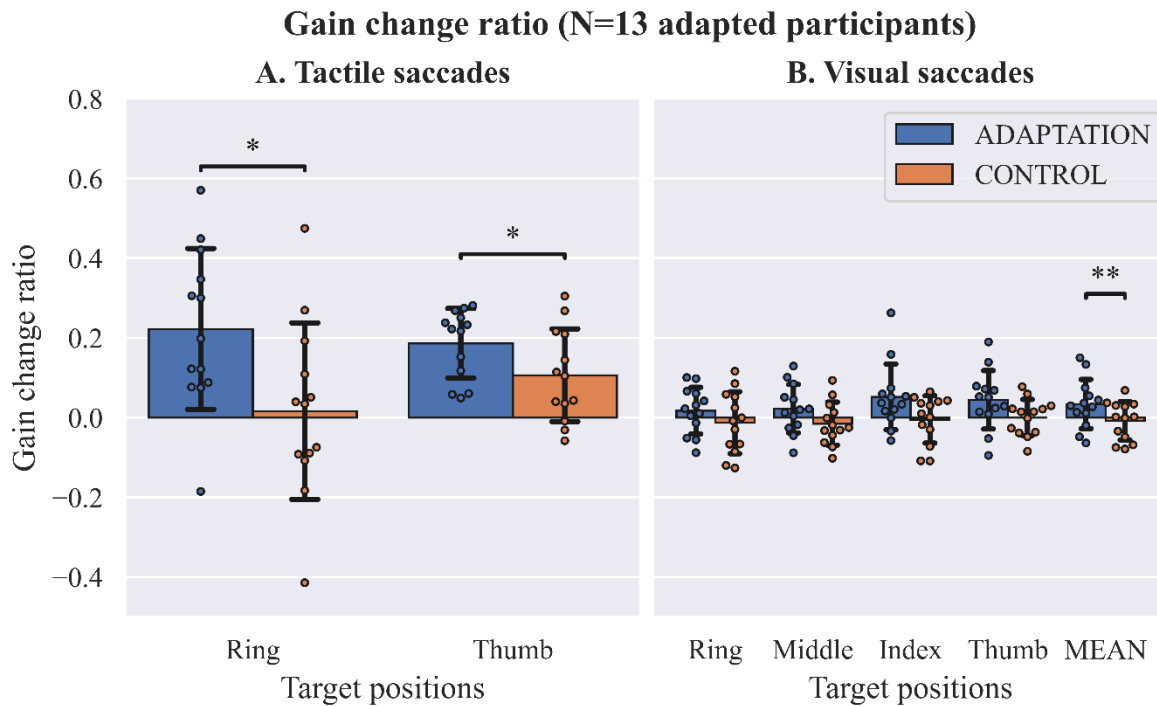


Figure 8: Experiment 2 generalization and transfer results (only adapted participants). Mean saccadic gain change ratio in the ADAPTATION and the CONTROL sessions, plotted as a function of the target location separately for tactile (Panel A) and visual (Panel B) saccades, as well as the grand mean (MEAN) of gain change ratio across all locations for visual saccades. Only non-adapted locations are plotted in this figure. Error bars represent standard deviations. *t*-tests : * ($p < .05$), ** ($p < .01$).

Proprioceptive drift

As shown in Figure 9, participants underestimated the location of their unseen middle finger location. This proprioceptive drift increases with time from PRE to POST phase (Figure 9B), but importantly, it did so similarly in both the ADAPT and the CTRL sessions (Figure 9A). Indeed, the repeated measure ANOVA indicates a significant main effect of the factor Phase ($F(1, 24) = 18.59, p < 0.001$) (mean estimations (in degree) \pm s.d.: PRE = 9.49 ± 3.1 , POST = 7.9 ± 3.9), but no significant main effect of the factor Session, and no significant Session \times Phase interaction (all $F \leq 1.453$, all $p \geq 0.240$). Therefore, the decrease of saccadic gain observed for tactile RS in the ADAPT session (see previous sections) appears unrelated to the proprioceptive drift.

Proprioceptive drift (N=25)

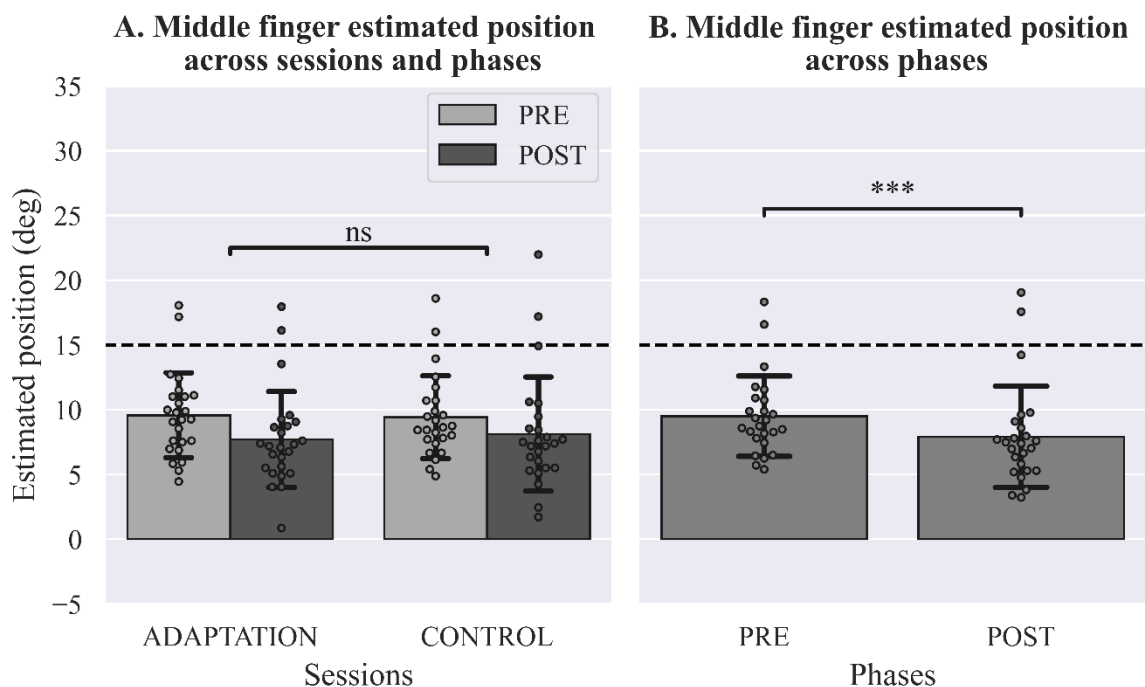


Figure 9: Experiment 2 proprioceptive drift results (all participants). Mean estimated position of the middle finger location in the PRE- and POST- proprioceptive location assessment phases of the ADAPTATION and CONTROL sessions plotted separately (Panel A) and as a grand mean pooled over both sessions (Panel B). The dotted line represents the actual middle finger real location. Error bars represent the standard deviation. ns : t -test ($p > .05$), *** : t -test ($p < .001$).

Discussion

In this study, we sought to determine whether RS adaptation operates at the motor level, i.e., modifying the saccadic command. To test this hypothesis we adapted, separately, reactive visual or tactile saccades and we investigated the transfer of adaptation to the non-adapted modality, the reasoning being that if motor, then saccadic adaptation should also transfer to saccades triggered by other sensory modalities. We found in Experiment 1 that adaptation of reactive visual saccades strongly transferred to tactile saccades and we reported for the first time in Experiment 2, experimental support for the existence of adaptation of tactile saccades, although this adaptation transferred to visual saccades only slightly. In the following sections, we discuss the results obtained in this study in respect to the existing literature on saccadic adaptation.

Within the visual modality, saccadic adaptation has been shown to transfer to non-adapted saccades according to a spatial gradient known as the adaptation field (Frens & van Opstal, 1994; Pélisson et al., 2010). This means that adaptation of a given saccade fully transfers to all saccades with the same vector, i.e., direction and amplitude, irrespective of their initial/final position and that, conversely, the rate of transfer progressively decreases as the amplitude and/or the direction of the tested saccades deviates from the adapted vector. When the deviation of direction between the two

saccade vectors reaches 90° no transfer of adaptation is observed at all, but with a deviation of 45° a transfer of about 50% occurs, reflecting a large adaptation field. The visual adaptation field is also quite extended along the saccade amplitude dimension and is asymmetric (Collins et al., 2007), with a higher rate of adaptation transfer to saccades larger than the adapted saccade compared to smaller-sized saccades.

Here, while we replicate the adaptation field finding (Experiment 1) for the visual modality, we reveal for the first time (Experiment 2) the existence of adaptation for tactile saccades (discussed below). In addition, we further disclose that tactile saccades adaptation also displays an adaptation field. Indeed, after the adaptation of tactile saccades toward the middle and the index finger a generalization of adaptation has been shown to non-adapted tactile saccades toward the ring and the thumb fingers. Moreover, the high amount of adaptation spatial generalization seen for both sensory modalities in the present experiments fits with the existence of wide adaptation fields and can further be attributed to the simultaneous training of two slightly different saccade vectors (to the middle and the index finger). Importantly, this spatial generalization further argues that the decrease in tactile saccades gain during the exposure phase of the adaptation session in Experiment 2 is not related to a strategy followed by participants to saccade directly toward the second tactile stimulation but rather to a plastic gain reduction resulting from backward adaptation mechanisms. This interpretation is also compatible with the significant after-effect on the saccade gain observed in the POST-exposure phase in comparison to the PRE-exposure phase.

The transfer of visual saccades adaptation to saccades in a different modality has been reported so far for auditory saccades only, as indicated in the introduction (Collins et al., 2010; Frens & van Opstal, 1994). With Experiment 1, we were able to show that an adaptation transfer exists also from visual to tactile saccades. These cross-modal, visual-to-auditory, and visual-to-tactile, transfers of adaptation argue for a motor functional locus of RS backward adaptation common for saccades in all modalities and possibly situated at the cerebello-brainstem level. Furthermore, this hypothesis would also predict a significant cross-modal transfer of adaptation in the reverse direction, i.e., from tactile saccades to visual saccades. Indeed, Experiment 2 provided evidence for the existence of such transfer, which however, turned out to be much smaller than the visual-to-tactile transfer of adaptation. Note that the mere presence of some transfer provides another piece of evidence for our interpretation that adaptive processes largely dominated potential strategies in the decrease of tactile saccade gain observed during exposure. This strong asymmetry of adaptation transfers between visual-to-tactile versus tactile-to-visual suggests multiple adaptation functional loci for tactile saccades, with at least one located upstream from the adaptation locus of visual saccades and from of the oculomotor commands common to all saccade's modalities.

Vision is known to be the dominant sensory modality that we rely on to localize in our environment the targets of our motor responses, including saccades (Neggers & Bekkering, 1999; Sullivan et al., 2004). When auditory and visual or tactile and visual targets are presented

simultaneously at relatively close locations, the perception of auditory and tactile targets is biased toward the visual ones if the latter provides clear information about its location, a phenomenon known as the ventriloquist effect (Alais et al., 2010). Furthermore, the dominance of vision and its important role in shaping the perception from other senses can be seen in the deficits in auditory localization in children with visual impairment compared to normal-sighted children (Cappagli & Gori, 2016). The separation of functional adaptation loci that we suggest based on the asymmetrical cross-modal transfer can be also thought as a higher weight given by the adaptation processes to visual information in comparison to other sensory modalities, leading to a generalization of saccadic adaptation induced by a visual error to saccades performed toward tactile or auditory targets but only partially in the other way around. According to this hypothesis, the adaptation of auditory saccades, if possible, should also transfer asymmetrically to visual saccades. Further studies will test this prediction and should first determine whether auditory saccades can be adapted at all.

The second main finding of our study is that RS toward tactile targets can be adapted, even though its prevalence appears reduced as compared to visual RS adaptation (several individual participants failed to demonstrate a significant after-effect). To our knowledge, this is the first demonstration that the gain of non-visual saccades can be reduced with a modified version of the double step target paradigm. Tactile saccades (like other non-visual saccades) differ from visual saccades by their longer latency, their reduced speed and, critically in the context of saccade adaptation, their gain is much more variable and lower on average. Also, the modified double step paradigm used here to adapt tactile saccades may differ from the double step paradigm originally designed to adapt visual saccades by the way that the change of stimulated finger during the ongoing saccade is interpreted by participants' central nervous system. In particular, since this double tactile stimulation was consciously detected by all except one participant (as confirmed by report at debriefing), as opposed to the intra-saccadic target step of the visual saccade adaptation procedure, which is frequently masked by saccadic suppression, one may wonder whether it can truly yield an adequate error signal for adaptation mechanisms. These peculiarities lead us to consider whether the decrease in tactile saccades gain seen in the adaptation exposure of Experiment 2 is related to genuine adaptation mechanisms and to discuss potential alternative explanations. The first alternative cause is strategy, that our participants could have used during exposure as they consciously detected the change in location of tactile stimulation during their saccades. However, the gain of tactile saccades 1) progressively decreased (see supplemental figures) during the adaptation exposure phase and 2) remained low in the post-exposure phase (after-effect) despite the fact that the tactile target no longer 'jumped'. These observations differ i) from the sudden drop of saccade gain which can be expected at the beginning of the exposure phase if participants only used a conscious strategy, and ii) from the immediate recovery of saccade gain which can be expected at the beginning of the post-exposure phase when target no longer jumps, and the potentially associated strategy, are discontinued. As explained in the method sections the order of the visual and tactile saccades block was

counterbalanced between participants. Therefore, in experiment 2 half of our participants performed the visual POST-exposure block directly after the exposure phase and only then, the tactile POST-exposure block, making highly unlikely the possibility that they maintained a strategy across a complete block of visual saccades. In addition, if such strategy was used by the remaining participants who performed the tactile POST-exposure block immediately after exposure, we should have seen an effect of ‘block order’ when tested as a between subjects factor in the ANOVA of gain change ratio, which was not the case. In previous saccadic adaptation studies, including when the intra-saccadic visual target step is consciously detected (Fujita et al., 2002; Heins et al., 2019; Heins & Lappe, 2024), both the slow gain change during exposure and the post-exposure after-effect are considered as hallmarks of true (or implicit) adaptation. Furthermore, a recent study by Heins and Lappe (Heins & Lappe, 2024) showed that saccadic adaptation takes place even when the error was attributed to external sources i.e. to error in machine decoding. In their experiment, participants were presented with a fixation point around which multiple objects were placed in a circular array. They were instructed to choose a certain object while fixating and then to communicate this object to the computer by performing a saccade toward it once the fixation point disappeared. At the end of the saccade, a feedback about the decoded chosen target was presented to the participants. Participants were warned that some bias could be erroneously added to the saccade endpoint information used to decode which target they chose, and that in such case they have to take into account these mistakes to keep trying enabling the machine to correctly decode the chosen targets. The results of this experiment show that changes in saccades trajectory occurred progressively during exposure and were preserved in post exposure indicating a genuine adaptive learning even though participants applied some strategies in order to reach a better machine decoding performance. In addition, another study performed by the same team (Heins et al., 2019) showed that backward saccadic adaptation occurs when participants were aware of the intrasaccadic step irrespective of whether they were told to follow the target step at the end of the primary saccade, or to ignore this second step and maintain fixation on the first target location. Also, in the tactile modality, it is well-established that healthy people make frequent errors in determining the identity of touched fingers (Rusconi et al., 2009; Tamè et al., 2017). Therefore, in Experiment 2 even if participants can clearly feel that 2 fingers were touched, it cannot be taken for granted that they know which ones, nor which exactly was the last one, therefore making the use of a strategy less likely. Despite all these considerations, and according to a reviewer’s suggestion, the hypothesis that changes in tactile saccade gain in Experiment 2 are due to strategic responses of participants to the double-finger stimulation during exposure cannot be ruled out in full. For this, further experiments will be necessary, for example by testing whether these changes of tactile saccade gain do transfer to other spatial locations/body parts.

The second alternative is fatigue, which would also account for the decrease of the amplitude of the tactile saccades in Experiment 1. Yet, our control sessions of both Experiments 1 and 2 argue against this possibility. Indeed, we have seen no significant changes in tactile or visual saccades gain

either during the exposure phase or between the PRE- and the POST-exposure phases of the control sessions. Thus, the gain changes observed during the exposure of adaptation sessions were specific, ruling out any explanation based on fatigue.

A third alternative explanation of the tactile saccades gain decrease seen in the adaptation sessions of this study is the proprioceptive drift. In the dark, the perception of our hands placed in an eccentric position tends to drift toward our midline progressively over time, as shown by Wann and Ibrahim (Wann & Ibrahim, 1992) and we still don't know why it occurs. In this study we showed that our participants' perception of their right hand's middle finger did drift toward their midline, with a higher drift rate reached in the POST- vs PRE- proprioceptive assessment blocks. Importantly however, this drift did not differ between the adaptation and the control sessions, which provided evidence that the proprioceptive drift was not responsible for the decrease in tactile saccades gain seen both in Experiment 1 and in Experiment 2.

Thus, altogether and in addition to the partial tactile-to-visual transfer demonstrated, these observations led us to propose that saccades toward tactile targets can both be modified via transfer of visual saccade adaptation (Experiment 1) and can themselves be directly adapted (Experiment 2).

An interesting issue raised by the present findings concerns the nature of error signals driving saccadic adaptation. Four main candidates have been considered in the literature: corrective saccades, post-saccadic retinal error, prediction error and postdiction error. Although corrective saccades and post-saccadic retinal error are the simplest motor or sensory signals the brain can use to monitor the accuracy of primary saccades, experimental evidence soon argued in favor of the prediction error (Bahcall & Kowler, 2000; Guillaume et al., 2018; Herman et al., 2013; Wallman & Fuchs, 1998). This prediction error hypothesis (Collins & Wallman, 2012; Wong & Shelhamer, 2011) states that the error signal is the result of a comparison between the predicted error (target location relative to the saccade landing position predicted from the efference copy) and the actual error (post-saccadic target retinal image relative to the fovea). In their recent modeling study, Masselink and Lappe (Masselink & Lappe, 2021) proposed the postdictive error hypothesis, according to which error signals driving saccadic adaptation mechanisms result from a comparison between the motor command of the saccade and the post-saccadic visual error postdicted back to pre-saccadic space based on the efferent copy. Note that in all these four different accounts, saccadic adaptation always relies on visual information of post-saccadic target location either directly (post-saccadic retinal error hypothesis) or indirectly through the generation of a corrective saccade, or through the computation of the prediction error or of the postdiction error. In sharp contrast, the present Experiment 2 suggests that saccades toward tactile targets, thus executed in absence of any visual feedback, could still be adapted. Therefore, our study highlights that the saccadic error feedback involved in saccadic adaptation is not necessarily visual but can be extracted from tactile information about the target location on the body. Further studies are required to determine how this non-visual information is transformed from its native anatomical frame of reference into an eye-centered frame of reference suitable for the saccadic adaptation mechanisms.

In conclusion, we showed that the adaptation of visual RS transfers strongly to tactile RS, in favor of a motor functional locus of RS adaptation. We also revealed for the first-time evidence for a possible induction of backward adaptation of tactile RS via a tactile double step target paradigm and that this adaptation transfers very partially to visual RS, suggesting that an adaptation locus specific of tactile RS is upstream the locus of visual RS adaptation.

Data Availability

Source data for this study are openly available at

https://osf.io/ehjd2/?view_only=8fe4eda5446847be84ee6dc0968cd057

Supplemental Material

Supplementary analysis can be found at

https://osf.io/ehjd2/?view_only=8fe4eda5446847be84ee6dc0968cd057

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Disclosures

The authors declare that they have no competing interests.

Author Contributions

Conception and design of the study: A.B., V.G., M.T.N.P., A.F., and D.P; Setup preparation and Software: A.B., V.G., E.K., and R.S.; Data collection: A.B. and V.G.; Data analysis: A.B.; Data interpretation: A.B., A.F. and D.P; Original draft: A.B.; Critical revisions: A.F. and D.P; All the authors approved the final manuscript for submission.

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Study 2: Saccades adapt to visual and auditory stepping targets but with asymmetrical cross-modal transfers

Ali Batikh¹, Arthur Bertin¹, Frederic Volland¹, Eric Koun¹, Alessandro Farnè^{1§}, and Denis Pélisson^{1§}

¹*IMPACT Team of Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University Claude Bernard Lyon 1, France.*

[§]*These authors contributed equally to this work.*

Abstract

Reactive saccades are rapid eye movements performed toward salient stimuli. Saccadic adaptation maintains the accuracy of visual reactive saccades throughout life and is thought to occur at the motor level of the saccade circuitry. Recently, we demonstrated that saccadic adaptation can also correct for inaccuracies of reactive saccades toward non-visual tactile targets. However, such adaptation of tactile saccades transferred partially to non-adapted visual reactive saccades of the same amplitude, compared to a complete visual-to-tactile transfer, suggesting the adaptation occurred upstream of the motor level common to all saccade modalities. Here, we test whether those findings also apply to auditory saccades. Experiment 1 tested the visual-to-auditory transfer of both backward and forward adaptation and conversely, Experiment 2 investigated the possibility of adapting auditory saccades and the extent to which such adaptation might transfer to visual saccades. Experiment 1 revealed a complete visual-to-auditory transfer of both forward and backward adaptations. In Experiment 2, stepping the auditory target to another location while the saccade was in flight induced a significant backward adaptation, but could not elicit a significant forward adaptation. Furthermore, we found a partial auditory-to-visual transfer of backward adaptation, in agreement with our previous findings regarding tactile saccades adaptation. This work brings additional knowledge to our understanding of saccadic adaptation, highlighting the adaptive functional levels of the different saccade modalities and the underlying encoding processes of post-saccadic error signals.

Keywords: Saccadic adaptation, Vision, Audition, Cross-modal transfer

Introduction

Saccades are rapid eye movements allowing the alignment of the objects of interest with the fovea, the central part of the retina characterized by its high acuity. Saccades triggered by the sudden appearance of targets in the visual field are classified as reactive while those performed based on our internal

goals as voluntary. Saccadic adaptation is the mechanism surveilling the precision of our saccades and maintaining their accuracy throughout life. Saccadic adaptation has been studied widely thanks to the double-step target paradigm introduced by McLaughlin in 1967 (McLaughlin, 1967). This paradigm consists of shifting the visual target while the saccade is in flight, thus creating a mismatch between the eye landing position and the visual target location. Typically, this target shift is not consciously perceived due to saccadic suppression. Shifting the visual target toward the eye's initial position (backward) results in an overshooting error of the saccade. The repetition of such trials induces an adaptive decrease in saccade amplitude, also known as backward adaptation, in order to nullify the encountered error. In contrast, shifting the target in the direction of the saccade (forward) leads the saccade to undershoot the target, and across repetitions, the saccadic system increases progressively the saccade amplitude, known as forward adaptation (for review, see: (Iwamoto & Kaku, 2010; Pélisson et al., 2010).

Saccadic adaptation was shown to generalize to saccades of the same vector performed from different initial eye positions. The extent to which saccadic adaptation generalizes to nearby non-adapted locations defines the adaptive field. The adaptive field is broad along its two dimensions, i.e. saccade direction and amplitude. Indeed, adaptation generalizes significantly to saccades which direction deviates up to 60° from the adapted saccade direction but not to orthogonal saccades (90°) nor saccades toward the opposite direction (Alahyane et al., 2008). Saccadic adaptation also generalizes to saccades of various amplitudes around the adapted saccade size (Collins et al., 2007; Schnier et al., 2010). Whereas it is symmetric along the direction dimension, the generalization is asymmetric along the amplitude dimension, being higher for saccades larger, compared to those shorter, than the adapted saccade. These adaptation field characteristics are similar for both types of adaptation, backward and forward.

Forward and backward adaptation rely on partially distinct mechanisms. Indeed, forward adaptation is less prevalent, slower to develop over time and results in lower adaptation aftereffects compared to backward adaptation (for the same number of trials and the same target's second step size) in both humans and monkeys (M. Panouillères et al., 2009, 2013; M. T. N. Panouillères et al., 2012; Robinson et al., 2003). In addition, a transfer to hand pointing movements has been observed only for forward, but not backward, adaptation of reactive saccades, suggesting that the latter occurs downstream the visual representation of the target, at the motor level of saccadic commands generation, while forward adaptation occurs partly at that motor level but also at the level of visual target representation (Hernandez et al., 2008). Furthermore, backward (but not forward) adaptation of reactive saccade transfers to anti-saccades performed in the adapted direction (M. Panouillères et al., 2009), which suggests again that backward adaptation occurs at a motor level, namely downstream from the vector inversion process of anti-saccades (which has been suggested to take place in the posterior parietal cortex (PPC) and/or the frontal eye field (FEF) (Jaun-Frutiger et al., 2013; Zhang & Barash, 2004)). Finally, the two types of adaptation have been shown to be accompanied by different

kinematics changes, an increase in saccade duration for forward adaptation compared to a decrease in both the saccade duration and peak velocity for backward adaptation (Golla et al., 2008).

Different adaptation mechanisms were also suggested for reactive and voluntary saccades. Several studies showed an asymmetrical pattern of adaptation transfer, with a stronger transfer from voluntary to reactive saccades than in the opposite direction (Alahyane et al., 2007; Collins & Doré-Mazars, 2006; Cotti et al., 2007; Zimmermann & Lappe, 2009). In addition, adaptation of voluntary saccades, but not of reactive saccades, transfers to hand-pointing responses (Bekkering et al., 1995; Cotti et al., 2007) which suggests the involvement of a target representation level common to both types of movement (saccades and hand movements). Furthermore, (Cotti et al., 2009) found that backward adaptation of reactive saccades transfers to anti-saccades performed in the adapted direction, while backward adaptation of voluntary saccades transfers to anti-saccades performed in both the adapted and the non-adapted directions. These authors thus proposed that voluntary saccade adaptation acts at two levels, both upstream and downstream of the vector inversion site(s) of anti-saccades, whereas reactive saccade adaptation acts only downstream of the inversion site(s), at the motor level of saccadic commands generation.

Saccades are frequently made to visual targets, but can also be performed toward non-visual targets such as sound and touch stimuli. Saccades toward tactile (or somatosensory) as well as auditory targets are characterized by their lower accuracy, longer latency, and lower peak velocity in comparison to visual saccades of similar size (Frens & Van Opstal, 1995; Groh & Sparks, 1996a; Sullivan et al., 2004; Yao & Peck, 1997). Saccades aimed at non-visual targets require the target location information to be translated into an oculocentric frame of reference usable by the saccadic system. Such coordinate transformation was proposed to occur at the level of the deep and intermediate layers of the superior colliculus (SC) for both tactile (Groh & Sparks, 1996b, 1996c) and auditory saccades (Jay & Sparks, 1987a, 1987b). Tactile and auditory saccades can be used as tools to investigate saccadic adaptation. For instance, if as previously described, adaptation of visual reactive saccades occurs at a motor level common to all saccade modalities, it should then transfer to saccades performed toward auditory and tactile targets at the same location as the adapted saccade visual target. Indeed, we have previously shown (Batikh et al., 2024) that backward adaptation of reactive visual saccades showed a full cross-modal transfer to tactile saccades (toward stimulated fingers) performed toward the adapted locations and toward nearby non-adapted locations. Some preliminary supports for a transfer of adaptation from visual to auditory reactive saccades have also been reported, but based on a limited sample (Frens & van Opstal, 1994) or in the absence of a direct comparison to visual saccades adaptation after-effects (Collins et al., 2010). In addition, neither of these studies did investigate whether the transfer occurred for nearby auditory targets. Finally, the visual-to-tactile and the visual-to-auditory transfers of adaptation were investigated only for backward adaptation, such that possible cross-modal transfers of forward adaptation remain completely unknown to date.

In our previous study (Batikh et al., 2024) we went further and investigated the possibility of adapting tactile saccades using a modified double-step target paradigm. Our results showed that backward adaptation of tactile saccades can indeed be induced, as evidenced both by a progressive decrease of amplitude during the exposure phase and by an adaptation after-effect in the post-exposure phase, therefore providing evidence that saccadic adaptation can take place in the absence of post-saccadic visual error. We further showed that backward adaptation of tactile saccades generalizes completely to tactile saccades performed toward nearby non-adapted locations, thus extending to somatosensation the well-established adaptive field features that are the fingerprint of saccadic adaptation towards visual targets. Importantly, we additionally found that tactile saccadic adaptation only partly transferred to saccades performed toward visual targets, despite the latter being displayed at the same locations as tactile targets, suggesting that the locus of adaptation may differ depending on the sensory modality. Nevertheless, as most of our participants were aware of the double step of the tactile stimulation that we used to induce adaptation of tactile saccades, we couldn't completely rule out the possible influence of a strategy being employed by the participants to reduce their tactile saccade amplitude.

In this study, we aim first (Experiment 1) to replicate the visual-to-auditory transfer of backward adaptation (Collins et al., 2010; Frens & van Opstal, 1994), test whether this cross-modal transfer extends to non-adapted locations, and further examine whether a visual-to-auditory transfer also exists for forward adaptation. Second (Experiment 2), using a strategy similar to the one we previously used for tactile saccades (Batikh et al., 2024), we investigate whether it is possible to induce both backward and forward adaptation of reactive auditory saccades and whether this adaptation transfers to reactive visual saccades. Answering these questions will increase our understanding of the functional levels and error signals of saccadic adaptation.

General Methods

Sample size estimation

We calculated our sample sizes with the open-access software G*Power 3.1.9.7, using effect sizes of 0.4 (strong effect) and 0.25 (moderate effect) for Experiments 1 and 2, respectively. These effect sizes were chosen based on the visual-to-auditory transfer reported in Collins et al.'s study (Collins et al., 2010) and the moderate adaptation of tactile saccades showed by Batikh et al. (Batikh et al., 2024). The other G*Power parameters used for both experiments were $\alpha = 0.05$, power = 0.8, non-sphericity correction $\epsilon = 1$, and correlation among repeated measures = 0.5. This resulted in 15 and 34 participants being estimated for Experiment 1 and 2, respectively.

Participants had normal or corrected-to-normal vision, and they reported normal audition. They were selected if they were not simultaneously participating in other sensorimotor adaptation experiments and if they had no history of neurological, psychiatric, or cognitive disorders. They were

notified that the consumption of psychotropic drugs or alcohol and severe sleep deprivation during the last 24 hours was not permitted. Participants were asked not to wear makeup or to remove it before the experiment (to prevent any difficulty with the eye tracker).

Ethical statement

Both Experiment 1 and Experiment 2 of the present study conformed with the Code of Ethics of the World Medical Association (Declaration of Helsinki 1964) and were approved by the ethics committee of INSERM U1028 (IRB00003888; decision n° 21-762). Informed consent was obtained from every participant before each experiment. Participants were paid 15 euros per session for their participation.

Experimental setup

Participants were seated on a chair, facing a table supporting an ensemble of 6 speakers and 7 light-emitting diodes (LED, 2 mm in diameter) positioned 76 cm from their eyes, mounted on thin, black-painted sticks, which were placed on a semi-circular wooden support. The participant's head was stabilized using a chin rest and forehead support, and their hands were placed on the table. The central LED served as a fixation point, the six remaining LEDs served as visual targets situated at 10, 15, and 20 degrees to the left and the right of the fixation point. Auditory targets were six speakers (15 mm in diameter, LSM-S20K, Ekulit), each placed 3 cm above the corresponding peripheral LED (see Figure 1). The sound emitted by speakers consisted of a pink noise, the intensity at the subject's ear level was 60 dB on a background of 30 dB.

Experiments were performed in a dark room and several additional measures were taken to prevent participants from seeing the speakers' positions and from getting any information about the location or number of auditory targets: the whole setup and the background behind it (curtain) was black; the LEDs intensity used during the experiment was kept low; the setup (visual and auditory targets) were hidden with a large black cardboard at the beginning of each session when the participants first entered the room, as well as at the end of the experiment while the participants were leaving. Binocular eye movements were recorded at a frequency of 1000 Hz using the desktop configuration of the EyeLink 1000 plus infrared tracker (SR Research EyeLink® 1000 plus, Canada).

The LEDs and the speakers were connected via parallel ports to a display computer, and the sequences of events were programmed and controlled by the Experiment Builder software (SR Research).

Each session started with a calibration of the eye tracker by asking participants to fixate on five targets consisting of the fixation LED as well as 4 LEDs other than the ones that served as saccade targets, 2 located 25 degrees to the left and the right of the fixation point and 2 located 10 degrees above and below the fixation point.

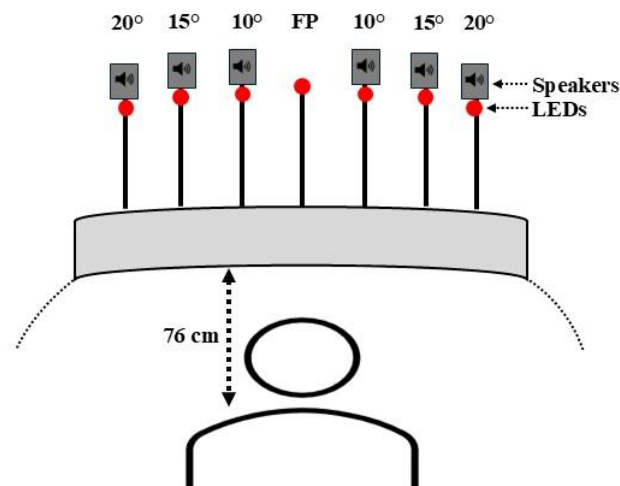


Figure 1: Schematic representation of the experimental setup. The participants sat at 76 cm from a semi-circular wooden support. Seven black-painted sticks were fixed on the support, 6 of them holding both a speaker and a LED (peripheral auditory and visual targets), the remaining one containing a LED only (central fixation point).

Experiment 1: The Adaptation Of Visual Saccades And Its Subsequent Transfer To Auditory Saccades.

Materials And Methods

Participants

Seventeen naïve volunteers were included in this experiment. Two participants had hypermetric auditory saccades that exceeded the camera's detection range; therefore, they were excluded after their first session. The remaining fifteen volunteers were right-handed, including three males and 12 females. Their mean age was 25.67 ± 5.38 years old (range 18 to 40).

Design

Each participant performed two experimental sessions in which we induced either backward or forward adaptation of visual reactive saccades. The order of the sessions was counterbalanced between participants (7 participants started with the backward adaptation session and 8 with forward adaptation). In each session, saccadic adaptation was induced for a single direction of saccades

(leftward or rightward) ; therefore, saccades in the opposite, non-adapted, direction served as control. The direction of adapted saccades (hence that of control saccades as well) was switched between the two sessions for each participant, and assigned in the following way in two groups of participants: the first group of participants (N=7) performed backward adaptation of rightward saccades (B-R) in one session and forward adaptation of leftward saccades (F-L) in the other session (B-R/F-L) whereas the second group (N= 8) had the opposite pattern (B-L/F-R). Both sessions were separated by at least seven days to avoid any cross-over effects related to the retention of adaptation (Alahyane & Pélisson, 2005; Wang et al., 2012)

Each experimental session consisted of three phases: a PRE- and a POST-exposure phase, in which participants performed simple visual and auditory reactive saccades, separated by an Exposure phase where visual saccades were adapted.

During PRE-exposure, the baseline performance of visual and auditory saccades was measured. Participants performed first 72 saccades directed toward one of the six auditory targets (auditory block, 12 saccades per target) followed by 60 saccades directed toward one of the six visual targets (visual block, 10 saccades per target). All trials started with the participants looking at the fixation point. After a random duration (2000 to 2750 ms), the fixation point was turned off, and simultaneously one of the peripheral stimuli (visual or auditory, depending on the block) was presented randomly. Participants were instructed to move their eyes toward the target location as rapidly and precisely as possible. During the saccadic response, when the eye exceeded a $60^{\circ}/s$ velocity threshold, the target was terminated, but participants had to maintain gaze fixation on the now-absent target until the reappearance of the fixation point (1000 ms later). When the fixation point reappeared, the participant had to prepare for the next trial by looking back to the fixation point and, when necessary, to blink during this return period in order to reduce the amount of blinking during the recorded saccades period.

In the Exposure phase, participants performed 120 visual reactive saccades randomly directed toward the LEDs located 15 degrees to the left or the right of the fixation point. As in the PRE-exposure phase, each trial started with a fixation period, which ended when the visual stimulus appeared. In the backward adapted saccade trials, the detection of the saccade onset ($60^{\circ}/s$ velocity) triggered a 5 degrees backward intra-saccadic displacement of the target (the 15° LED extinguished simultaneously with the illumination of the 10° LED). In the forward adapted saccade trials, the detection of the saccade onset triggered a 5 degrees forward intra-saccadic displacement of the target (the 15° LED extinguished simultaneously with the illumination of the 20° LED). In the non-adapted saccades trials (Control trials), the visual target remained at its initial 15° location. In all trials, the target remained visible for 500 ms after the saccade onset, disappearing 1000 ms before the re-appearance of the fixation point.

The POST-exposure phase was identical to the PRE-exposure phase except that the visual block was performed immediately after the Exposure phase, then followed by the auditory block.

At the beginning of each session, participants performed a short training phase consisting of a block of visual saccades (2 saccades per target location) followed by a block of auditory saccades (6 saccades per target location). These saccade trials were similar to the Control trials performed in the Exposure phase (the target did not jump and remained visible for 500 ms after saccade onset). The data from this training phase were not analyzed.

Data processing and parameter extraction

Horizontal and vertical eye positions were analyzed offline using MATLAB. Saccades onset and offset were identified based on a velocity threshold of 15°/s. Saccade amplitude was measured as the difference between eye positions 50 ms before the saccade onset and 50 ms after the saccade offset. We extracted the following variables for each saccade: 1) gain: ratio between the saccade amplitude and the target initial eccentricity (difference between target position and saccade starting position); this parameter presents the advantage, over saccade amplitude, of being expressed relative to the target distance, thus allowing us to measure the mean accuracy of saccades toward targets of different eccentricities pooled together; 2) latency: time between the appearance of the initial target and the saccade onset; 3) duration: time between saccade onset and saccade offset; 4) peak velocity: maximum eye velocity reached during the saccade. The following trials were excluded from the analysis (2.92% of the trials in total): trials where the saccadic gain fell outside the range defined by the mean gain $\pm 3 \times$ standard deviations (calculated and applied for each participant across each session, phase, modality, and target location separately), trials where the saccade latency was lower than 80 ms or higher than 700 ms, and trials where a blink occurred during the primary saccade.

Two additional parameters were then calculated. First, in the exposure phase, the slope of the linear relationship between visual saccade gain and trial number was calculated separately for leftward and rightward saccades. Second, for each target location and separately in the adapted and the non-adapted modality, the ratio of saccadic gain change between the PRE- and POST-exposure phases was calculated as:

$$\text{Gain change ratio} = (\text{Gain PRE} - \text{Gain POST}) / \text{Gain PRE}.$$

A positive gain change ratio indicates a decrease in saccadic gain in the POST-exposure phase compared to the PRE-exposure, compatible with backward adaptation. In contrast, a negative gain change ratio indicates an increase in saccadic gain, compatible with forward adaptation.

Analysis

Statistical analyses were performed using IBM SPSS statistics 29.0.0.0. First, to check if the double-step exposure successfully elicited adaptation of visual reactive saccades, we analyzed visual saccades performed toward the 15° targets. In each session, saccades associated during exposure to a double-step target were considered as the ‘adapted saccades’ (referred to as ADAPT). Such saccades were compared to ‘non-adapted’ saccades (referred to as CTRL) of the other session, i.e. saccades performed to the same no-jump target (same direction and eccentricity). The slope of the linear

relationship between saccadic gain and trial number, as well as the gain change ratio, were submitted to two separate repeated measures ANOVAs with the factor ‘Adaptation type’ (FORWARD vs. BACKWARD), ‘Saccade type’ (ADAPT vs. CTRL) as a within-subjects factor. In order to check for effects of ‘Group’ (B-R/F-L vs. B-L/F-R) as well as of ‘Session order’ (backward-first vs. forward-first), we performed two separate ANOVAs similar to the just presented ones but with the two additional between-subjects factors ‘Group’ and ‘Session order’.

In order to investigate whether the adaptation of saccades to the 15° visual target (VIS 15) generalizes to saccades toward the 10° and 20° targets (VIS 10 and VIS 20), as well as if this adaptation transfers to saccades toward different auditory targets (AUD 10, AUD 15, and AUD 20), we submitted separately for each adaptation type (FORWARD vs. BACKWARD) the gain change ratio to a 2-way repeated measures ANOVA with the factors ‘Saccade type’ (ADAPT vs. CTRL) and ‘Target’ (VIS 10, VIS 20, AUD 10, AUD 15, and AUD 20) as within-subjects factors.

The above transfer analysis was performed only for participants who showed a significant forward or backward adaptation, as assessed by the results of t-tests comparing the gain of the adapted visual saccades between the PRE- and the POST-exposure phases.

Finally, we investigated the effect of adaptation on the latency, duration, and peak velocity of the adapted saccade (visual saccade to 15° target). Therefore, we submitted each of those variables, and only for the participants who showed significant adaptation, to a 2-way repeated measures ANOVA with the factors ‘Phases’ (PRE- vs. POST-exposure) and the factor ‘Saccade type’ (ADAPT vs CTRL) as within-subjects factors.

Results

Slope of gain change during the exposure phase

The 2-way ANOVA performed on the slope of gain change during the exposure phase showed a significant main effect for the factors ‘Adaptation type’ ($F(1, 14) = 26.397$, $p\text{-value} < 0.001$) and ‘Saccade type’ ($F(1, 14) = 22.866$, $p\text{-value} < 0.001$), as well as a significant Adaptation type \times Saccade type interaction ($F(1, 14) = 24.786$, $p\text{-value} < 0.001$). Post-hoc pairwise Bonferroni comparison investigating the Adaptation type \times Saccade type interaction showed a significant difference between BACKWARD and FORWARD conditions for the ADAPT saccade ($p\text{-value} < 0.001$) but not for the CTRL saccade ($p\text{-value} = 0.120$). Furthermore, it showed significant differences between ADAPT and CTRL saccades for both the BACKWARD (mean gain slope \pm s.d.: ADAPT = $-10.8 \times 10^{-4} \pm 4.89 \times 10^{-4}$, CTRL = $2.84 \times 10^{-4} \pm 6.29 \times 10^{-4}$, $p\text{-value} < 0.001$) and the FORWARD (ADAPT = $3.12 \times 10^{-4} \pm 5.08 \times 10^{-4}$, CTRL = $-0.26 \times 10^{-4} \pm 2.89 \times 10^{-4}$, $p\text{-value} = 0.015$) conditions. The results of this ANOVA are represented in Figure 2A.

We then tested the effects of the session order and of the adapted hemifield by adding to the previous ANOVA the following two between-subjects factors: ‘Group’ (B-R/F-L vs. B-L/F-R), ‘First session’ (backward-first vs. forward-first). This analysis showed neither significant main effect for

these between-subjects factors nor interactions among them and the other factors of the ANOVA (all $F \leq 2.593$, all p -values ≥ 0.136).

Overall, these results suggest that the double-step paradigm was successful in both reducing and increasing the size of visual saccades for backward and forward conditions, respectively, as compared to control conditions.

Gain change ratio between PRE- and POST-exposure phases

The 2-way repeated measures ANOVA showed a significant main effect for the factors ‘Adaptation type’ ($F(1, 14) = 45.720$, p -value < 0.001) and ‘Saccade type’ ($F(1, 14) = 6.718$, p -value = 0.021), as well as a significant Adaptation type \times Saccade type interaction ($F(1, 14) = 58.750$, p -value < 0.001). Post-hoc pairwise Bonferroni comparison evaluating this interaction showed a significant difference between BACKWARD and FORWARD conditions for the ADAPT saccade (p -value < 0.001) but not for CTRL (p -value = 0.408). Furthermore, it showed significant differences between ADAPT and CTRL saccades for both the BACKWARD (mean gain change \pm s.d.: ADAPT = 0.101 ± 0.041 , CTRL = -0.007 ± 0.057 , p -value < 0.001) and the FORWARD (ADAPT = -0.058 ± 0.050 , CTRL = -0.019 ± 0.0245 , p -value = 0.038) conditions. The results of this ANOVA are represented in Figure 2B.

We then tested the effects of the session order and of the adapted hemifield by adding to the previous ANOVA the following two between-subjects factors: ‘Group’ (B-R/F-L vs. B-L/F-R), ‘Session order’ (backward-first vs. forward-first). This analysis showed neither significant main effect for these between-subjects factors nor interaction among them and with the other factors of the ANOVA (all $F \leq 1.960$, all p -values ≥ 0.189).

Overall, these results show significant backward and forward adaptation aftereffects, which were larger than the changes in saccadic gain observed when, in the control condition, the visual target remained at its location at the saccade onset.

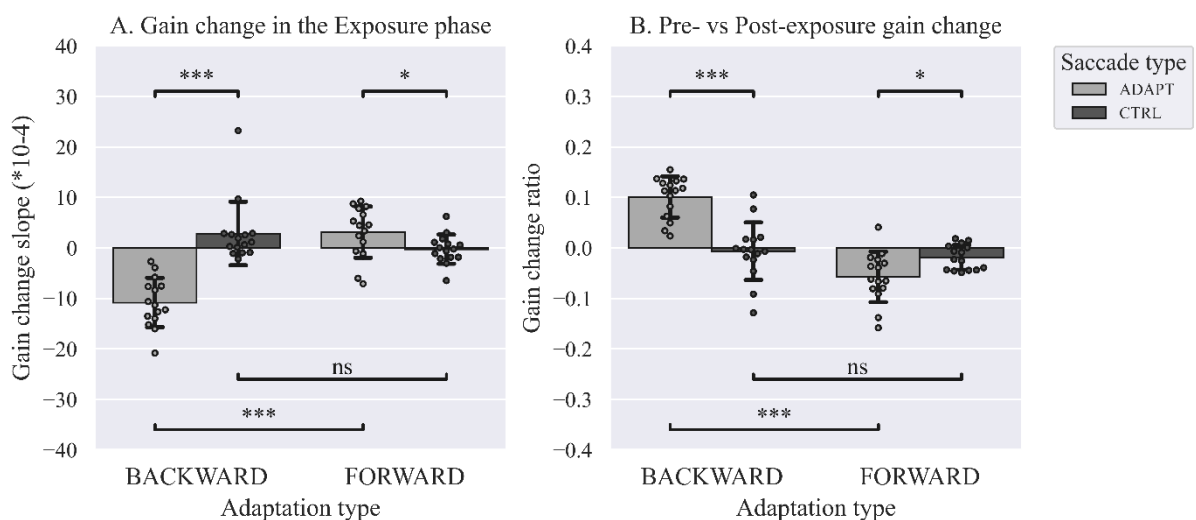


Figure 2: Experiment 1 adaptation results. A) mean saccadic gain change (\pm s.d.) in the exposure phase (slope of the linear regression between saccadic gain and trial number). B) mean saccadic gain change ratio (\pm s.d.) between the PRE- and the POST-exposure phases. Both the gain

*change slope and ratio are plotted as function of the adaptation type (BACKWARD vs. FORWARD) and the saccade type (legend: light grey for the ADAPT saccade and dark grey for the CTRL saccade). ns : t-test ($p > .05$), * : t-test ($p < .05$), ** : t-test ($p < .01$), *** : t-test ($p < .001$).*

Adaptation transfer

Here, we investigate whether the adaptation of visual saccades toward targets at 15 degrees transferred to visual saccades performed to nearby locations (10 and 20 degrees), as well as to auditory saccades performed toward sounds located at 10, 15, and 20 degrees. For this analysis, we considered only those participants who showed significant adaptation, according to student t-tests comparing the gain of the adapted saccades between the PRE- and the POST-exposure phases.

Backward adaptation transfer

All participants showed a decrease in the gain of the adapted visual saccade, however reaching significance for 11 out of 15 participants. Those 11 participants had an average gain change ratio equal to 0.1133 for the ADAPT saccade compared to an average gain change ratio equal to 0.0081 for the CTRL saccade (visual saccades to 15° targets). Based on this sample of 11 participants, the 2-way ANOVA showed a significant main effect for the factor ‘Saccade type’ ($F(1, 10) = 13.650$, p -value = 0.004) (ADAPT = 0.101 ± 0.078 , CTRL = 0.001 ± 0.045). There were no significant main effect for the factor ‘Target’ or the Saccade type \times Target interaction (all $F \leq 1.115$, all p -values ≥ 0.330).

This analysis, therefore, shows that backward adaptation of visual saccades led to significant changes of the size of visual saccades to non-adapted locations as well as to auditory saccades performed toward both the (visually) adapted and non-adapted locations.

Forward adaptation transfer

All participants except one showed an increase in the gain of the adapted visual saccade, however, this effect was statistically significant for 7 out of 15 participants. Those 7 participants had an average gain change ratio equal to -0.091 for the ADAPT saccade compared to an average gain change ratio equal to -0.011 for the CTRL saccade (visual saccades to 15° targets). Based on this sample of 7 participants, the 2-way ANOVA revealed significant main effects for the factor ‘Saccade type’ ($F(1, 6) = 16.997$, p -value = 0.006) (ADAPT = -0.049 ± 0.058 , CTRL = 0.055 ± 0.088) and ‘Target’ ($F(4, 24) = 4.578$, p -value = 0.007). There was no significant Saccade type \times Target interaction ($F(1.498, 8.990) = 1.100$, p -value = 0.354). Paired t-test assessing the main effect of the factor ‘Target’ showed no significant differences between the different levels (all p -values ≥ 0.223).

In conclusion, this ANOVA analysis shows that forward adaptation of visual saccades led to significant changes of the size of visual saccades to non-adapted as well as to auditory saccades performed toward both the adapted and the non-adapted locations.

Effect of adaptation on saccade metrics

Backward adaptation

a. Latency:

The latency of the adapted visual saccades was not affected by backward adaptation. Indeed, the 2-way Phase x Saccade type ANOVA showed neither significant main effect nor significant interaction (all $F \leq 2.033$, all p -values ≥ 0.184).

b. Duration:

The Phase \times Saccade type 2-way ANOVA showed a significant main effect for the factor Saccade type ($F(1, 11) = 10.002$, p -value = 0.01), as well as a significant Phase \times Saccade type interaction ($F(1, 11) = 38.858$, p -value < 0.001). There was no significant main effect for the factor Phase ($F(1, 11) = 0.137$, p -value = 0.719). The post-hoc pairwise Bonferroni comparison evaluating the significant Phase \times Saccade type interaction showed significant differences between the phases for both the ADAPT (p -value = 0.004, mean duration (ms) \pm s.d.: PRE = 50.92 ± 5.82 , POST = 48.87 ± 5.29) and the CTRL (p -value = 0.024, PRE = 51.61 ± 5.01 , POST = 53.27 ± 4.513) saccades. It also revealed a significant difference in the duration between the ADAPT and the CTRL saccades in the POST-exposure (p -value < 0.001) but not in the PRE-exposure (p -value = 0.396) phases.

c. Peak velocity

The 2-way ANOVA showed only a significant main effect for the factor Phase ($F(1, 11) = 9.001$, p -value = 0.013) (peak velocity ($^{\circ}$ /s) \pm s.d.: PRE = 449.369 ± 82.94 , POST = 427.932 ± 67.90). There was neither a significant main effect for the factor Saccade type nor a significant Phase \times Saccade type interaction (all $F \leq 2.023$, all p -values ≥ 0.185).

Forward adaptation

a. Latency:

The latency of the adapted visual saccade was not affected by forward adaptation, as revealed by the 2-way ANOVA showing no significant main effect for the factors Phases and Saccade type, as well as no significant interaction (all $F \leq 2.415$, all p -values ≥ 0.171).

b. Duration:

The 2-way ANOVA showed a significant main effect for the factor Phase ($F(1, 6) = 8.023$, p -value = 0.03), as well as a significant Phase \times Saccade type interaction ($F(1, 6) = 11.458$, p -value = 0.015). There was no significant main effect for the factor Saccade type ($F(1, 6) = 1.176$, p -value = 0.320). Post-hoc pairwise Bonferroni comparison showed a significant difference between the phases for the ADAPT saccade (p -value = 0.012, mean duration (ms) \pm s.d.: PRE = 50.09 ± 5.146 , POST = 53.95 ± 5.583), but not for the CTRL saccade (p -value = 0.710, PRE = 50.72 ± 4.063 , POST = 50.98 ± 3.871). It also revealed a significant difference in the duration between the ADAPT and the CTRL saccades in the POST-exposure (p -value = 0.049), but not in the PRE-exposure (p -value = 0.619) phase.

c. Peak velocity:

The peak velocity of the adapted visual saccade was not affected by forward adaptation, as the 2-way ANOVA showed no significant main effects for the factors Phases and Saccade type, as well as no significant interaction (all $F \leq 0.644$, all p -values ≥ 0.453).

In sum, backward and forward adaptation of visual reactive saccades were accompanied respectively by a decrease and an increase in saccade duration. There was also a decrease in the peak velocity in the backward condition, which was not specific to the adapted saccades as it was also present for control saccades.

Experiment 2: The Adaptation Of Auditory Saccades And Its Subsequent Transfer To Visual Saccades.

Experiment 1 showed that both forward and backward adaptations of visual reactive saccades generalize to non-adapted visual saccades and transfer to auditory saccades performed toward the adapted and nearby non-adapted locations. In Experiment 2, we investigated whether forward and backward adaptations can be induced for auditory saccades using a modified version of the double-step target paradigm and, in such case, whether they generalize to non-adapted auditory saccades and transfer to visual saccades.

Material And Methods

Participants

Thirty-four naïve volunteers were included in this experiment. Four participants had hypermetric auditory saccades that exceeded the detection range of the camera; therefore, they were excluded after their first session. The remaining thirty volunteers (11 males and 19 females, including three left-handed) had a mean age of 25.07 ± 4.43 years old (range 19 to 39).

Design

The design and procedures were the same as in Experiment 1, except that here, during the Exposure phases, auditory saccades toward sounds located at 15 degrees were adapted instead of visual saccades. In addition, the PRE- and POST-exposure phases differed from Experiment 1 only in the order of the auditory and visual blocks, the auditory blocks being performed immediately before and after the exposure phase, respectively.

As in Experiment 1, the backward and forward adaptations were investigated in two separate sessions presented in a counterbalanced order between participants (14 participants started with the backward adaptation session and 16 with the forward adaptation). Also, participants were divided in two groups depending on the assignment between backward (B) and forward (F) adaptations and the left (L) and right (R) hemifields: B-R/F-L (16 participants) vs. B-L/F-R (14 participants).

In the Exposure phase, participants performed 120 auditory saccades randomly directed toward the sound located 15° to the left or the right of the fixation point. In the backward adapted saccade trials, the detection of the saccade onset (at 60°/s velocity threshold) triggered a 5 deg backward intra-saccadic displacement of the target (the 15° sound turned off simultaneously with the activation of the 10° sound). In contrast, in the forward adapted saccade trials, the detection of the saccade onset triggered a 5 deg forward intra-saccadic displacement of the target (the 15° sound turned off simultaneously with the activation of the 20° sound). In the non-adapted saccades trials (Control trials), the activated auditory target did not change location (15°) after the detection of the saccade onset (no-jump trials). In all conditions, the auditory target remained for 500 ms after the saccade onset, disappearing 1000 ms before the re-appearance of the fixation point.

Data processing and parameter extraction

The data processing and parameter extraction procedures were the same as in Experiment 1 (Here, 4.68% of the trials in total were excluded).

Analysis

First, to check if the double-step exposure successfully elicited adaptation of auditory reactive saccades, we analyzed auditory saccades performed toward the 15° targets. The slope of the linear relationship between saccadic gain and trial number during Exposure, as well as the gain change ratio between PRE and POST-Exposure, were submitted to two separate repeated measures ANOVAs with the factors ‘Adaptation type’ (FORWARD vs. BACKWARD) and ‘Saccade type’ (ADAPT vs. CTRL) as within-subjects factors. In order to check for any effects of ‘Group’ (B-R/F-L vs. B-L/F-R) or ‘Session order’ (backward-first vs. forward-first), we performed two separate ANOVAs similar to the just presented ones but with the two additional, between-subjects, factors ‘Group’ and ‘Session order’.

In order to investigate whether the adaptation of auditory saccades to the 15° auditory target (AUD 15) generalizes to saccades to the 10° and 20° targets (AUD 10 and AUD 20), as well as if this adaptation transfers to saccades toward different visual targets (VIS 10, VIS 15 and VIS 20), we submitted separately for each adaptation type (FORWARD vs. BACKWARD) the gain change ratio to a 2-way repeated measures ANOVA with the factors ‘Saccade type’ (ADAPT vs CTRL) and ‘Target’ (AUD 10, AUD 20, VIS 10, VIS 15, and VIS 20) as within-subjects factors. VIS 10 represents visual saccades performed toward the LED located at 10 degrees, while AUD 10 represents auditory saccades performed toward the sound located at 10 degrees. The above transfer analysis was performed only for participants who showed a significant forward or backward adaptation, as assessed by the results of t-tests comparing the gain of the adapted auditory saccades between the PRE- and the POST-exposure phases.

Finally, we investigated the effect of adaptation on the latency, duration, and peak velocity of the adapted saccades (auditory saccades to 15° target). Therefore, we submitted each of those variables, and only for the participants who showed significant adaptation, to a 2-way repeated

measures ANOVA with the factors ‘Phases’ (PRE- vs. POST-exposure) and the factor ‘Saccade type’ (ADAPT vs CTRL) as within-subjects factors.

Results

Slope of gain change in the exposure phase

The 2-way ANOVA performed on the slope of gain change in the Exposure phase showed a significant main effect for the factor ‘Adaptation type’ ($F(1, 29) = 21.720$, $p\text{-value} < 0.001$), as well as a significant Adaptation type \times Saccade type interaction ($F(1, 29) = 14.759$, $p\text{-value} < 0.001$). There was no significant main effect for the factor ‘Saccade type’ ($F(1, 29) = 0.221$, $p\text{-value} = 0.641$). Post-hoc pairwise Bonferroni comparison showed a significant difference between BACKWARD and FORWARD conditions for the ADAPT saccade ($p\text{-value} < 0.001$) but not for CTRL one ($p\text{-value} = 0.756$). Furthermore, it showed significant differences between ADAPT and CTRL saccades for both the BACKWARD (mean gain change \pm s.d.: ADAPT = $-11.27 \times 10^{-4} \pm 13.94 \times 10^{-4}$, CTRL = $0.431 \times 10^{-4} \pm 15.91 \times 10^{-4}$, $p\text{-value} = 0.005$) and the FORWARD conditions (ADAPT = $11.29 \times 10^{-4} \pm 13.69 \times 10^{-4}$, CTRL = $1.82 \times 10^{-4} \pm 16.38 \times 10^{-4}$, $p\text{-value} = 0.009$). These results are plotted in Figure 3A.

We then tested the effects of the session order and of adapted hemifields by adding to the previous ANOVA the following two between-subjects factors: ‘Group’ (B-R/F-L vs. B-L/F-R), and ‘Session order’ (backward-first vs. forward-first). This 4-ways ANOVA showed significant Saccade type \times Group ($F(1, 26) = 4.325$, $p\text{-value} = 0.048$) and Saccade type \times Group \times Session order interaction ($F(1, 26) = 8.306$, $p\text{-value} = 0.008$). There were no significant main effects for the between-subjects factors, or interaction among them, or other interactions with the other factors of the ANOVA (all $F \leq 2.108$, all $p\text{-values} \geq 0.158$).

In summary, these results show that the forward and backward second step of the auditory target induced during exposure an increase and a decrease in auditory saccades gain, respectively, compared to control saccades performed toward a stationary auditory target.

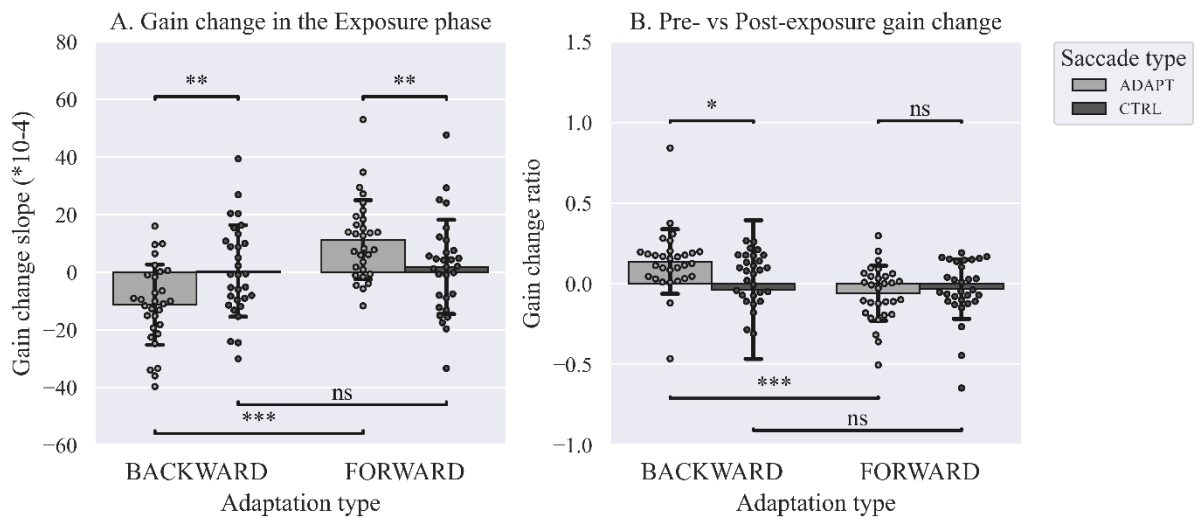


Figure 3: Experiment 2 adaptation results (all participants). Panel A: mean saccadic gain change (+/- s.d.) in the exposure phase (slope of the linear regression between saccadic gain and trial number). Panel B: mean saccadic gain change ratio (+/- s.d.) between the PRE- and the POST-exposure phases. Both the gain change slope and ratio are plotted as function of the adaptation type (BACKWARD vs. FORWARD) and the saccade type (legend: light grey for the ADAPT saccade and dark grey for the CTRL saccade). ns : t-test ($p > .05$), * : t-test ($p < .05$), ** : t-test ($p < .01$), * : t-test ($p < .001$).**

Gain change ratio in PRE- and POST-exposures

The 2-way repeated measures ANOVA showed a significant main effect for the factors ‘Adaptation type’ ($F(1, 29) = 5.969$, p -value = 0.021), as well as a significant Adaptation type \times Saccade type interaction ($F(1, 29) = 6.784$, p -value = 0.014). There was no significant main effect for the factor ‘Saccade type’ ($F(1, 29) = 3.261$, p -value = 0.081). Post-hoc pairwise Bonferroni comparison showed a significant difference between BACKWARD and FORWARD conditions for the ADAPT saccade (p -value < 0.001), but not for the CTRL saccade (p -value = 0.964). Furthermore, it showed a significant difference between ADAPT and CTRL saccades for the BACKWARD (ADAPT = 0.137 ± 0.200 , CTRL = -0.036 ± 0.430 , p -value = 0.02), but not the FORWARD condition (ADAPT = -0.059 ± 0.170 , CTRL = -0.034 ± 0.184 , p -value = 0.448) (See Figure 3B).

We then tested the effects of the session order and the adapted hemifields by adding to the previous ANOVA the following two between-subjects factors: ‘Group’ (B-R/F-L vs. B-L/F-R) and ‘Session order’ (backward-first vs. forward-first). This analysis showed a significant Saccade type \times Adaptation type \times Group interaction ($F(1, 26) = 7.266$, p -value = 0.012). The ANOVA showed no significant main effects for the two between-subjects factors and no other significant interaction between them and with the other factors (all $F \leq 1.676$, all p -values ≥ 0.207). Post-hoc pairwise Bonferroni comparison revealed that while the B-R/F-L group showed a significant difference between ADAPT and CTRL saccade in the BACKWARD condition (p -value = 0.004), the B-L/F-R group didn’t (p -value = 0.748). Note that this non-significant difference in the B-L/F-R group is

related to a gain decrease for the CTRL saccade of the BACKWARD condition, which is not the case for the rest of the CTRL saccades, as reported in Table 1. There were no significant differences between ADAPT and CTRL saccades in the FORWARD condition of both groups.

Overall, these results show that exposure of auditory saccades to the backward double-step procedure led to a significant adaptation aftereffect, further supporting the conclusion of the previous analysis of gain change slope, of a successful backward adaptation. In contrast, the forward double-step procedure, despite increasing auditory saccade gain during exposure (see results of the gain slope analysis), led to an after-effect which was not significantly larger than the gain change ratio of control saccades.

Table 1: mean gain change ratio (+/- s.d.) of the adapted (ADAPT) and the control (CTRL) saccades across groups in both BACKWARD and FORWARD conditions.

| Adaptation type | Saccade type | Groups | |
|-----------------|--------------|----------------|----------------|
| | | B-R/F-L | B-L/F-R |
| BACKWARD | ADAPT | 0.142 ± 0.269 | 0.132 ± 0.076 |
| | CTRL | -0.158 ± 0.557 | 0.102 ± 0.125 |
| FORWARD | ADAPT | -0.113 ± 0.117 | 0.003 ± 0.143 |
| | CTRL | -0.032 ± 0.233 | -0.035 ± 0.116 |

Adaptation transfer

Here, we investigated whether the adaptation induced for auditory saccades toward the 15° target generalized to auditory saccades performed to nearby locations (10° and 20°) and whether it transferred to visual saccades performed toward targets located at 10°, 15°, and 20°. We considered only the participants who showed a significant forward or backward adaptation, as revealed by a significant difference of their 15° auditory saccades gain between the PRE- and the POST-exposure phases (student t-tests).

Backward adaptation transfer

Twenty-eight out of thirty participants showed a PRE- vs POST-exposure decrease in their adapted auditory saccade gain, but this gain decrease was significant in only 12 out of 30 participants. The mean value of the gain change ratio for those 12 participants was equal to 0.2218 for the ADAPT saccade compared to 0.0622 for the CTRL saccade (auditory saccades to targets at 15°). Based on this sample of 12, the 2-way ANOVA showed a significant main effect for the factor ‘Saccade type’ only ($F(1, 11) = 5.772$, $p\text{-value} = 0.035$) (ADAPT = 0.048 ± 0.069 , CTRL = -0.014 ± 0.068). There was no significant main effect for the ‘Target’ factor and no significant Saccade type × Target interaction (all $F \leq 3.272$, all $p\text{-values} \geq 0.083$). These results indicate a general decrease of the gain for all non-adapted saccades, suggesting that auditory saccades adaptation generalizes to non-adapted auditory saccades and transfers to visual saccades.

Forward adaptation transfer

Sixteen out of thirty participants showed an increase in the gain of the adapted auditory saccade after exposure to the forward double-step procedure, but this gain increase was significant in only 8 out of 30 participants. The 2-way ANOVA showed no significant results (all $F \leq 2.770$, all p -values ≥ 0.135). This analysis thus provides no evidence of a transfer of auditory saccades forward adaptation to non-adapted auditory saccades and to visual saccades.

Effect of adaptation on saccade metrics

Backward adaptation

a. Latency:

The latency of the adapted auditory saccade was not affected by backward adaptation. Indeed the Phase \times Saccade type 2-way ANOVA showed neither significant main effect nor significant interaction (all $F \leq 1.663$, all p -values ≥ 0.224).

b. Duration:

The 2-way ANOVA on the auditory saccade duration showed only a significant main effect for the Phase factor ($F(1, 11) = 10.135$, p -value = 0.009) (mean duration (ms) \pm s.d.: PRE = 92.47 ± 33.46 , POST = 85.38 ± 29.10). There was no significant main effect for the Saccade type factor, and no significant Phase \times Saccade type interaction (all $F \leq 0.194$, all p -values ≥ 0.668).

c. Peak velocity

The 2-way ANOVA showed only a significant main effect for the Phase factor ($F(1, 11) = 25.051$, p -value < 0.001) (peak velocity ($^{\circ}/s$) \pm s.d.: PRE = 310.53 ± 61.93 , POST = 283.51 ± 61.03). There was no significant main effect for the Saccade type factor, and no significant Phase \times Saccade type interaction (all $F \leq 2.084$, all p -values ≥ 0.177).

Forward adaptation

The 2-way ANOVAs showed no significant main effect for the Phases and Saccade type factors, as well as no interaction between them for the analysis of the latency (all $F \leq 4.759$, all p -values ≥ 0.066), of the duration (all $F \leq 0.819$, all p -values ≥ 0.395) and of the peak velocity (all $F \leq 0.486$, all p -values ≥ 0.508).

Overall, no significant change of the latency, duration or peak velocity of auditory saccades were observed specifically after either forward or backward adaptation.

Discussion

In this study, we elicited both forward and backward adaptation of visual reactive saccades and were able to reveal in both cases a strong adaptation transfer to auditory saccades (Experiment 1). In Experiment 2 we further established, for the first time, the possibility to adaptively decrease the size of auditory saccades in the backward condition, but in this case a very low transfer to visual saccades

was observed. Both experiments also illustrated that the adaptation characteristics and transfer pattern in the forward condition differed from the backward condition.

The cross-modal visual-to-auditory transfer of backward adaptation revealed in Experiment 1 replicates the findings of two previous studies (Collins et al., 2010; Frens & van Opstal, 1994). In addition, the generalization of such backward adaptation to visual saccades toward nearby targets agrees with the well-known adaptive field characteristics (Collins et al., 2007). Note that the cross-modal visual-to-auditory transfer of adaptation was not restricted to the (auditory) target location matching the adapted (visual) one but extended also to nearby auditory targets. Concerning the forward condition, adaptation of visual saccades was elicited, but with a lower efficiency than backward adaptation, confirming several previous studies (M. Panouillères et al., 2009, 2013; M. T. N. Panouillères et al., 2012; Robinson et al., 2003). Nonetheless, forward adaptation of visual saccades was characterized by the same pattern of generalization and cross-modal transfer as backward adaptation. These characteristics can provide cues as to the neural substrates of visual saccades adaptation. It is known that neurons in the PPC, FEF and SC show vigorous motor-related discharge for saccades of a given vector, with the discharge decreasing progressively for saccades showing an increasing deviation from this preferred vector (Hopp & Fuchs, 2004). This spatial tuning characteristics define the so-called movement field of saccade-related neurons. The similarities in the shape of both the neuron movement fields and the adaptation field have been taken as supporting evidence for the hypothesis that saccadic adaptation modifies saccade motor commands encoded as 2-D vectors, rather than commands encoded downstream at the level of the brainstem as separate vertical and the horizontal components (Alahyane et al., 2008). Saccade-related neurons responsive to auditory stimuli were found in the PPC (Grunewald et al., 1999; Linden et al., 1999), in the FEF (Hu & Vetter, 2024; Leszczynski et al., 2023) and in the SC (Jay & Sparks, 1987a, 1987b). The FEF and SC are known to be sites where, to trigger saccadic eye movements, auditory information is encoded as desired vectorial eye displacements in an oculocentric reference frame. Here, our results argue that reactive visual saccade adaptation act on the saccade's motor command at sites where auditory (and tactile, see (Batikh et al., 2024)) has been translated into an oculocentric frame of reference.

To date, the cross-modal transfer of saccadic adaptation (visual-to-tactile : (Batikh et al., 2024); visual-to-auditory: (Collins et al., 2010; Frens & van Opstal, 1994)) has been investigated only after backward adaptation of reactive saccades but not forward adaptation. Consistent with the literature (see Introduction), our results in Experiment 1 show that forward adaptation is less prevalent (fewer participants were adapted), slower to develop over time (the gain increase in the exposure phase was slower than the gain decrease), and results in lower adaptation aftereffects compared to backward adaptation. Note that, as will be detailed below, similar differences were also found in Experiment 2 for the newly-attempted induction of auditory saccades adaptation. Interestingly, despite the differences between forward and backward adaptation of visual saccades, they both significantly

and almost completely transferred to auditory non-adapted saccades. This last finding suggests that both backward and forward visual reactive saccades adaptations involve a motor functional locus.

In Experiment 2, we investigated whether it is possible to induce backward and forward adaptation of reactive auditory saccades. We adapted the double-step target paradigm (McLaughlin, 1967) to auditory targets, i.e. the intra-saccadic, forward or backward, shift of the auditory target was achieved by activating a sound sequentially in two neighboring speakers. It is important to note that, contrary to our previous study of tactile adaptation in which participants were aware of the double step of tactile stimulations (Batikh et al., 2024), our participants in Experiment 2 were unaware of the intra-saccadic change in location of the auditory target, as confirmed by reports at debriefing. Therefore, it is highly unlikely that participants employed a strategy to cope with target perturbations during exposure. Furthermore, in the backward condition, the decrease of auditory saccades gain observed during the exposure phase was progressive and was retained in the post-exposure phase (adaptation after-effect) despite the fact that the auditory target no longer ‘jumped’. These observations argue for true adaptation mechanisms elicited during exposure, rather than an involvement by the participants of a strategy. Still, the backward adaptation of auditory saccades appeared overall less consistent than visual saccades adaptation as, at the level of individual participants, less than half of them showed a significant adaptation after-effect. Nevertheless, auditory saccades backward adaptation generalized to non-adapted auditory saccades, which is reminiscent of the adaptation field described for visual saccades. In addition, the backward adaptation of auditory saccades showed a partial but significant transfer to visual saccades. These two last findings provide further support to the conclusion that the decrease in auditory saccades gain cannot be attributed to a strategy employed by the participants and therefore demonstrate the existence of backward adaptation of auditory saccades. When considered alongside the adaptation of tactile saccades we reported recently (Batikh et al., 2024), these findings underline the flexibility of the saccadic system in correcting errors encoded in the absence of post-saccadic visual information, therefore challenging the current models investigating the nature of the error signal that drives saccadic adaptation (Bahcall & Kowler, 2000; Collins & Wallman, 2012; Masselink & Lappe, 2021).

Comparing the outcomes of Experiments 1 and 2 revealed an asymmetrical pattern of adaptation transfers between the visual and the auditory saccades, with a complete visual-to-auditory transfer but only a partial auditory-to-visual transfer. Note that a similar asymmetrical pattern was found when comparing the visual-to-tactile transfer to the tactile-to-visual transfer of backward adaptation (Batikh et al., 2024). Together, these findings suggest the existence of multiple functional loci for the backward adaptation of non-visual saccades, with at least one located upstream from the adaptation locus of visual saccades which is supposedly the final oculomotor pathway common to all saccade’s modalities.

Finally, in Experiment 2, stepping the auditory target in the direction of the saccades (i.e., forward) progressively increased saccade gain in the exposure phase but failed to produce at the group

level any significant adaptation after-effect, with only eight out of thirty participants showing a significant after-effect. Also no significant transfer to visual reactive saccades was observed. Noteworthy, the differences between backward and forward adaptation of auditory saccades mirror those reported for visual saccades in Experiment 1 as well as in the literature (M. Panouillères et al., 2009, 2013; M. T. N. Panouillères et al., 2012). Therefore, the failure to reveal any forward auditory adaptation in our study could stem from the difficulty encountered in general when inducing forward adaptation and/or to the relatively low number of double-step trials we used, which leads us to consider our findings too preliminary to conclude about the presence or absence of forward adaptation -and transfer- of auditory saccades..

In conclusion, we showed that both forward and backward adaptation of visual reactive saccades transfers strongly to auditory saccades. These visual-to-auditory transfers of adaptation argues in favor of a motor functional locus of visual reactive saccades adaptation. We also demonstrated for the first time that it is possible to induce adaptation of auditory saccades in the backward direction with, in this case, a partial transfer to visual reactive saccades, suggesting an additional, upstream, adaptation locus for auditory saccades compared to visual saccades.

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Authors Contributions

Conception and design of the study: A. Batikh, A. Farnè, and D. Pélisson; Setup preparation and Software: A. Batikh, F. Volland, E. Koun; Data collection: A. Batikh and A. Bertin .; Data analysis: A. Batikh; Data interpretation: A. Batikh, A. Farnè and D. Pélisson; Original draft: A. Batikh; Critical revisions: A. Farnè and D. Pélisson; All the authors approved the final manuscript for submission.

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Disclosures

The authors declare that they have no competing interests.

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Study 3: Tactile spatial attention modulates saccadic adaptation

Ali Batikh¹, Éric Koun¹, Roméo Salemmé¹, Alessandro Farnè^{1§}, and Denis Péliçon^{1§}

¹*IMPACT Team of Lyon Neuroscience Research Center INSERM U1028 CNRS UMR5292 University Claude Bernard Lyon 1, France.*

[§] *These authors contributed equally to this work.*

Abstract

Eye movements and spatial attention are both crucial to visual perception. Orienting gaze to objects of interest is achieved by voluntary saccades (VS) driven by internal goals or reactive saccades (RS) triggered automatically by sudden environmental changes. Both VS and RS are known to undergo plastic adaptation processes so-called saccadic adaptation, to maintain accurate vision throughout life. Spatial attention enhances visual processing within a restricted zone where it can be shifted voluntarily following our internal goals (endogenous), or automatically in response to unexpected changes of sensory stimulation (exogenous). Despite the widely accepted notion that saccadic and attention shifts are governed by distinct but highly interconnected systems, the relationship between saccadic adaptation and spatial attention is still unclear. To address this relationship, we conducted two experiments combining modified versions of the attention orienting paradigm (Posner 1980) and the adaptation double-step paradigm (McLaughlin 1967). Experiment 1 tested the effect on RS adaptation of shifting exogenous attention by a tactile cue near -or away from- the saccade's target. Experiment 2 also used tactile cueing but now to investigate the effect of shifting endogenous attention on VS adaptation. Both experiments (RS/exogenous and VS/endogenous) revealed that the degree and the speed of saccadic adaptation correlated positively with the amount of attention oriented toward the saccade's target and negatively with the amount of attention oriented away from the saccade's target. Overall these findings suggest an effect of spatial attention on saccadic adaptation.

Keywords: Saccadic adaptation, spatial attention, cross-modal link

Introduction

The fovea is restricted to 1-2% of the retinal surface, where visual acuity is the highest. To inspect in detail an object of interest in our visual environment, it is thus necessary to bring its image into the fovea via rapid eye movements called saccades. Saccades elicited by the sudden appearance of objects are classified as reactive (also called 'reflexive' or 'automatic') saccades (RS), and those generated based on internal goals are classified as voluntary saccades (VS). Because of their high speed, saccades toward visual targets differ from actions involving the skeletal system in that they cannot

benefit from visual feedback signals to control their execution ‘online’ (except for large saccades (Gaveau et al., 2003) or pathologically-slowed saccades (Zee et al., 1976)). Therefore, the motor programming of saccades must be optimal to ensure their accuracy despite short to long-term modifications of the body-space relationships (growth, aging, etc.) or consequences of cerebral or neuro-muscular lesions. A critical mechanism contributing to such oculomotor calibration is the so-called saccadic adaptation, a plastic phenomenon by which saccades’ metrics are modified to maintain visual accuracy (Hopp & Fuchs, 2004; Pélisson et al., 2010). Saccadic adaptation has been intensively studied, largely thanks to the "double-step target paradigm" established long ago (McLaughlin, 1967). In this paradigm, participants follow with their eyes a target appearing in the visual field (1st step) and then changing position (2nd step) during the execution of the saccadic response to the first target step. Unless the 2nd step exceeds ~30% of the 1st step amplitude, it usually goes undetected due to saccadic suppression (Bridgeman et al., 1975; Wurtz, 2008). Nonetheless, it is systematically interpreted by the sensorimotor system as an aiming error of the primary saccade. Repeated exposure to such aiming error in successive "double-step" trials entails the adaptation process to gradually modify the primary saccade amplitude, either reducing or increasing it depending on the direction of the 2nd target step relative to the 1st step (“backward” or “forward”, respectively), resulting in a reduction of the aiming error.

The many features that compose our visual field continuously and simultaneously stimulate our retinal receptors, leading to a high throughput of information transmitted to the visual system. To avoid neural processing overload, our attentional system selects salient or task-relevant information (based on our current priorities) and discards non-essential information (Posner, 1980). Individuals are able to orient their attention whenever changes in the environment or the task at hand require it (Corbetta et al., 2008), calling for two types of spatial attention shifts. The first process (involuntary, “bottom-up”, or “stimulus-driven”) corresponds to the automatic capture (exogenous) of attention by salient stimuli. The second process (voluntary or “top-down”) directs attention toward stimuli defined endogenously, according to the ongoing task (Corbetta et al., 2008; Groner & Groner, 1989). Corbetta and Shulman showed evidence that different neuronal networks underlie these two types of attention orientation (Corbetta et al., 2008; Corbetta & Shulman, 2002). The dorsal fronto-parietal network, including the intraparietal sulcus (IPS) and the superior parietal lobule (SPL) in the parietal cortex, as well as the frontal eye field (FEF) in the frontal cortex, generates endogenous attention signals, and the ventral fronto-parietal network situated in the right hemisphere, including the right temporo-parietal junction (rTPJ), the ventral part of the supramarginal gyrus (SMG), and the ventral frontal cortex (VFC), generates exogenous attention signals.

Spatial attention and eye movements are known to strongly interact. Both spatial attention and saccades preparation are reflected within the activity of the FEF, the superior colliculi (SC), and the PEF (Hunt et al., 2019). In particular, a series of studies have suggested the existence of a coupling between visuospatial attention and saccadic adaptation. Behavioral studies in healthy participants have

shown that the adaptation of VS favors the orienting of endogenous visual attention (Nicolas, Bidet-Caulet, et al., 2019), while the adaptation of RS facilitates the orienting of exogenous attention (Habchi et al., 2015; Nicolas et al., 2020). Saccadic adaptation has also been suggested to alter the attentional field, expanding and shrinking in relation to forward and backward adaptation, respectively (Wick et al., 2016). In addition, at the neurophysiological level, Nicolas et al. (Nicolas, Bompas, et al., 2019) demonstrated through magnetoencephalography (MEG) that the adaptation of RS is accompanied by activation of an extended parietal-temporal zone overlapping with the visuospatial attention networks. Furthermore, combining the findings of fMRI studies of attention (Corbetta et al., 2008) and saccadic adaptation ((Corbetta et al., 2008; Gerardin et al., 2012) shows that the neural substrates of exogenous spatial attention and those of RS adaptation overlap at the level of rTPJ, while those of endogenous spatial attention and VS adaptation overlap at the level of IPS. Taken together, these previous studies suggest that saccadic adaptation and visuospatial attention are functionally coupled.

Here, to further test this functional coupling hypothesis, we aimed at verifying whether, in addition to the effect of adaptation on attention mentioned above (Habchi et al., 2015; Nicolas, Bidet-Caulet, et al., 2019; Nicolas, Bompas, et al., 2019; Nicolas et al., 2020; Wick et al., 2016), there is also an effect of attention on adaptation. To date, a few studies provide arguments in favor of this prediction. First, ADHD patients display reduced saccadic adaptation, possibly resulting from their altered attentional capabilities (Connolly et al., 2016). Second, (Bock et al., 2017) used a scrambled sentence task to prime the participants' attentional focus prior to RS adaptation. Although they did not observe any changes in adaptation after-effect, they suggested that the postulated widening, relative to narrowing, of attentional focus increased saccadic adaptation induced during a subsequent exposure phase. The same team however had previously found no evidence for an impact on saccadic adaptation of diverting attentional resources toward a secondary task performed concurrently (Bock et al., 2014), suggesting that saccadic adaptation does not draw on spatial attention. Third, in a visually-triggered saccade task, Khan et al. (Khan et al., 2014) presented at the time of saccade onset a visual distractor in the vicinity of the saccade target (± 3 degrees) which could be either salient or not (relative to the saccade target). They found that despite the saccade target remained stationary, the salient distractor was enough to induce saccadic adaptation, thus suggesting that the locus of attention drawn toward the distractor can, on its own, act as an error signal for the saccadic adaptation process. In contrast, another study where either the target or the distractor jumped intra-saccadically (Madelain et al., 2010) concluded that adaptation is unhampered by distractors, but note here that the distractor saliency was equal to that of the target (two stimuli of identical size but with different shapes and colors were pseudo-randomly assigned as target and distractor across trials). Two further studies argue in favor of the effect of attention on saccadic adaptation (McFadden et al., 2002; Gerardin et al., 2015). In the first (McFadden et al., 2002), the authors modified the line motion illusion protocol (a static visual line presented immediately after a flashed cue is perceived as growing over time from the cue location) to

adapt the ‘covert’ displacement of the focus of visual attention. In doing so, they noticed that the postulated adaptation of covert attention led to a change in the size of RS. However, whether their line motion illusion procedure really adapted spatial attention remains uncertain. In the second study (Gerardin et al., 2015), Gerardin et al. tested the effect on RS adaptation of the attentional load deployed during the adaptation exposure. In every exposure trials, participants performed a double-task (saccade and discrimination), the saccadic targets that jumped during the saccade to elicit adaptation consisting of Gabor stimuli that the subjects had to discriminate. The attentional load level was varied in separate sessions as ‘low’ or ‘high’ by providing participants with different instructions for the discrimination task. The results showed stronger saccadic adaptation in the high load condition (difficult discrimination) compared to the low load condition (easy discrimination). However, this study does not allow to disentangle whether this effect on oculomotor adaptation is due to spatial attention or to a general effect of alertness.

Here, thus, we investigated more directly the effect of spatial attention on saccadic adaptation. To this aim, we focused on backward adaptation: it is indeed well known that forward adaptation is harder to induce than backward adaptation, and both types of adaptation were suggested to rely on different mechanisms (Ethier et al., 2008; Panouillères et al., 2009; Pélisson et al., 2010), and most of the studies presented above investigated the interaction between spatial attention and saccadic adaptation used backward adaptation. To more specifically investigate spatial attention than in (Gerardin et al., 2015), 1) we combined the Posner paradigm (Posner, 1980) with a double-step target paradigm (McLaughlin 1967) in a dual (attention and saccade) task. To reduce as much as possible the interference with the saccade (visual) targets, we implemented a tactile version of Posner paradigm (cue and target consisting of tactile stimuli). Indeed, we leveraged the intermodal nature of spatial attention (Driver & Spence, 1998), notably the fact that orienting spatial attention to tactile stimuli boosts visual processing, and hypothesized that tactile spatial attention would facilitate saccadic adaptation, similar to the facilitatory effect of visual attention proposed by (Gerardin et al., 2015). In this dual task, the ‘covert’ orienting of attention (without eye movement) towards an area of the peripersonal space was induced by a tactile cue delivered on the fingers and measured by the difference in the speeded response to a second tactile stimulation delivered either on the cued side (valid trials) or the opposite side (invalid trials). The specific parameters of both the tactile attention and the saccadic adaptation procedures were adapted across two experiments to investigate the effect of exogenous tactile spatial attention on the adaptation of RS (Experiment 1) and that of endogenous tactile spatial attention on the adaptation of VS (Experiment 2). Based on the hypothesis of a functional relationship between saccadic adaptation and attention, we predicted that in both cases, the orienting of tactile spatial attention would facilitate the adaptation of saccades.

General Methods

Sample size estimation

We calculated our sample size with the open-access software G*Power 3.1.9.7, using an effect size based on the results obtained by Gerardin et al (Gerardin et al., 2015). In that study, saccadic adaptation was compared between two conditions (Low attentional demand ‘LAD’ versus High attentional demand ‘HAD’), as assessed by the saccadic gain difference between the pre- and post-exposure phases (mean \pm standard deviation: LAD = -0.10 ± 0.034 , HAD = -0.13 ± 0.033). Using the resulting effect size of 0.447 (other G*Power parameters: $\alpha = 0.05$, Power = 0.8, non-sphericity correction $\epsilon = 1$, and correlation among repeated measures = 0.5) the recommended sample size was 12 participants for this study. As our task meant to more accurately orient spatial attention toward or away from the saccade target, we cautiously increased the number of participants to 20 per experiment.

Inclusion criteria were: normal or corrected-to-normal vision; no simultaneous participation in other experiments involving sensorimotor adaptation; no history of neurological, psychiatric, or cognitive disorders preventing the comprehension of the instructions; no consumption of psychotropic drugs or alcohol and no severe sleep deprivation during the last 24 hours. Participants were asked not to wear high heels (so they could be comfortable using a pair of response pedals) and not to use makeup or remove it before the experiment (to facilitate eye tracker set-up and improve eye movement data).

Ethical statement

The study adheres to the World Medical Association's code of ethics and the 2008 Declaration of Helsinki and received the approval of the INSERM Ethics Committee (notice 21-762, IRB00003888). All participants were given 15 euros per session for their participation.

Experimental setup

The experiment was performed in a dimly lit room. Participants were seated on a chair facing a computer screen (1920×1080 pixels, 53.5×31.5 cm; 144 Hz refresh rate) positioned 35 cm from their eyes and tilted backward by $\sim 35^\circ$ from the vertical plane. Their head was stabilized using a chin rest and forehead support, and their hands were placed on a tilted support behind the screen (subtending a horizontal angle of about -30 deg and $+30$ deg relative to the body midline). Visual targets consisted of a light grey circle (0.5 deg of visual angle) shown against a dark grey background. The position of the right eye was recorded at a 1000 Hz frequency using the tower configuration of the EyeLink 1000 infrared tracker (SR Research EyeLink® 1000, Canada).

Each session started with a calibration of the eye tracker by asking participants to fixate on five targets located at the center and near the screen's borders. In Experiment 1, two electrode pairs (Ambu® Neuroline 700; connector: 1.5 mm; Length: 150 cm/60") were attached to the distal

phalanxes of each participant's index finger, and each pair was connected to a stimulator delivering constant current electro-cutaneous stimulations (Digitimer® DS7A, controlled by the parallel port of the display computer). In Experiment 2, four pairs of the same electrodes were used (two pairs on each hand, one on the index and one on the thumb), each electrode pair being controlled by one of four stimulators.

The supra-threshold stimulation intensity was manually adjusted to be detectable easily and comfortably. Participants were asked to steadily press with their right foot two pedals (under the toes and the heel) and to provide their answer to the tactile target stimulation by releasing one of the two pedals (connected to the parallel port of the display computer). Visual targets and stimulators were controlled by a computer program running in the Experiment Builder environment (SR Research), and signals from the eye tracker and the pedals were sampled through the same program and stored at 1000 Hz for offline analyses.

Experiment 1: The Effect Of Exogenous Spatial Attention On The Adaptation Of Reactive Saccades.

Materials And Methods

Participants

Twenty participants were recruited for this experiment, including 11 females (one left-handed) and nine males (all right-handed) with mean age = 22.85 ± 3.84 years old (range 18 to 31).

Design

The central part of the experiment consisted of the Exposure phase (320 trials), during which RS adaptation and exogenous tactile attention orienting were simultaneously elicited using modified versions of, respectively, the “double step” paradigm (McLaughlin, 1967) and the exogenous attention paradigm (Posner, 1980). The double-step paradigm consists of repeatedly inducing a post-saccadic error by displacing the visual target during saccade execution (see Introduction). In parallel the orienting of exogenous tactile attention was induced by a first tactile stimulus (tactile cue) delivered on one hand and its effect was measured by asking subjects to report as fast as possible with foot pedals the location of a second tactile stimulus (tactile target) on the same or the opposite hand.

As represented in Table 1, saccades directed towards the left or the right hemifield (equiprobable) were randomly elicited. Whereas half of the leftward saccades (25% in total) were exposed to an amplitude shortening adaptation (backward double-step target procedure), the remaining leftward saccades and all the rightward (control direction) saccades were performed to a target disappearing after the saccade onset (no jump). Tactile exogenous attention was also randomly directed towards the left or the right hemifield (equiprobable). Each participant performed two sessions during which tactile attention in the adapted leftward saccade trials was systematically

directed either to the left (tactile cue on left hand, “IPSI” session) or to the right (tactile cue on right hand, “CONTRA” session). Specifically, during the “IPSI” session, trials with a tactile cue on the left were associated with a systematic double step of the saccadic target when presented on the left (to induce an adaptation of the saccades directed ipsilaterally to the attentional displacement) and to a disappearance of the saccadic target when shown on the right. In contrast, trials with a tactile cue on the right were associated with the disappearance of all saccadic targets (left and right). During the “CONTRA” session, the association was made between attentional cueing on the right and systematic double step of the saccadic target presented on the left (to induce an adaptation of the saccades directed contralaterally to the attentional displacement) and the disappearance of the saccadic target in all other trials.

The order of the sessions was counter-balanced between participants: 10 participants performed the IPSI session first, and 10 started with the CONTRA session. Knowing that the retention of saccadic adaptation can remain statistically significant for up to five days (Alahyane & Pélisson, 2005), the two sessions were separated by at least seven days. The Exposure phase was divided into four blocks of 80 trials each, between which participants could take a short break. Feedback about the discrimination task performance (number of correct answers and the mean reaction time) was presented on the computer screen at the end of each block.

In each session, the Exposure phase was preceded and followed by, respectively, a PRE-exposure phase and a POST-exposure phase, identical to each other and between the two experimental sessions (except for the random ordering of the target appearance in the right or left hemifield). Each PRE-exposure and POST-exposure phase consisted of 30 simple RS toward a target disappearing after the saccade onset (15 rightward and 15 leftward saccades in random order).

Before starting the experiment, a short training session was performed to accustom participants to the double task (oculomotor response and tactile discrimination) and ensure they complied with the instructions. This training session was identical to the Exposure phase of the experiment but without any adaptation (the visual target disappeared at the time of saccade onset in all trials).

Table 1: Table representing the different trial types in the exposure phase of Experiment 1 and specifying the trials where the second step of the visual target occurred.

| Tactile Cue | Left Hand | | Right Hand | |
|--|-----------|-------|------------|-------|
| | Left | Right | Left | Right |
| Saccade target (T1) | Left | Right | Left | Right |
| 2 nd step (T2): IPSI Session | <u>ON</u> | OFF | OFF | OFF |
| 2 nd step (T2): CONTRA Session | OFF | OFF | <u>ON</u> | OFF |

| | | | | | | | | |
|-----------------------|--------------|---------------|--------------|---------------|--------------|---------------|--------------|---------------|
| Tactile target | Left Hand | Right Hand | Left Hand | Right Hand | Left Hand | Right Hand | Left Hand | Right Hand |
|-----------------------|--------------|---------------|--------------|---------------|--------------|---------------|--------------|---------------|

Procedure

Saccadic tasks

All PRE- and POST-exposure phase trials started with participants fixating on a central fixation point (FP) for 1000 ms. As soon as a peripheral target (T1) replaced the fixation point to its left or right (eccentricity of 15 degrees of visual angle), participants had to perform a saccade toward it as rapidly and as precisely as possible. Once the saccade onset was detected (30°/s velocity threshold), the target disappeared, but participants had to maintain their gaze on this location until the fixation point reappeared 200 ms after the saccade's offset. An inter-trial period of 1500 msec with the fixation point still present allowed the subject to prepare for the subsequent trial and to blink if needed.

At the beginning of each trial of the Exposure phase, participants had to fixate the fixation point for 1000 ms. Then, a peripheral saccade target (target T1) replaced the fixation point, located 15 degrees away to the left or right. For leftward adaptation trials, the target jumped as soon as the reactive saccade was detected: T1 (15 deg to the left) disappeared and was replaced by T2 (11 degrees to the left), representing a 4-degree jump in the direction opposite to the saccade (backward jump) (see Figure 1). T2 turned off 100 ms after the saccade offset. For all other trials (no-jump), T1 disappeared at the saccade onset until the fixation point's re-appearance.

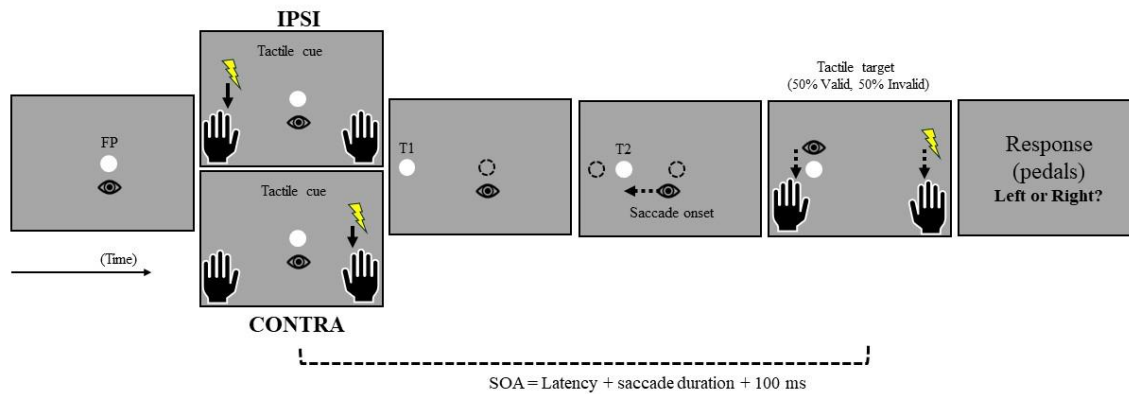


Figure 1: Schematic representation of the experimental protocol for leftward adapted saccades in the exposure phase of Experiment 1. After a random fixation time, participants tactile exogenous attention was oriented using a tactile stimulation (tactile cue) delivered on the index of the left hand (in *IPSI* session) or the right hand (in *CONTRA* session) 50 ms before the appearance of the saccade target *T1* (15 degrees of eccentricity). *T1* appearance was accompanied by the disappearance of the *FP*, and participants were instructed to saccade as rapidly and precisely as possible toward its location. Once saccade onset was detected, *T1* disappeared, and a second visual target, *T2*, appeared at 11 degrees of eccentricity, thus forming a backward step of the visual target. Fifty ms after the detection of saccade offset, a second tactile stimulation (tactile target) was delivered on the cued (Valid trials, 50%) or the uncued hand (Invalid trials, 50%). The participants had to report the location of the tactile target (left or right) using a pair of pedals placed under their right leg.

Tactile discrimination task

In all trials of the Exposure phase (see Figure 1), two tactile stimulations were delivered to induce an exogenous orienting of tactile attention: 1) a tactile cue was delivered 50 ms before the appearance of the saccadic target *T1* on the index finger of one hand, and 2) a tactile target was delivered, 50 ms after the saccade offset, on the index finger of the cued hand (valid trials) or of the other hand (invalid trials). Participants were instructed to report the tactile target's location (which hand) as quickly as possible by releasing one of the two pedals. Ten participants released the heel pedal for the left hand and the toe pedal for the right hand, and the remaining ten subjects were assigned to the opposite combination (both groups being equally divided across the two testing orders: *IPSI*-first versus *CONTRA*-first). We used orthogonal response-stimulation mapping to prevent the

stimulus-response spatial compatibility effect (Simon, 1990) and thus to specifically reveal attentional effects on target processing (Spence et al., 1998). Once the response was detected or the 850 ms timeout had elapsed, the central fixation point appeared again for a 1500 ms inter-trial period, allowing the participant to blink and prepare for the subsequent trial.

Analysis

Eye position data were analyzed offline using MATLAB code developed in our laboratory. This software automatically detects the beginning and end of saccades based on a velocity threshold (15°/s) and allows for manual corrections whenever necessary (blinks, artifacts...). Saccade amplitude was measured as the difference between eye positions 50 ms before the saccade onset and 50 ms after the saccade offset. Saccade gain was calculated as the ratio between the saccade amplitude and the target initial eccentricity (distance between target T1 and saccade starting positions). The slope of the gain change during time was calculated separately for rightward and leftward saccades of the Exposure phase. Saccade's latency was calculated as the time between the appearance of T1 and the saccade onset.

Trials were excluded from the analysis when: the saccade gain was outside the mean \pm 2.5 standard deviations, the saccade latency was less than 80 ms or outside the mean \pm 3 standard deviations, or when a blink occurred during the primary saccade (means and standard deviations calculated for each participant and across each hemifield, phase, and session). This led to the exclusion of 4.73% of all trials.

Tactile discrimination performance was evaluated by the speed (reaction time RT) of correct responses, trials with no or wrong responses being excluded. We used the Tukey method to check whether individual participants qualified as outliers according to their mean percentages of correct responses (Chica et al., 2007), and found that none of our participants was concerned (median percentage of correct answers: IPSI = 75.47%, CONTRA = 80.47 %). We then calculated the difference of mean tactile discrimination RT between invalid trials and valid trials. This "tactile validity index" reflects the temporal benefit of tactile discrimination responses brought about by tactile exogenous attention orienting.

Statistical analyses were performed using SPSS software (IBM SPSS Statistics). We first performed two analyses on saccade latency. First, we investigated whether the latency of saccades in the PRE-exposure phase differed between the sessions and the saccades' direction by submitting the median saccade latency to a 2-way repeated-measures (rm) ANOVA with the Saccade direction (Leftward vs. Rightward) and the Session (IPSI vs. CONTRA) as within-subjects factors. Second, we looked for a potential effect of the tactile cue delivered 50 ms before the saccade target on the saccade latency: we submitted the latency of saccades from the PRE-exposure and the Exposure phases to a 3-way rm-ANOVA with the factors 'Session' (IPSI vs. CONTRA), 'Saccade direction' (Leftward vs. Rightward) and 'Tactile Cue' [Same side as saccade target vs. Opposite side relative to saccade target vs. None (Saccades in PRE-exposure phase with no Cue)] as within-subjects factors.

Then, to test our main hypothesis, we evaluated the effect of attentional cueing on saccadic adaptation time-course during Exposure (slope of gain change) and on adaptation after-effect in the POST- relative to PRE-Exposure phases (gain) as follows. The slope of gain change during the Exposure phase was submitted to a 2-way rm-ANOVA with “Session” (IPSI vs. CONTRA) and “Saccade direction” (Rightward-Control vs Leftward-Adapted) as within-subjects factors. The saccadic gain in PRE- and POST-exposure phases was submitted to a similar rm-ANOVA with the “Phase” (PRE vs. POST) as an additional within-subjects factor (3-way rm ANOVA : Session x Saccade direction x Phase).

We also analyzed the speed of discrimination responses to check whether tactile exogenous spatial attention was successfully oriented toward the cued locations. To this aim, we submitted the RT of correct discrimination responses to the following 4-way rm-ANOVA: “Session” (IPSI vs. CONTRA) × “Cue direction” (Right vs. Left) × “Saccade direction” (Rightward vs Leftward) × Validity (Valid vs Invalid).

We tested the effect of session and pedal counterbalancing across participants on the saccadic gain and the discrimination RT, respectively, by including them as additional between-subjects factors in the above analyses.

We calculated the ratio of gain change in each session and each saccade direction as follows: Gain change ratio = (Gain PRE - Gain POST) / (Gain PRE) (for example, a gain change ratio of +0.2 corresponds to a 20% decrease in saccadic gain in the POST-exposure compared to the PRE-exposure phase). We then separately correlated (one-sided Pearson’s correlation), for the leftward adapted trials, the tactile validity index with the gain change ratio and the gain change slope, in order to investigate whether the strength of adaptation depended on the efficiency of attentional shifts, as measured by our participants’ discrimination performance.

When the sphericity was violated in the ANOVAs, Greenhouse-Geisser correction was applied. Results were considered significant when p value < 0.05 at $\alpha = 0.05$.

Results

Saccade latency in PRE-exposure

The latency of saccades in the PRE-exposure phase did not differ between the 2 sessions nor between the 2 saccade directions, as disclosed by the Session x Saccade direction rm-ANOVA (no significant main effect or interaction, all $F \leq 2.551$, all p-values ≥ 0.127). The grand mean of the median saccade latencies was $185.01 \text{ ms} \pm 18.64$, which is consistent with the latency of RS (Nikolov, 2020).

Cue effect on saccade latency

The 3-way Session x Saccade direction x Tactile Cue rm-ANOVA showed only a significant main effect of the Tactile Cue factor ($F(1.226, 23.303) = 16.751$, p value < 0.001) (all others $F \leq 3.761$, p values ≥ 0.067). Pairwise comparisons showed that the saccade median latency was 6 ms lower when the cue was ipsilateral vs contralateral to the saccade target (p-value = 0.002) and was in both cases

lower than with no cue (PRE-exposure phase), by 18 ms for ipsilateral cues (p-value < 0.001) and by 12 ms for contralateral cues (p-value = 0.018). Crucially, this acceleration of saccade onset by the tactile cue did not interact with Session or Saccade direction.

The slope of gain change

The mean slope values of gain change measured during Exposure are plotted in Figure 2. The 2-way Saccade direction x Session rm-ANOVA showed a significant main effect of Saccade direction ($F(1, 19) = 14.918$, p-value = 0.001) (mean slope \pm S.D.: Leftward saccades = $-0.3987 \times 10^{-3} \pm 0.345 \times 10^{-3}$, Rightward saccades = $-0.064 \times 10^{-3} \pm 0.278 \times 10^{-3}$). There was neither a significant main effect of Session ($F(1, 19) = 0.935$, p-value = 0.346) nor a significant Session \times Saccade direction interaction ($F(1, 19) = 3.749$, p-value = 0.068). These results show that the gain of leftward RS decreased during exposure due to the repetition of backward double-step trials, and in comparison, the gain of rightward RS toward no-jump targets remained stable.

To test if there was an effect of the session order on the gain slopes, we performed a separate rm-ANOVA similar to the previous one but with an additional between-subjects factor, the ‘Group’ (IPSI-first vs CONTRA-first) factor. This analysis showed no significant main effect or interaction of this ‘Group’ factor (all $F \leq 4.076$, all p-values ≥ 0.059). Altogether, these findings are consistent with the adaptation of leftward RS, which, however, did not differ between the IPSI and CONTRA sessions.

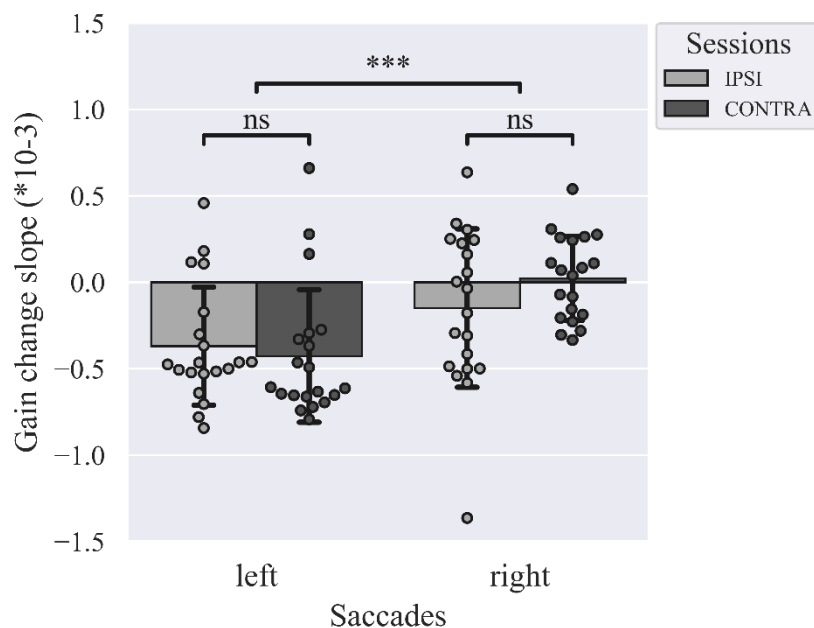


Figure 2: Experiment 1, mean slope (\pm s.d.) of the linear relationship between saccadic gain and trial number in the exposure phase, separately for leftward and rightward saccades and for IPSI (light grey) and CONTRA sessions (dark grey). t-tests: ^{ns} $p > 0.05$, ^{*} $p < 0.001$.**

Gain variation

The mean gain values measured in the PRE- and POST-exposure phases are illustrated in Figure 3. The 3-way Saccade direction x Session x Phase rm-ANOVA revealed a significant main effect of the factors Phase ($F(1, 19) = 27.636$, $p\text{-value} < 0.001$) and Saccade direction ($F(1, 19) = 23.150$, $p\text{-value} < 0.001$), as well as significant Session \times Phase ($F(1, 19) = 10.563$, $p\text{-value} = 0.004$) and Phase \times Saccade direction interactions ($F(1, 19) = 51.061$, $p\text{-value} < 0.001$). No other significant effect or interactions were found (all $F \leq 2.113$, all $p\text{-values} \geq 0.162$). Post hoc pairwise Bonferroni comparisons assessing the Session \times Phase interaction showed no significant difference of gain between sessions in the PRE-exposure ($p\text{-value} = 0.452$) and the POST-exposure phases ($p\text{-value} = 0.166$) while revealing significant differences between PRE- and POST-exposure phases in both the IPSI ($p\text{-value} < 0.001$) and the CONTRA sessions ($p\text{-value} = 0.002$). Post hoc pairwise Bonferroni comparisons investigating the significant Phase \times Saccade direction interaction revealed significant differences between phases for leftward saccades (mean gain \pm standard deviation (S.D.): PRE: 0.939 ± 0.045 , POST: 0.858 ± 0.044 , $p\text{-value} < 0.001$), but not for rightward saccades (PRE: 0.956 ± 0.044 , POST: 0.960 ± 0.065 , $p\text{-value} = 0.731$), also showing significant differences between Saccade direction in the POST-exposure phases ($p\text{-value} < 0.001$), but not the PRE-exposure ($p\text{-value} = 0.196$).

Next, we verified whether the session order affected the above results by submitting the saccade gain to the same ANOVA with the additional between-subjects factor 'Group' (IPSI-first vs CONTRA-first). This 4-way ANOVA showed no significant main effect of this Group factor ($F(1, 18) = 0.160$, $p\text{-value} = 0.694$) but a significant Group \times Saccade direction interaction ($F(1, 18) = 6.285$, $p\text{-value} = 0.022$). Post hoc pairwise Bonferroni comparisons showed a significant gain difference between the groups for leftward ($p\text{-value} = 0.045$) but not rightward saccades ($p\text{-value} = 0.379$), as well as a significant gain difference between saccade directions in the IPSI-first group ($p\text{-value} < 0.001$) but not in the CONTRA-first group ($p\text{-value} = 0.053$). None of the interactions between the group factor and the other within-subjects factors were significant (all $F \leq 2.594$, all $p\text{-values} \geq 0.125$).

These results are consistent with and confirm those reported above for the gain slope, indicating that, as expected, backward adaptation after-effects were successfully induced for leftward (double-step trials) but not rightward RS (no jump trials). However, the absence of triple interaction Session \times Phase \times Saccade direction did not support our hypothesis of a stronger adaptive after-effect of leftward RS in the IPSI versus CONTRA sessions.

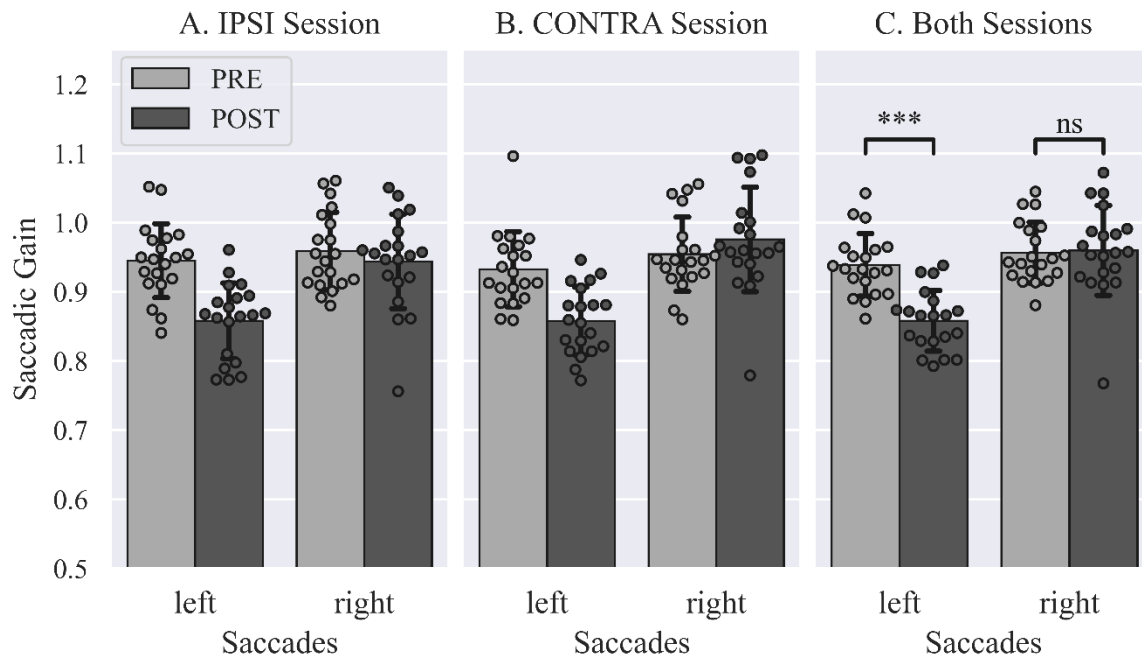


Figure 3: Experiment 1, mean saccadic gain (+/- s.d.) of leftward and rightward saccades in the PRE (light grey) and POST phases (dark grey), in IPSI (A) and CONTRA sessions (B) and both sessions pooled together (C). t-tests: ^{ns} $p > 0.05$, ^{*} $p < 0.001$.**

Discrimination RT

To ensure that our participants' tactile attention was successfully oriented toward the cued locations in both the IPSI and CONTRA sessions, we analyzed the RT of their correct discrimination responses to the tactile targets. The mean RT values measured in the Exposure phase are plotted in Figure 4. The 4-way rm-ANOVA (Session x Validity x Cue direction x Saccade direction) showed significant main effects of the factors Saccade direction ($F(1, 19) = 16.030$, p -value < 0.001 , corresponding to a 17.6 ms faster discrimination of the tactile target location in rightward saccades trials than in leftward saccades trials) and Validity ($F(1, 19) = 139.310$, p -value < 0.001 , with a 65.9 ms faster discrimination in valid trials than in invalid trials). The 2-way interactions involving the Cue direction factor were all significant: Cue direction x Session ($F(1, 19) = 4.970$, p -value = 0.038), Cue direction x Saccade direction ($F(1, 19) = 19.373$, p -value < 0.001), and Cue direction x Validity ($F(1, 19) = 24.816$, p -value < 0.001). The following 3-way interactions were also significant: Session x Cue direction x Saccade direction ($F(1, 19) = 13.842$, p -value = 0.001) and Cue direction x Saccade direction x Validity ($F(1, 19) = 7.358$, p -value = 0.014). The ANOVA showed no other significant main effects or interactions (all $F \leq 1.694$, all p -values ≥ 0.209). Post hoc pairwise Bonferroni comparisons assessing the Session x Cue direction x Saccade direction interaction showed no significant difference in RT between sessions for saccades or cue directions. In addition, they showed that for leftward saccades in the CONTRA session, participants responded significantly faster when the cue was delivered on the left hand than when the cue was delivered on the right hand (36 ms difference, p -value < 0.001). The

cue direction had no further significant effect (all p -values ≥ 0.168). Finally, this post hoc analysis showed that participants were significantly faster in discriminating the target location after rightward saccades (all p -values ≤ 0.018) except in the CONTRA session when the cue was presented on the left hand (p -value = 0.665). A second series of post hoc pairwise Bonferroni comparisons was performed to investigate the Cue direction \times Saccade direction \times Validity interaction. It revealed that participants were significantly faster at discriminating the target location after rightward versus leftward saccades (all p -values ≤ 0.034) except for valid trials when the cue was delivered on the left hand (p -value = 0.314). In addition, there was a significant validity effect with right cues for both saccades directions (all p -values ≤ 0.001) (Figure 4B) but not with left cues (all p -values ≥ 0.115) (Figure 4A), participants being faster in discriminating the target location in valid trials than invalid ones, but only when the cue was delivered on the right hand. In summary, participants' tactile exogenous attention was successfully oriented when the cue was presented to the right but not to the left, an asymmetry observed in both IPSI and CONTRA sessions. Thus, these discrimination RT results confirm that tactile exogenous spatial attention was successfully oriented away from the (leftward) adapted saccades in the CONTRA session but provide no evidence that it was oriented toward the adapted saccades in the IPSI session.

We also checked whether there was an effect of pedals assignment on the discrimination RT results. To do so, we performed a new ANOVA similar to the above analysis, except here we included a between-subjects factor, 'Toes pedal' (Left vs. Right), representing which tactile target the participants designated by releasing the pedal under the toes. Results showed no significant main effect of the 'Toes pedal' factor ($F(1, 18) = 0.425$, p -value = 0.523), but this factor significantly interacted with the 'Saccade direction' ($F(1, 18) = 13.364$, p -value = 0.002) (when the pedal under the toes was assigned to left tactile targets, participants responded 20 ms faster after performing leftward saccades compared to rightward saccades) as well as with the 'Cue direction' ($F(1, 18) = 4.944$, p -value = 0.039) (when the pedal under the toes was assigned to right tactile targets, participants responded 26 ms faster after a rightward cue in comparison to a leftward one). There were no other significant interactions involving the between-subjects factor 'Toes pedal' (all $F \leq 3.619$, all p -values ≥ 0.073).

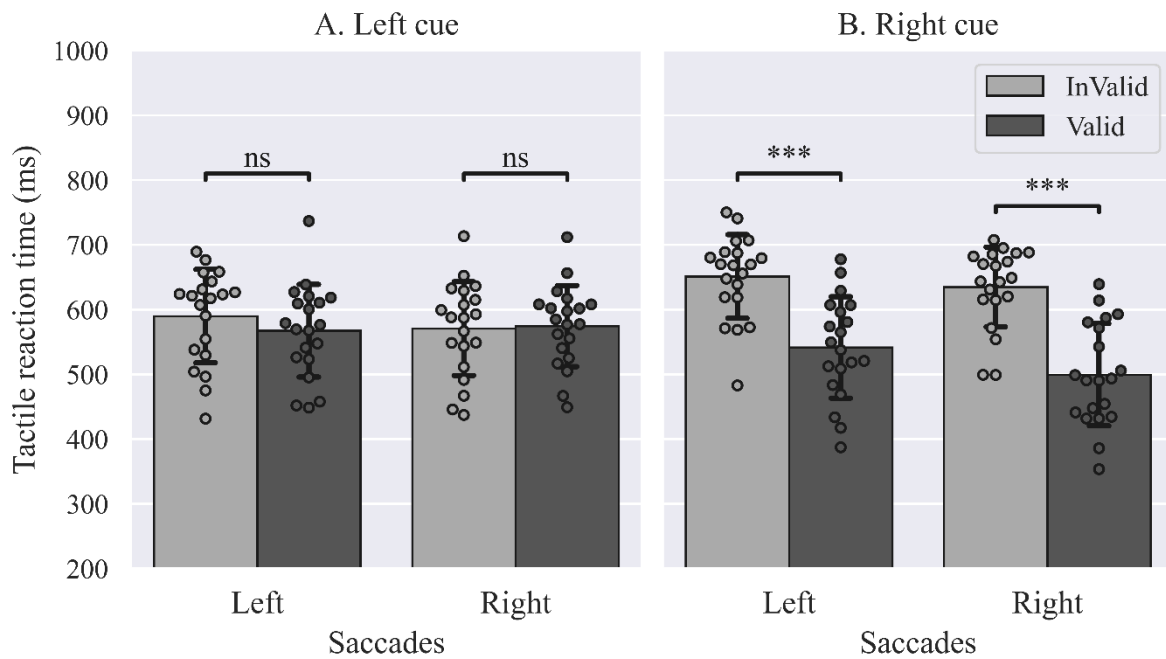


Figure 4: Experiment 1, mean reaction time to the tactile target (+/- s.d.) in leftward and rightward saccade trials for valid (dark grey) and invalid trials (light grey) when the tactile cue was delivered on the left (A) or the right (B) hand. t-tests: ^{ns} $p > 0.05$, ^{*} $p < 0.001$.**

Correlations

The discrimination performance described in the previous section suggested that tactile spatial attention may not have been similarly oriented in the IPSI and CONTRA sessions during the adaptive exposure of leftward saccades. Further, this group-level analysis of discrimination performance may hide some inter-subject variability in the capability of shifting tactile attention. Our hypothesis of coupling between attention and adaptation would predict that participants who best shifted attention (highest validity index) should show the strongest effects on the adaptation of RS. Thus, we analyzed the correlation between the tactile validity index –indexing tactile attention orienting- and the two measures of leftward saccades adaptation (gain change slope and gain change ratio). These correlation analyses are illustrated in Figures 5 and 6. Starting with the CONTRA session, we found a significant positive correlation between the slope of gain change and the tactile validity index (Figure 5A, $R = 0.512$, $p\text{-value} = 0.011$), as well as a significant negative correlation between the gain change ratio and the tactile validity index (Figure 6A, $R = -0.396$, $p\text{-value} = 0.042$). In the IPSI session, the correlation analysis showed neither a significant correlation between the slope of gain change and the tactile validity index (Figure 5B, $R = 0.004$, $p\text{-value} = 0.494$) nor a significant correlation between the gain change ratio and the tactile validity index (Figure 6B, $R = -0.104$, $p\text{-value} = 0.332$).

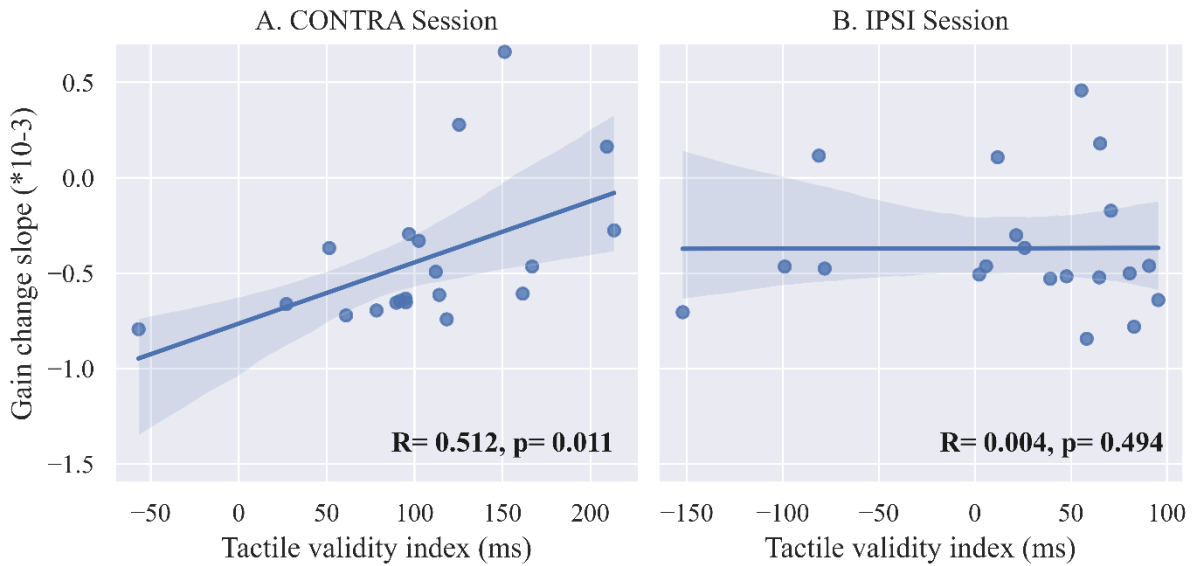


Figure 5: Experiment 1: correlation between the slope of gain change during time and the tactile validity index (ms) for leftward saccades in the CONTRA (A) and IPSI (B) sessions. R represent the Pearson's correlation value and p represent the p -value for the one-sided Pearson's correlation.

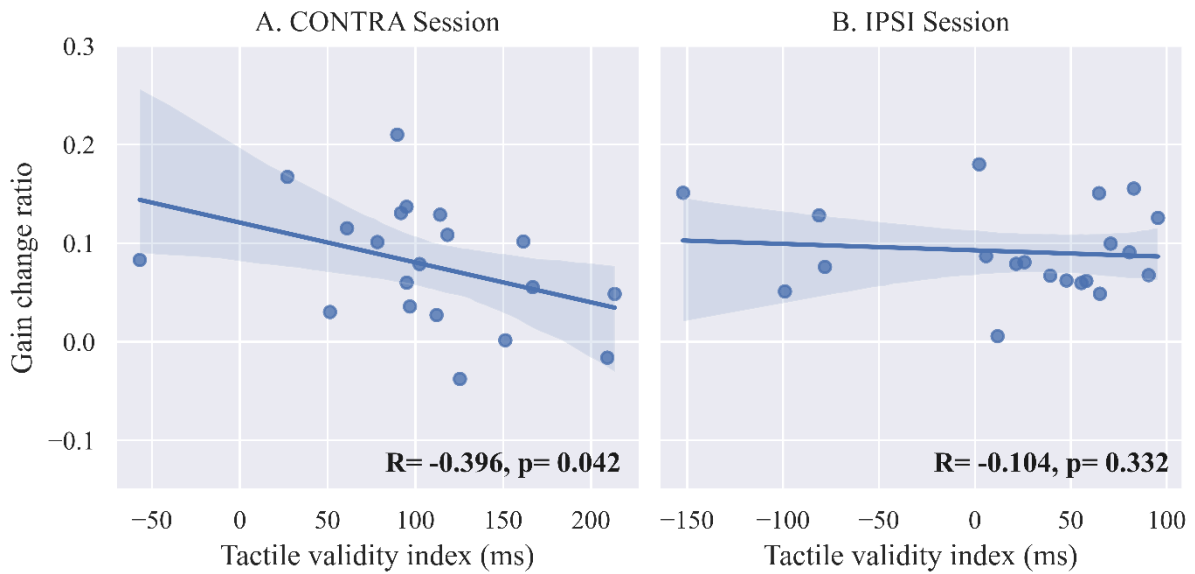


Figure 6: Experiment 1: correlation between the gain change ratio and the tactile validity index (ms) for leftward saccades in both CONTRA (A) and IPSI (B) sessions. R represent the Pearson's correlation value and p represent the p -value for the one-sided Pearson's correlation.

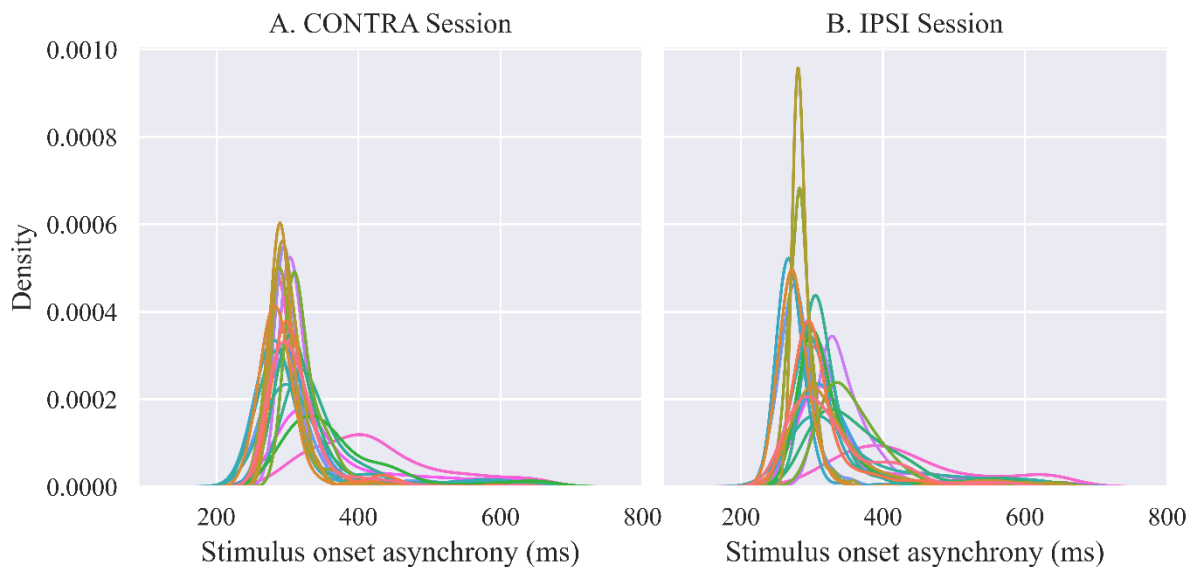


Figure 7: Experiment 1: A graph showing the densities of the stimulus onset asynchronies for different participants (different colors) in the CONTRA (A) and the IPSI (B) sessions.

Interim Discussion

In this experiment, we investigated the effect of the exogenous orienting of spatial attention on the adaptation of leftward RS. We were able to reliably induce adaptation of those saccades (saccadic gain decreased during Exposure and remained lower in the POST- versus PRE-exposure phases), but group-level statistical comparisons between the IPSI and CONTRA session did not argue for an effect of the direction of exogenous tactile attention on RS adaptation. However, this analysis may have been insufficiently sensitive, all the more so since participants' tactile discrimination performance failed to reveal any successful orienting of tactile exogenous attention for leftward cues. Nevertheless, if our hypothesis is valid, the gain decrease due to saccadic adaptation should correlate with the amount of attention shifts obtained in each session. Indeed, when exogenous orienting of tactile attention was successful (for leftward saccades in the CONTRA session), correlation analyses did show that orienting tactile exogenous attention away from the location of the saccade's target during adaptation made this adaptation slower and weaker (significant positive correlation with slope and negative correlation with gain change, respectively), thus providing partial support to our hypothesis. However, the second prediction of this hypothesis could not be supported by our results, as the absence of significant correlations for leftward saccades in the IPSI session does not argue for a facilitatory effect of exogenous attention when oriented toward the saccade's target on RS adaptation.

In Experiment 2, using the same strategy as in Experiment 1, we investigated whether endogenous tactile attention could also modulate the adaptation of voluntary saccades (VS).

Experiment 2: The Effect Of Endogenous Spatial Attention On The Adaptation Of Voluntary Saccades.

Material And Methods

Participants

Twenty new participants were recruited for this experiment, including ten females (one left-handed) and ten males (one left-handed) with mean age = 26.1 ± 4.49 years old (range 20 to 37).

Design

Each participant performed two sessions, with a minimum seven-day interval in between, where tactile endogenous attention in the adapted saccade trials was directed either towards (‘IPSI’ session) or away from (‘CONTRA’ session) the location of the VS target. Contrary to Experiment 1, both leftward and rightward VS were simultaneously exposed to the adaptive double-step procedure (there was no exposure trial with the target disappearing at saccade onset); thus, the ‘IPSI’ and ‘CONTRA’ association between adapted saccades direction and attention orienting applied simultaneously to both hemifields (see Table 2).

Each session comprised three phases: the PRE- and POST-exposure phases (30 trials each) consisting of simple VS towards transient visual targets (disappearing at saccade onset), and the Exposure phase (160 trials) wherein each trial combined adaptation (McLaughlin, 1967) and endogenous spatial attention-orienting paradigms (Chica et al., 2007). The second (intra-saccadic) target step was directed backward relative to the saccade direction in order to induce a saccade-shortening adaptation (see Table 2). During all 3 phases, saccades directed towards the left or right hemifield were randomly elicited with equal probabilities (50% each).

The order of the IPSI and CONTRA sessions was counter-balanced among participants, with ten starting with the former and the remaining ten with the latter.

Table 2: Table representing the different trial types in the exposure phase of Experiment 2.

| Session | IPSI | | | | CONTRA | | | |
|---------------------------|-----------|------------|------------|------------|-----------|------------|------------|------------|
| Tactile cue | Left Hand | | Right Hand | | Left Hand | | Right Hand | |
| Saccade target (T1) | Left | | Right | | Right | | Left | |
| 2 nd step (T2) | <u>ON</u> | | <u>ON</u> | | <u>ON</u> | | <u>ON</u> | |
| Tactile target | Left Hand | Right Hand | Left Hand | Right Hand | Left Hand | Right Hand | Left Hand | Right Hand |

Procedure

Saccadic tasks

All trials of the PRE- and POST-exposure phases started with a central FP appearing for 1200 ms. Then, a visual target T1 was presented at 15° to the left or right (FP still visible). Participants were asked to maintain fixation on FP for a random duration (average 1100 ms), after which a go-signal, consisting of a green circle (diameter = 0.25°), appeared inside the fixation point (the trial was aborted and replaced by a new one if a saccade was detected during this interval). The go-signal prompted participants to perform a saccade toward T1. Once the saccade onset was detected (velocity threshold = 30°/s), both T1 and FP disappeared, and participants were instructed to keep fixating on the location of T1 until the re-appearance of FP, indicating the end of the trial.

In the Exposure phase, the sequence of visual events was the same as in the PRE- and POST-exposure phases until saccade detection. At that time, the saccade target T1, the fixation point FP including the incrustrated go-signal all stepped 4° in a backward direction, and participants had to maintain fixation over the stepped peripheral target (T2 located at 11°) as represented in Figure 8.

Tactile discrimination task

In the Exposure phase, a tactile stimulation (cue) was delivered to both the index and thumb of one hand at a constant interval of 380 ms preceding the go signal (i.e., at a random delay –averaging 720 ms- after T1 onset). One hundred milliseconds after the saccade onset, a second tactile stimulation (target) occurred on a single finger (index or thumb, 50% probability) of either the cued hand (Valid condition, 80% of the total number of trials) or the opposite, un-cued hand (Invalid condition, 20% of the trials) (see Figure 8). Participants used foot pedals to report as fast and accurately as possible whether the tactile target was on the index or thumb finger. Upon response (or after the 1500 ms time-out), T2 disappeared, and performance feedback was displayed for 200 ms around the location of T2 to indicate whether their answer was correct (“+1”), “incorrect,” or “too late”. Then, a blank screen followed for 750 ms until the beginning of the subsequent trial, a period during which participants could blink if necessary. The Exposure phase was divided into two blocks of 80 trials each, followed by a short break of a few seconds, allowing the participants to rest while their mean performance (percentage of correct answers and mean RT) during the last block was displayed on the screen.

Before starting the experiment, a short training session was performed to accustom participants to the double task (oculomotor response and tactile detection) and ensure they complied with the instructions. This training session was identical to the exposure phase of the experiment but was shorter and without any adaptation elicited (T1 and FP disappeared at the saccade onset).

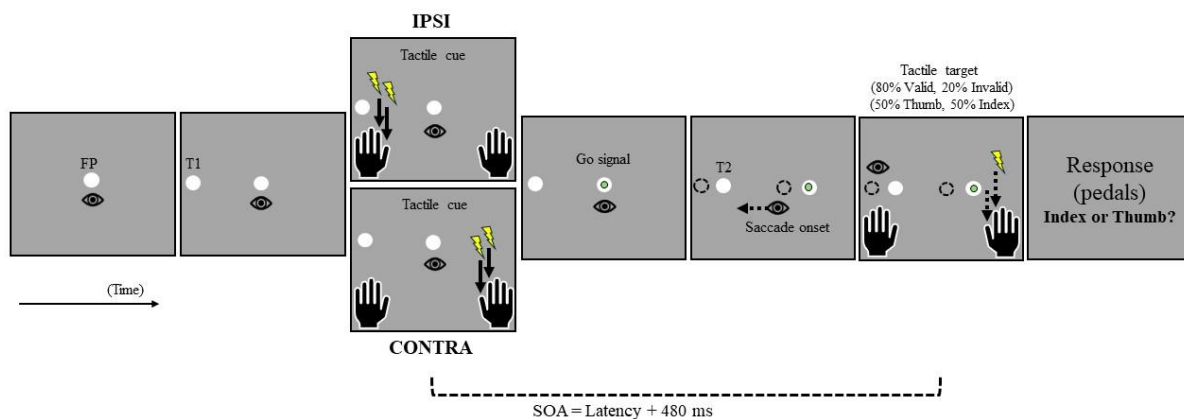


Figure 8: Schematic representation of the experimental protocol for leftward saccades in the exposure phase of Experiment 2. After a random fixation time (on FP), the saccade target T1 was presented at 15 degrees eccentricity. However, the participants were instructed to maintain fixation. Participants tactile endogenous attention was oriented using a tactile stimulation (tactile cue) delivered on both the index and the thumb fingers of the left hand (in IPSI session) or the right hand (in CONTRA session) at a random duration after T1 appearance and 380 ms before the appearance of the saccade's go-signal (green circle inside the FP). Participants were instructed to saccade as rapidly and precisely as possible toward T1 once the go-signal was presented. At the saccade's onset, the visual scene shifted 4 degrees toward the right, thus forming a backward step. One hundred ms after saccade onset, a second tactile stimulation (tactile target) was delivered on the cued (Valid trials, 80%) or the uncued hand (Invalid trials, 20%). The tactile target can occur on either the stimulated hand's thumb or the index (50% chance each). The participants had to report the location of the tactile target (Index or Thumb) using a pair of pedals placed under their right leg.

Analysis

The data processing and parameter extraction of the saccadic and tactile discrimination responses were similar to those of Experiment 1. For the saccade latency, the minimum latency of VS was set at 120 ms (instead of 80 ms for RS in Experiment 1). Overall, 10.8 % of trials were excluded. The Tukey method was again used to identify participants as outliers according to their mean percentage of correct answers in the attentional task (group median: IPSI = 75.31%, CONTRA = 75.94 %) (Chica et al., 2007). Two participants were identified as outliers and thus removed. Therefore, the analyses described in the following were based on a final dataset of 18 participants.

Firstly, we used a 2-way rm-ANOVA with the Session (IPSI vs. CONTRA) and Saccade direction (Leftward vs. Rightward) as within-subjects factors to analyze the median values of saccade latency in the PRE-exposure phase. Second, we investigated the effect of the tactile cue on saccade latency: we submitted the median latency of saccades collected in the Exposure phase along with those measured in the PRE-exposure phase where no tactile cues were delivered (the IPSI and CONTRA sessions were collapsed after checking the absence of significant difference) to a 2-way rm-ANOVA with the factors ‘Saccade direction’ (leftward vs. Rightward) and ‘Tactile Cue’ (Same side vs. Opposite side vs. None) as within-subjects factors.

Third, to test our main working hypothesis of a modulation of VS adaptation by shifts of endogenous attention, the slope of gain change during Exposure was subjected to a 2-way rm-ANOVA, with Session (IPSI vs. CONTRA) and Saccade direction (Rightward vs. Leftward) as within-subjects factors. In the second ANOVA testing our hypothesis, we submitted the saccade gain measured in the PRE- and POST-Exposure phases to a 3-way rm-ANOVA with the factors Phase (PRE vs. POST) x Session (IPSI vs. CONTRA) x Saccade direction (Rightward vs. Leftward).

Additionally, to check whether endogenous attention was adequately oriented to the cued location, we submitted the tactile discrimination RT to a 3-way rm-ANOVA with Session (IPSI vs. CONTRA), Saccade direction (Rightward vs. Leftward), and Validity (Valid vs. Invalid) as within-subjects factors.

We tested the effect of session and pedal counterbalancing across participants on the saccadic gain and the discrimination RT, respectively, by including them separately in the above analyses as additional between-subjects factors (‘Group’: IPSI-first vs. CONTRA-first or ‘Toes pedal’: Finger vs. Thumb).

Lastly, as in Experiment 1, we explored the correlations (one-sided Pearson’s correlation) between the tactile validity index and the Gain change ratio, as well as between the tactile validity index and the Gain change slope.

When the sphericity was violated in the ANOVAs, Greenhouse-Geisser correction was applied. Results were considered significant when p value < 0.05 at $\alpha = 0.05$.

Results

Saccade latency in PRE-exposure

The 2-way rm-ANOVA on median values of saccade latency showed that the main effects of the Session and Saccade direction factors and their interaction were not significant (all $F \leq 0.588$, all p -values ≥ 0.454). The grand mean of saccade median latency pooled across the two saccade directions and the two sessions was equal to $274.52 \text{ ms} \pm 71.01$, which is consistent with the latency of VS (Nikolov, 2020).

Cue effect on saccade latency

The 2-way Saccade direction x Tactile cue rm-ANOVA showed a significant main effect only of the Tactile cue ($F(2, 34) = 6.272$, $p\text{-value} = 0.005$) (all other effects $F \leq 0.334$, $p\text{ values} \geq 0.718$). Pairwise comparisons showed no significant difference in saccade median latency when the cue and the saccade were ipsilateral in comparison to when they were contralateral, but also showed that, in both cases, latency was higher than for saccades in the PRE-exposure phase with no preceding cue, by respectively 53 ms ($p\text{-value} = 0.013$) and 57 ms ($p\text{-value} = 0.028$). Note that this increased latency of VS by tactile cues did not interact with Session or Saccade direction.

The slope of gain change

The slope of gain change during Exposure is illustrated in Figure 9, showing a decreased gain for both saccade directions. This is consistent with the use, in this experiment, of backward double-step targets for both saccade directions. This pattern is confirmed by the 2-way rm-ANOVA showing no significant main effect of Saccade direction ($F(1, 17) = 2.076$, $p\text{-value} = 0.168$) (mean slope \pm S.D.: Leftward saccades = $-1.258 \times 10^{-3} \pm 0.658 \times 10^{-3}$, Rightward saccades = $-1.513 \times 10^{-3} \pm 0.329 \times 10^{-3}$) or Session ($F(1, 17) = 1.105$, $p\text{-value} = 0.308$) or any significant Saccade direction \times Session interaction ($F(1, 17) = 2.052$, $p\text{-value} = 0.170$). Comparing the mean slope to zero (one-sample t-test with Bonferroni correction to multiple comparisons) showed significantly negative values in both sessions and for both saccade directions (all $p\text{-values} \leq 0.001$). In addition, the mean slopes did not differ between sessions (paired t-tests, leftward saccades: $p = 0.082$ and rightward saccades: $p = 0.618$). These results show that backward adaptation was successfully induced in both sessions and for both saccade directions. However, they also did not reveal any significant difference in gain slope values between the IPSI and the CONTRA sessions.

As in Experiment 1, we tested if there was an effect of the session order on the slope analysis. To this aim, we performed a rm-ANOVA similar to the previous one, but with the ‘Group’ factor (IPSI-first vs. CONTRA-first) added as a between-subjects factor. This analysis showed no significant main effect or interaction for the ‘Group’ factor (all $F \leq 3.206$, all $p\text{-values} \geq 0.092$).

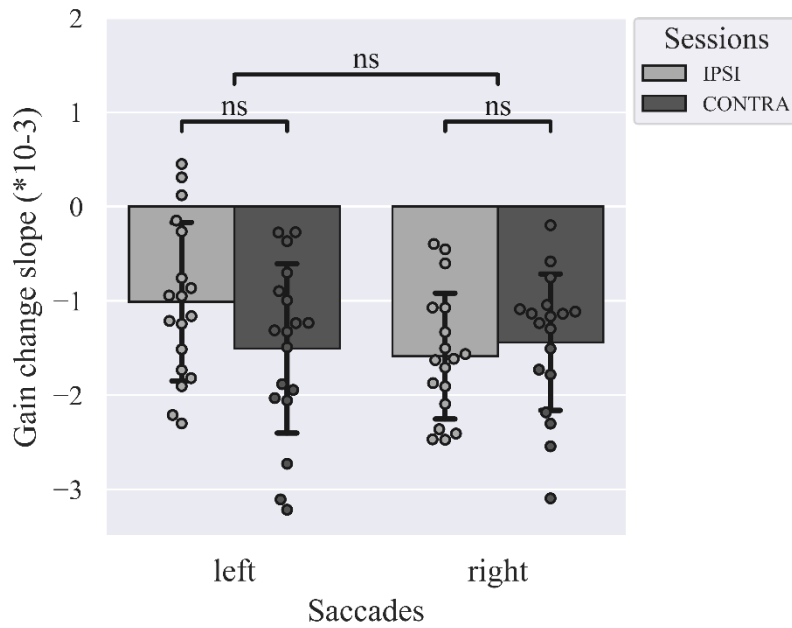


Figure 9: Experiment 2, mean slope (\pm s.d.) of the linear relationship between saccadic gain and trial number in the exposure phase, separately for leftward and rightward saccades and for IPSI (light grey) and CONTRA sessions (dark grey). *t*-tests: ^{ns} $p > 0.05$.

Gain variation

The mean gain values measured in the PRE- and POST-exposure phases are illustrated in Figure 10. Note that the gain decreased in POST- relative to PRE- for both leftward and rightward saccades, consistent with the findings reported above for the gain changes during Exposure. The 3-way rm-ANOVA revealed a significant main effect of the Phase factor ($F(1, 17) = 148.558$, p -value < 0.001) (mean gain \pm S.D.: PRE = 0.961 ± 0.043 , POST = 0.862 ± 0.043), without any additional main effect or interaction (all $F \leq 4.043$, all p -values ≥ 0.06). Thus, in continuity with the slope of gain change results, these findings reveal that backward adaptation led to a significant after-effect in both IPSI and CONTRA sessions, without any significant difference between the two sessions.

We tested the effect of session order on this saccadic gain analysis by including the Group (IPSI-first vs. CONTRA-first) as a between-subjects factor in the rm-ANOVA. This Group factor had no significant main effect ($F(1, 16) = 0.059$, p -value = 0.811) and did not interact with any other factor (all $F \leq 3.322$, all p -values ≥ 0.087) except for the triple interaction Group \times Saccade direction \times Phase ($F(1, 16) = 5.042$, p -value = 0.039). However, post hoc pairwise Bonferroni comparisons for this interaction showed neither significant differences between groups (all p -values ≥ 0.226) nor significant differences between saccades (all p -values ≥ 0.109), while the phases differed significantly for both saccades and the counter-balanced groups (all p -values ≤ 0.001).

In summary, we succeeded in inducing backward adaptation of both leftward and rightward VS in both IPSI and CONTRA sessions but did not observe any significant difference in adaptation between sessions that might result from differences in the orienting of attention.

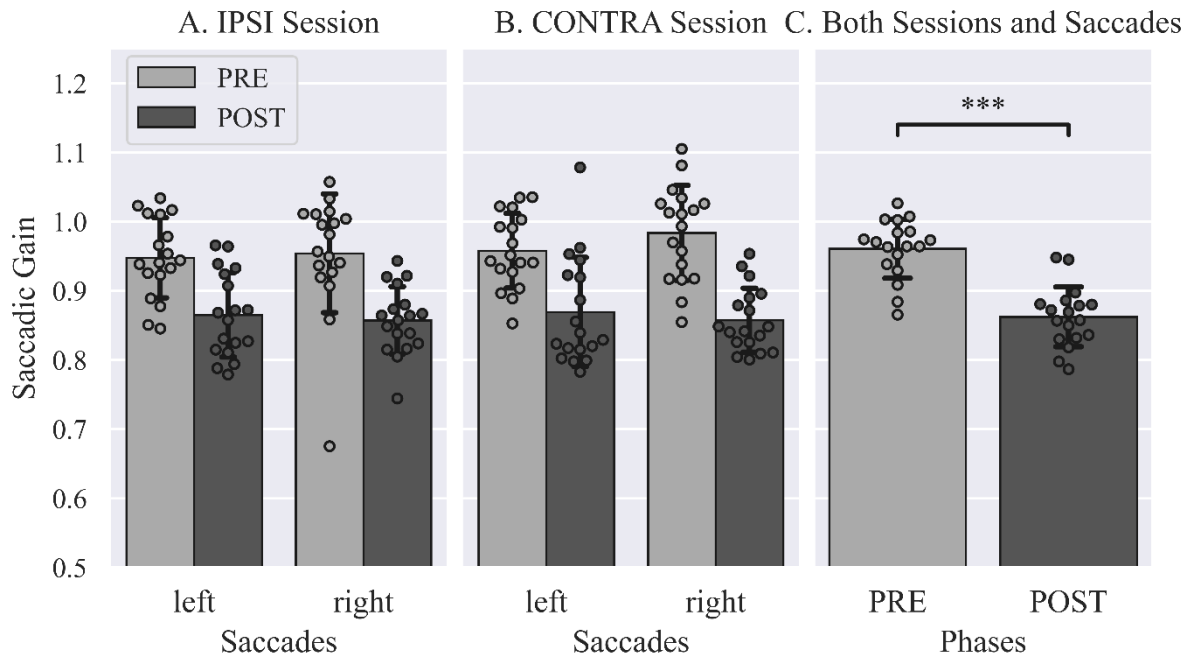


Figure 10: Experiment 2, mean saccadic gain (+/- s.d.) of leftward and rightward saccades in the PRE (light grey) and POST phases (dark grey), in IPSI (A) and CONTRA sessions (B) as well as the average PRE- and POST-exposure saccadic gain over both sessions and saccades (C). t-tests: * $p < 0.001$.**

Discrimination RT

As in Experiment 1, we analyzed the RT of the tactile discrimination responses to verify that the participants' endogenous tactile attention was successfully oriented in both the IPSI and CONTRA sessions. The mean RT values of correct responses are plotted in Figure 11. The 3-way Session \times Saccade direction \times Validity rm-ANOVA showed a significant main effect of Validity ($F(1, 17) = 57.101$, p -value < 0.001 , participants were 55.4 ms faster responding in valid versus invalid trials), as well as of the Saccade direction \times Validity ($F(1, 17) = 5.418$, p -value = 0.033) and Session \times Saccade direction \times Validity interactions ($F(1, 17) = 18.239$, p -value < 0.001). There were no other significant effects or interactions (all $F \leq 1.772$, all p -values ≥ 0.201). Bonferroni corrected post hoc comparisons for the Session \times Saccade direction \times Validity interaction revealed significant differences between valid and invalid trials for all saccades and sessions (all p -values < 0.001) except for rightward saccades in the CONTRA session (p -value = 0.098). In addition, this post hoc analysis showed no significant difference in RT between saccade directions (all p values ≥ 0.120) except for invalid trials in the CONTRA session where rightward saccades had faster RT than leftward saccades (41 ms

difference, p -value = 0.004), which might explain the absence of validity effect for rightward saccades in CONTRA session.

In conclusion, tactile spatial attention could be oriented toward both sides in the IPSI session but only for leftward saccades in the CONTRA session.

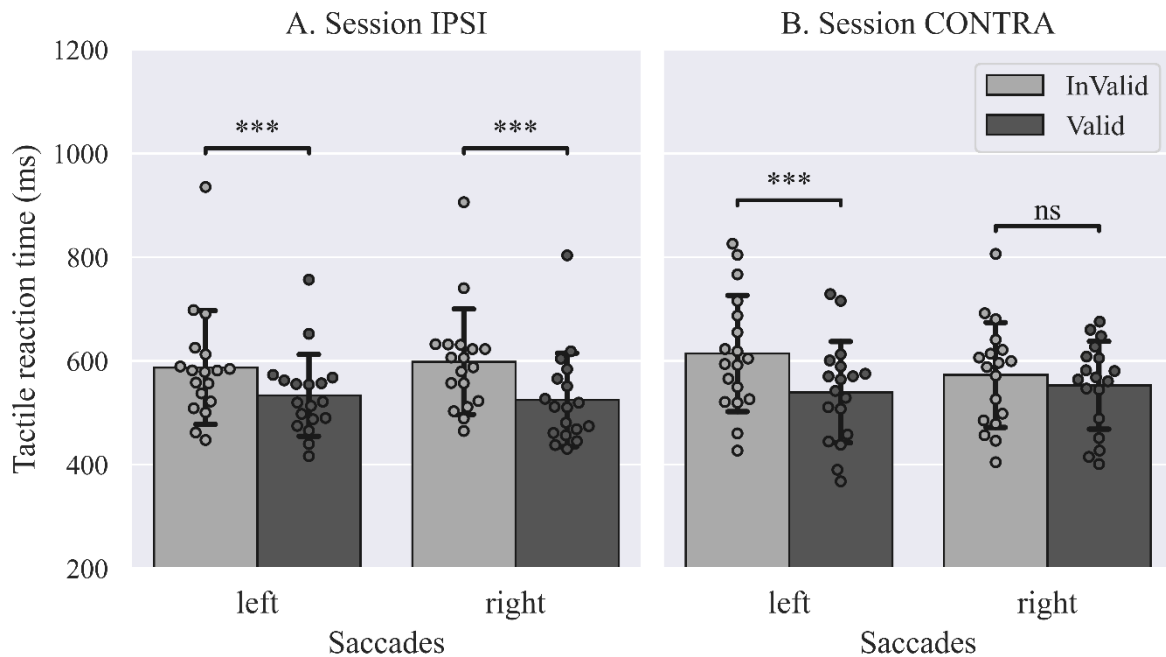


Figure 11: mean reaction time to the tactile target (+/- s.d.) in leftward and rightward saccade trials for valid (dark grey) and invalid trials (light grey) across the IPSI (A) and the CONTRA (B) sessions. *t*-tests: ^{ns} $p > 0.05$, ^{***} $p < 0.001$.

Correlations

As in experiment 1, we investigated the correlations between the tactile validity index –indexing tactile attention orienting- and the two measures of VS adaptation (gain change slope and gain change ratio). These correlation analyses are illustrated in Figures 12 and 13. Considering first the relationship with the gain slope (Figure 12), a significant negative correlation was found in the IPSI session for leftward saccades ($R = -0.533$, p -value = 0.011) but not for rightward saccades ($R = 0.106$, p -value = 0.337). In the CONTRA session, there was a significant positive correlation again for leftward saccades ($R = 0.426$, p -value = 0.039) but a significant negative for rightward saccades ($R = -0.625$, p -value = 0.003).

Moving now to the relationship between tactile validity index and gain change ratio (Figure 13), significant positive correlations were found in the IPSI session for both leftward ($R = 0.543$, p -value = 0.010) and rightward saccades ($R = 0.519$, p -value = 0.014), but not in the CONTRA session for either leftward saccades ($R = -0.248$, p -value = 0.161) or rightward saccades ($R = 0.128$, p -value = 0.307).

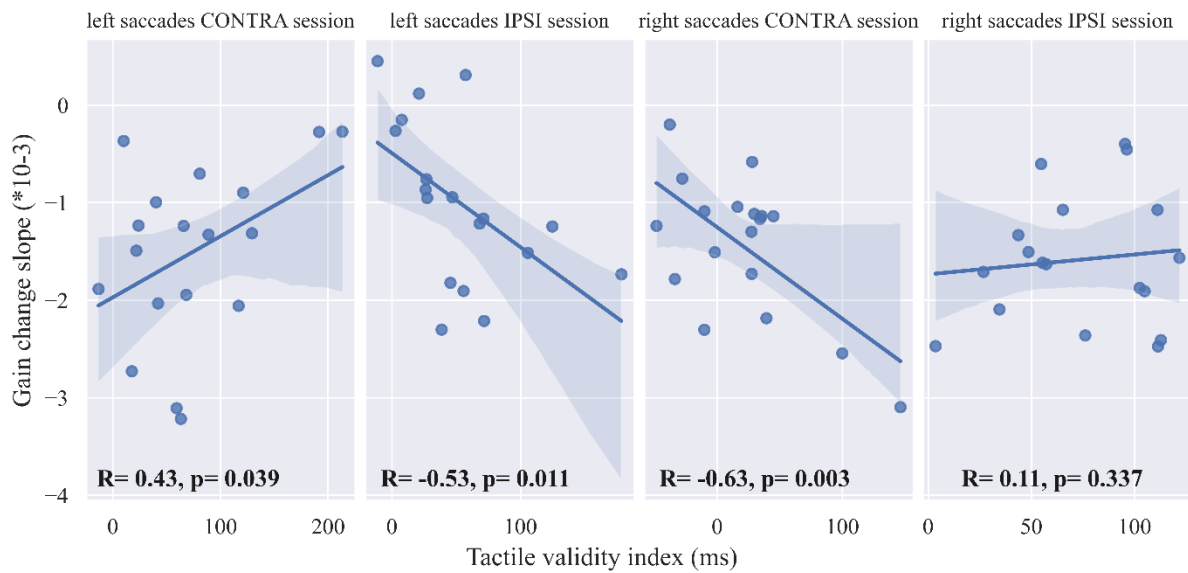


Figure 12: Experiment 2, correlation between the slope of gain change during time and the tactile validity index (ms) for leftward and rightward saccades in the IPSI and the CONTRA sessions. R represent the Pearson's correlation value and p represent the p -value for the one-sided Pearson's correlation.

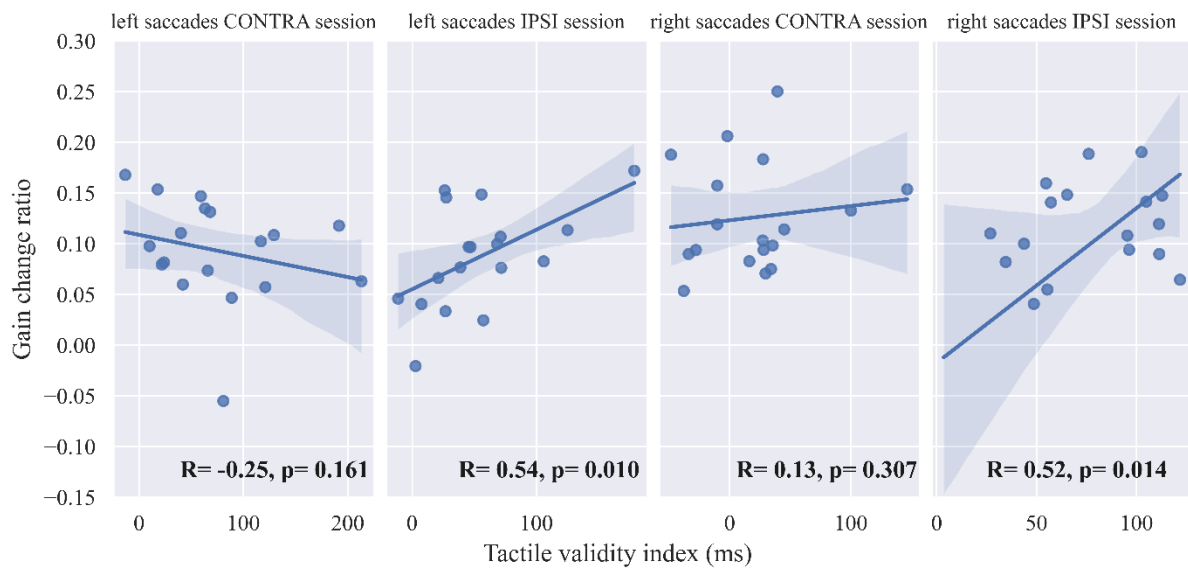


Figure 13: Experiment 2: correlation between the gain change ratio and the tactile validity index (ms) for left and rightward saccades in both IPSI and CONTRA sessions. R represent the Pearson's correlation value and p represent the p -value for the one-sided Pearson's correlation.

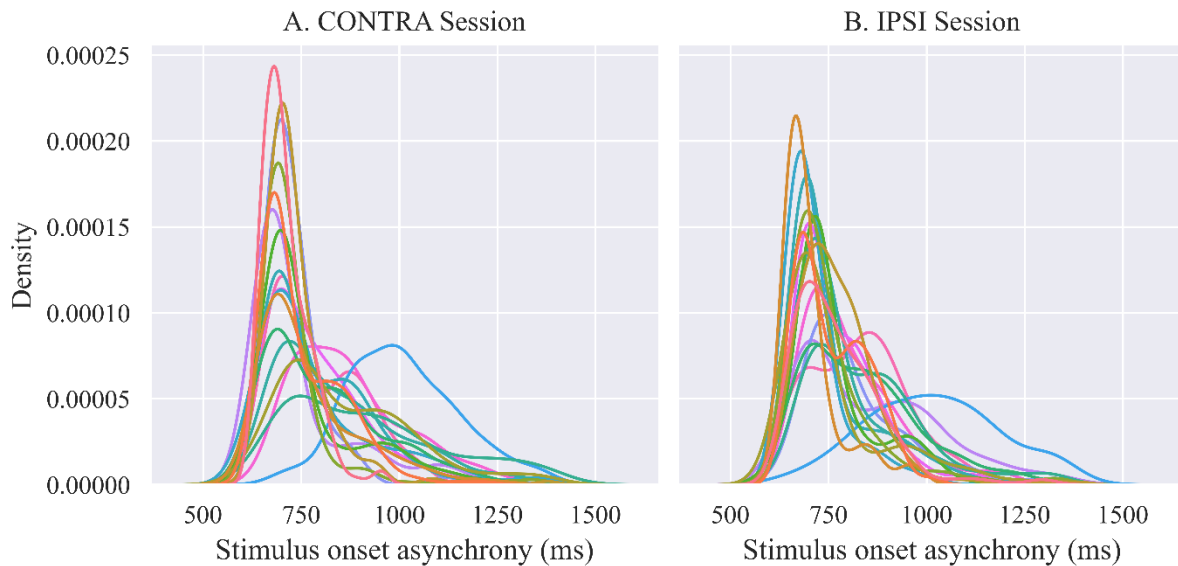


Figure 14: Experiment 2: A graph showing the densities of the stimulus onset asynchronies for different participants (different colors) in the CONTRA (A) and the IPSI (B) sessions.

Interim Discussion

In Experiment 2, we investigated the effect of the endogenous orienting of spatial attention on the adaptation of leftward and rightward VS. Similarly to Experiment 1, we were able to induce adaptation of those saccades, but statistical comparisons between the IPSI and CONTRA sessions did not argue for an effect of the direction of endogenous tactile attention on VS adaptation. Since the orienting of tactile endogenous attention wasn't equivalent in all our conditions, we further investigated the correlation between the individually-measured tactile validity index and each of the gain change ratio and slope.

In conditions where we observed successful orientation of tactile endogenous attention, correlation results indicate that, on the one hand, the more tactile endogenous spatial attention is oriented toward the location of the saccade's target, the faster the adaptation (IPSI session, leftward saccades) as well as the higher the adaptation after-effect (IPSI session, leftward and rightward saccades) and on the other hand, the more tactile spatial attention is oriented away from the saccade's target, the slower saccadic adaptation (CONTRA session, leftward saccades). This provides evidence for an effect of endogenous orienting of attention on the adaptation of voluntary saccades. Yet, one correlation seems contradictory As the slope of gain change for rightward saccades in the CONTRA session correlated negatively with the tactile validity index, meaning that when endogenous attention was oriented toward the opposite location of the visual target, the gain decrease due to backward adaptation in the exposure phase was faster.

General Discussion

In this study, we investigated the impact of spatial attention on saccadic adaptation. We used tactile cueing to orient crossmodally participants' exogenous (Experiment 1) and endogenous (Experiment 2) spatial attention toward or away from the location of the saccade's target while inducing backward adaptation of reactive (Experiment 1) and voluntary saccades (Experiment 2).

In neither experiment, we observed a difference in the adaptation after-effect or the slope of the saccadic gain change during the exposure between the conditions whereby spatial attention was oriented towards or away from the saccade target. However, validly cued tactile targets were not uniformly speeded up across participants and conditions in comparison to invalidly cued ones, contrary to what one would expect from efficient orienting of spatial attention. This might, therefore, hamper the comparison of adaptation parameters between sessions.

Nevertheless, we found several correlations between the tactile validity index, reflecting at the individual level the attentional orienting capability, and both the gain change ratio (an indicator of the amount of adaptation's after-effect) and the gain change slope (an indicator of the speed of adaptation). Specifically, results obtained in Experiment 1 revealed a decrease in the speed and the amount of RS adaptation when exogenous attention was oriented away from the saccade's target. Results obtained in Experiment 2 revealed that, first, the amount of VS adaptation increases when endogenous attention is oriented toward the visual target (for both leftward and rightward saccades). Second, the speed of adaptation is also affected by the orienting of endogenous attention for leftward VS: it decreases (or increases) with the increasing amount of attention when oriented away (or toward) the visual target, which both argue in favor of our hypothesis.

Besides its main objective, our study provided another outcome. It has been previously shown that presenting a non-visual stimulation before a visually-triggered saccade reduces the saccade latency, specifically when the stimulus onset asynchrony (SOA) between the sensory stimulation and the saccade visual target ranges between 200 ms and 0 ms (Diederich & Colonius, 2008; Vidal et al., 2020). This effect has also been shown to be stronger when the sensory stimulus is ipsilateral to the saccade target. Those findings suggest a multisensory integration effect on saccade preparation, possibly taking place at the level of the superior colliculus (SC) (Diederich & Colonius, 2008; Vidal et al., 2020). The SC is indeed known to be a critical site of multisensory integration. Visual, auditory, and tactile sensory information converge in the intermediate and deep layers of the SC after being totally or partially translated into the oculocentric reference frame in which the oculomotor commands of the appropriate saccadic response toward these stimuli are generated (Groh & Sparks, 1996a, 1996b; Jay & Sparks, 1987a, 1987b). In Experiment 1, we did observe a pattern of cue-related latency modulation compatible with multisensory integration. Indeed, RS preceded by an ipsilateral tactile cue were triggered after a shorter latency than those preceded by a contralateral cue, and, in both cases, ipsilateral and contralateral cues reduced the saccade latency as compared with saccades performed in the PRE-exposure phase without tactile cues. In contrast, for VS in Experiment 2 we found a

significant increase in the latency of saccades preceded by a cue compared to the saccades in the PRE-exposure without a cue, with no significant difference between the cue types (ipsi vs. contra). Thus, the findings in Experiment 1 point toward a pre-saccadic facilitatory effect of tactile cueing on saccades preparation, resulting from the multisensory integration process probably at the level of the superior colliculus. In Experiment 2 we did not see such pre-saccadic facilitatory effect, which is not surprising as the tactile cue was delivered outside the temporal window (-200 to 0 ms) in which multisensory effects take place. Nevertheless, for both experiments the effect of attention on saccadic adaptation should originate from the effect of the tactile cueing after the saccade offset while the error signal is being generated and processed.

In their reviews, Corbetta et al. (Corbetta et al., 2008; Corbetta & Shulman, 2002) proposed that the orienting of spatial attention relies on two separate but interconnected frontoparietal networks, a ventral one responsible for the exogenous orienting of spatial attention and a dorsal one responsible for the endogenous orienting (see Introduction). The dorsal premotor cortex and the IPS, both belonging to the dorsal frontoparietal network, were shown to be activated irrespectively of whether the participants prepare for visual or tactile discrimination (Macaluso et al., 2003). Similarly, the TPJ and the inferior frontal gyrus of the ventral frontoparietal network also show significant activations in both visual and tactile discrimination tasks (Macaluso et al., 2002). One possibility would be that attention acts on the adaptation's neural substrates at the level of this multimodal structures. As pointed out in the introduction, Gerardin et al. (Gerardin et al., 2012) showed an activation of the rTPJ during RS adaptation and of the IPS during VS adaptation. Altogether, these observations suggest that the interaction between spatial attention and saccadic adaptation might result from interactions at the level of the TPJ (for exogenous attention and RS adaptation in addition to a possible implication of the SC mentioned above) and the IPS (for endogenous attention and VS adaptation).

The activation of the IPS and the TPJ during saccadic adaptation (Gerardin et al., 2012) has also been reported in Guillaume et al. study (Guillaume et al., 2018) and attributed to the processing of the error signal involved in saccadic adaptation (the mismatch between the predicted and the actual target position relative to the saccade landing position). Another fMRI study (Métais et al., 2022) also demonstrated the involvement of the PPC in error signal processing. Furthermore, as pointed out in the Introduction, the locus of attention itself can act as an error signal to induce saccadic adaptation (Khan et al., 2014; McFadden et al., 2002). When considered in the light of the extant literature, these findings suggest that spatial attention may act on saccadic adaptation by allowing better processing of the error signals. Further studies are needed to decipher whether this entails facilitating the processing of post-saccadic visual information on which the error signal is built and/or directly supplying a complementary source of information for the error signal computation.

The correlation analyses revealed that all significant relationships were compatible with the facilitation of adaptation by attention when both are ipsilateral and an inhibitory effect of attention when contralateral to the adapted target, with the notable exception of the relationship between the

slope of gain change and the tactile validity index for rightward saccades when attention was oriented contralaterally to the saccade target. On the one hand, orienting tactile spatial attention toward the left hemifield implicates activation of attentional areas, mostly in the right hemisphere (Macaluso & Driver, 2001). On the other hand, performing saccades toward the right hemifield implicates an orienting of visuospatial attention toward the target location, including the activation of attentional regions not only in the left but also in the right hemisphere characterized by its attentional dominance (Capotosto et al., 2009, 2012; Corbetta & Shulman, 2002). Therefore, visuospatial attention allocated to the saccade target might be indirectly boosted by the increased activation of the right hemisphere, resulting in the observed negative correlation between the slope of gain change and the tactile validity index. This hypothesis is also supported by the corresponding RT analysis, which shows that for rightward saccades in the CONTRA session, discriminating targets in the invalid (tactile target on the right) trials was as fast as in the valid (tactile target on the left) trials. Therefore, while attention was intended to be oriented contralaterally to the saccade target, unexpected facilitation also took place ipsilaterally.

Limits of the study: In this study, we leveraged the cross-modality of spatial attention to use tactile cues to orient spatial attention because visual cues would more directly conflict with the saccade visual targets and hamper the participants' task. Thus, it is necessary to assess whether this procedure and associated temporal and spatial parameters allowed an adequate shift in attention toward or away from the direction of the adapted saccade. In this study, the tactile cue and target were delivered on the hands located behind the visual display, in close alignment with the saccade targets. This way, any cueing effect induced unimodally (tactile attention orientation) should transfer cross-modally and boost visual-spatial attention at the location of the saccade target. Results from the discrimination task showed that for most participants, the tactile cueing facilitated (speeding up) the discrimination of the tactile target in valid trials compared to invalid ones. However, this effect was not seen in certain conditions, which might result from the following causes. First, using the right foot in a discrimination task has been suggested to speed up the participants' response to targets presented ipsilaterally to the foot pedal, leading to mask any difference in RT between invalid and valid trials (Lloyd et al., 2010). In our study this might have artificially masked the validity effect (even with the orienting of spatial attention maintained) for Left-Cued trials, while increasing it for Right-Cued trials. Both effects are indeed compatible with the pattern of results in Experiments 1 and 2. Second, it has been suggested that discriminating a target is faster when fixating on its location even if the stimulated location is not visible (Honoré et al., 1989). In our study, the participants discriminated the unseen target location while fixating its location which might have an impact on the discrimination RT. Third, the within-subject variation of reactive and voluntary saccades latency might impact the cue-target interval such that an inhibition, instead of facilitation, may occur (especially for RS). Indeed, when exogenous spatial attention is oriented tactually, the discrimination of both tactile and visual targets presented at the cued location is facilitated (faster response) in comparison to the opposite location, for

cue-target intervals ranging between 150 ms and 400 ms (Spence et al., 1998; Spence & McGlone, 2001). With longer intervals, this effect vanishes, and around 600 ms, it reverses into faster responses in invalid than in valid trials, a phenomenon, known as inhibition of return (IOR) (Plax, 2021). Similarly to the tactile-visual cross-modal effects in exogenous attention, orienting tactile endogenous attention toward a certain location also facilitates the discrimination of both tactile and visual targets at the cued location for cue-target intervals ranging between 500 and 1000 ms (Chica et al., 2007; Spence et al., 2000). In our experiments, the cue-target interval could not be constant across trials because it included the saccadic response and thus varied with the saccade's latency and duration. Nevertheless, while implementing and piloting the protocol, we took into consideration the median latency value reported in the literature for both reactive (around 180 ms) and voluntary (around 300 ms) saccades, as well as their duration (50 ms), ensuring that in both experiments the mean delay between the cue and the target were adequate for a facilitatory cueing effect as described in the previous paragraph. As depicted in Figures 7 and 14, most of our participants' SOAs fall between 150 and 400 ms in Experiment 1 and between 500 and 1200 ms in Experiment 2. According to the literature presented above and for both SOA ranges, we should have a successful orienting of tactile spatial attention and, therefore, a cross-modal facilitatory effect of the tactile cueing on visual targets presented at the tactually cued location compared to the un-cued location.

In conclusion, by leveraging the cross-modal link of attention between touch and vision, this study reports initial evidence that both exogenous and endogenous shifts of spatial attention affect the adaptation of reactive and voluntary saccades, respectively. We suggest that these effects might be related to spatial attention acting on the processing of error signals underlying saccadic adaptation.

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Disclosures

The authors declare that they have no competing interests.

Author contributions

Conception and design of the study: A.B., A.F., and D.P; Setup preparation and Software: A.B., E.K., and R.S.; Data collection: A.B.; Data analysis: A.B.; Data interpretation: A.B., A.F. and D.P; Original draft: A.B.; Critical revisions: A.F. and D.P; All the authors approved the final manuscript for submission.

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C. GENERAL DISCUSSION

In this section, we will discuss the different outcomes of the experiments done during this thesis. Those outcomes can be classified into three main parts. First, we will discuss the results obtained on the transfer of visual reactive saccades adaptation to non-visual saccades. Second, we will interpret our findings on the adaptation of non-visual saccades. Finally, the third part will be devoted to the results related to the effect of spatial attention on saccadic adaptation.

Part 1: The transfer of visual reactive saccades adaptation to non-visual saccades

Summary of results

Study 1, Experiment 1:

This experiment included 15 participants, each of whom performed a control session and an adaptation session. Each session included three major phases: in the pre- and post-exposure phases, participants performed simple saccades toward peripheral tactile or visual targets, which disappeared at the saccade onset. Between these two phases, we had an exposure phase in which we either adapted our participants (adaptation session) or not (control session). In the exposure phase of the adaptation session, visual reactive saccades performed toward two target eccentricities (located at 20° and 25° from the fixation point) were submitted to backward adaptation. We investigated the effect of this adaptation on non-adapted visual saccades of 15° and 30° and tactile saccades performed toward the adapted (20° and 25°) as well as the non-adapted locations (15° and 30°). The results obtained in the adaptation session were contrasted to the control session where no backward target step occurred in the exposure phase, the target remaining at its initial location after the detection of the saccade onset. We compared the ratio of gain change between pre- and post-exposure as well as the slope of gain change during the exposure phase between adaptation and control sessions. Our results in the adaptation session, compared to the control session, showed:

1. a significant decrease in the adapted visual saccades gain, as revealed by a progressive gain decrease during the exposure phase and a significant adaptation after-effect
2. a generalization of visual saccades backward adaptation to non-adapted visual saccades at nearby locations
3. a transfer of backward adaptation to tactile saccades performed toward both adapted and non-adapted nearby locations.

Study 2, Experiment 1:

Each of our 15 participants included in this experiment performed two sessions: a forward and a backward adaptation session. As in Study 1, each session included three major phases: in the pre- and post-exposure phases, participants performed simple saccades toward auditory or visual targets located in the periphery and which disappeared at the saccade onset. In the exposure phase, visual reactive saccades to the 15° target in one hemifield were either submitted to forward (forward session) or to backward (backward session) adaptation (5° intrasaccadic step), whereas for visual saccades of 15° performed toward the opposite hemifield the visual target remained at its location after the saccade onset (control saccades). We investigated the effect of these adaptations on non-adapted visual saccades of 10° and 20° and on auditory saccades performed toward the adapted (15°) as well as the non-adapted locations (10° and 20°). In this experiment, backward and forward adaptations were performed not only in two different sessions but also in two different hemifields. We compared saccades submitted to backward intrasaccadic steps in one session to control saccades performed in the same hemifield but in a different session. Similar comparisons were made for forward adaptation. For each adaptation type, we compared the gain change ratio as well as the gain change slope between the adaptation and control conditions. Our results showed that compared to control, both backward and forward adaptation of visual reactive saccades:

1. lead to, as expected, significant changes (decrease or increase, respectively) of the gain change slope and of the gain change ratio
2. generalize to non-adapted nearby visual saccades (10° and 20°)
3. transfer to tactile saccades performed toward both the adapted (15°) and the non-adapted nearby locations (10° and 20°).

Discussion I: The transfer

The two experiments presented above aimed to assess the transfer of visual reactive saccades adaptation to non-visual tactile (Study 1) and auditory (Study 2) reactive saccades. We were able to induce backward (Studies 1 and 2) as well as forward adaptations (Study 2), as evidenced by significant and progressive gain changes in the exposure phases as well as significant adaptation after-effects. The adaptation of visual saccades in these two experiments showed significant and complete generalization to non-adapted visual saccades aiming at targets located near the adapted ones. This is not surprising in light of the well-known pattern of spatial generalization of adaptation (adaptation field). Indeed, saccadic adaptation was shown to fully generalize to saccades of the same vector performed from different initial eye positions, whereas the amount of generalization decreases for increasing deviations of the saccade vector direction until it nullifies for saccades orthogonal to the adapted one as well as for those in the opposite direction (Alahyane, Devauchelle, et al., 2008). The generalization of saccadic adaptation was further shown to be asymmetric along the saccade vector amplitude as it decreases faster for smaller saccade's amplitudes compared to larger ones, with no

difference in the characteristics of this generalization between backward and forward adaptations (Collins, Doré-Mazars, et al., 2007; Schnier et al., 2010). In both of our experiments, the non-adapted visual saccades were in the same direction as the adapted ones, with amplitudes either 5° shorter or 5° larger than the adapted saccades. This explains the high amount of transfer, as a 5° difference is not large enough relative to the size of the adaptation field to entail a significant decrease in generalization.

In Study 1, we reported for the first time a transfer of backward adaptation of reactive visual saccades to tactile saccades. Concerning the third modality studied in this thesis, audition, the visual-to-auditory transfer of backward adaptation we found (Study 2) was previously reported in two different studies (Collins et al., 2010; Frens & van Opstal, 1994). Here, we further showed that this visual-to-auditory transfer also exists for forward adaptation, leading us to expect also a visual-to-tactile transfer of reactive saccade forward adaptation. In addition, we demonstrated that the transfer of adaptation affects not only non-visual saccades performed toward the adapted location but also those directed to different though close targets. In order to understand the candidate structure/process where such transfer happens, it is important to recall some of the studies reviewed in Chapter 2. Bimodal neurons responsive to both somatosensory and visual stimuli and exhibiting saccade-related activities were found in the intermediate and deep layers of the SC. These neurons were found to encode the saccade goal in an oculo-centric coordinate system, irrespective of stimulus modality. This, therefore, indicates that the somatosensory signals were translated from their native body-centered reference frame into eye-centered motor coordinates at the level of those bimodal neurons or upstream (Groh & Sparks, 1996b). Groh and Sparks (Groh & Sparks, 1996c) further suggested that this coordinate transformation takes place partially at the level of the SC, as well as upstream of this structure. Similarly, the intermediate layer of the SC was also found to contain neurons with motor bursts prior to saccades to both auditory and visual targets, and it was further suggested that the transformation of head-centered to eye-centered frame of reference of auditory signals takes place partially, and gradually in the SC (Jay & Sparks, 1987a, 1987b; Lee & Groh, 2012). The best upstream candidate for the coordinate transformation of auditory and somatosensory signals would be the PPC, as shown by several studies (Buchholz et al., 2011, 2014; Grunewald et al., 1999; Linden et al., 1999; Mullette-Gillman et al., 2009). In addition, a near-complete transformation of auditory signals to an eye-centered frame of reference was also shown to take place at the level of the FEF, known to contain neurons responsive to both auditory and visual stimuli but not somatosensory ones (Caruso et al., 2016); nevertheless, as the PPC project to the FEF (Munoz, 2002), it is probable that this latter receive information related to tactile saccades. Based on our transfer results and in accordance with the studies presented above, a parsimonious proposal is that both backward and forward adaptations of visual reactive saccades take place at a site(s) where different sensory signals (visual, auditory, and somatosensory) have converged into a common motor pathway and where neurons with saccade-related activities encode information in a common frame of reference, such as, therefore, the FEF, the

PPC, the SC, and/or brainstem structures. Also, and as was suggested in previous studies (Alahyane, Devauchelle, et al., 2008), adaptation is thought to act at a level where the oculomotor command is still encoded as vectorial eye displacement rather than downstream, at the level of the brainstem where the vertical and the horizontal saccade components are separately encoded, in order to account for both the generalization to non-adapted visual saccades and the transfer to non-visual saccades with various amplitudes reported in our studies. Previous studies have found that backward adaptation of voluntary - but not reactive - saccades transfers to hand-pointing movements (Bekkering et al., 1995; Cotti et al., 2007). This suggests that voluntary saccades adaptation occurs at the level of target representation common for both effectors (saccades and hand movements). Our cross-modal transfer results argue in favor of this conclusion, at least for the part related to reactive saccades: the large visual-to-auditory and visual-to-tactile transfer of adaptation we found indicate that it is not specific for visual reactive saccades and thus is not likely to mainly occur at the level of the visual target representation. Finally, Cotti et al. (Cotti et al., 2009) also found that reactive saccade adaptation acts only downstream of the vector inversion site(s) of anti-saccades, i.e., onto the saccade motor, rather than sensory, vector. While it is well known that both FEF (Jaun-Frutiger et al., 2013) and PPC (Zhang & Barash, 2000, 2004) participate in the anti-saccade vector inversion process, we are not aware of studies investigating whether the inversion takes place prior to or after the coordinate transformation of auditory and tactile signals into an oculo-centric frame of reference. Nevertheless, it seems likely that coordinate transformation could occur upstream of the vector inversion process, as the spatial localization and sensory information processing would logically need to be completed before the reversal of the saccade vector can be accurately performed. In such case, the results of Cotti et al. (Cotti et al., 2009) would provide additional support to our suggestion of a motor functional locus of adaptation downstream of the coordinate transformation level.

While saccadic adaptation in the laboratory is induced by an artificial error, under natural circumstances, it aims to correct for repeated inaccuracies that might be caused by fatigue and injuries. In these cases, our eye movement performance is affected no matter the nature (modality) of the stimulus that we are looking at. Therefore, the brain must adapt motor outputs based on spatial error, regardless of the sensory modality that provides the input, by acting along the saccadic network common to all modalities, consistent with what we found in the first experiments of Study 1 and 2.

Perspectives

In the introduction of this thesis, we reviewed studies that suggest the existence of different adaptation mechanisms for forward and backward adaptations, as well as for reactive and voluntary saccade adaptations. In the first experiment of our Study 2, while showing no difference in the visual-to-auditory transfer between backward and forward adaptations, it remains up to future studies to investigate whether our transfer results apply to the adaptation of visual voluntary saccades.

Part 2: The adaptation of non-visual saccades and its effect on visual saccades

Summary of the results

Study 1, Experiment 2:

Thirty participants were included in this experiment, which was similar to experiment 1 except that in the exposure phase, participants performed tactile saccades rather than visual saccades. Therefore, we either had a 5° backward step of the tactile stimulation (from 20° to 15° and from 25° to 20°) (adaptation session) or a second tactile stimulation was delivered at the previously stimulated location once the saccade onset was detected (control session). We found that in the adaptation session, compared to control:

1. the gain of the adapted tactile saccades decreased progressively during the exposure phase.
2. this decrease in gain seen for the adapted tactile saccades was maintained in the post-exposure phase.
3. the backward adaptation of tactile saccades generalized for saccades of the same modality performed toward non-adapted locations.
4. the backward adaptation of tactile saccades transferred partially but significantly to visual saccades performed toward the adapted and the non-adapted locations

Study 2, Experiment 2:

This experiment included 30 participants. Again, the experimental procedure was similar to that employed for the first experiment of this study. Here, instead of visual reactive saccades, we investigate the possibility of adapting auditory reactive saccades. Therefore, in the exposure phases, when the onset of saccades performed to the 15° auditory target was detected, the sound was switched to another speaker located either at 10° (backward session) or 20° (forward adaptation). These double steps of the auditory target were performed in two different sessions and two different hemifields. In each session, one hemifield was assigned to control trials, in which the sound remained at its location after the onset of the saccades. Therefore, as in experiment 1, we compared saccades submitted to backward intrasaccadic steps in one session to control saccades performed in the same hemifield but in a different session. Similar comparisons were made for forward adaptation. The comparison between saccades exposed to backward steps of the sound and the corresponding control saccades showed that:

1. the gain of the adapted auditory saccade decreased progressively during the exposure phase.
2. the decrease in gain seen for the adapted auditory saccades was maintained in the post-exposure phase.
3. the backward adaptation of auditory saccades generalized for saccades of the same modality performed toward non-adapted locations.

4. the backward adaptation of auditory saccades transferred partially but significantly to visual saccades performed toward the adapted and the non-adapted locations

In contrast, the comparison between saccades exposed to forward steps of the sound and the corresponding control saccades showed that:

1. while the gain of the adapted auditory saccades increased progressively during the exposure phase, no significant gain change was observed in the post-exposure phase.
2. the forward step of the auditory target affected neither the gain of non-adapted auditory saccades nor the gain of visual saccades.

Discussion II: Non-visual saccades adaptation

In the studies summarized above, we reported for the first time that backward adaptation can be induced for non-visual tactile (Study 1) and auditory saccades (Study 2) using the double-step target paradigm. Even though these adaptations were not as strong as the backward adaptation of visual reactive saccades seen in the first experiments of both studies as well as in the literature, we showed in our adaptation conditions a significant and progressive decrease of tactile and auditory saccades gain during the exposure phases, as well as a significant adaptation aftereffect, i.e., the gain decrease was maintained in the post-exposure phases where the saccade targets no longer changed location. These effects differed significantly from the control conditions, where the saccade target remained at its location following the saccade onset. Those two results –progressive change of saccade gain during exposure and after-effect in post-exposure- are usually considered evidence for a genuine adaptation mechanism. Indeed, the alternative explanation that participants adopted the strategy of looking directly toward the second location of the target in a double-step paradigm predicts, on the contrary, a sudden drop of saccade gain during exposure and a brisk restoration of the gain as soon as the double-steps are resumed during post-exposure. This alternative explanation had to be all the more seriously considered as, in the second experiment of the first study, the participants were all aware of the double steps during the exposure phase of the adaptation session, i.e., they reported after de-briefing the presence of two consecutive stimulations on two adjacent fingers. Interestingly, Study 2 revealed, in contrast, that the adaptation of non-visual (auditory) saccades was achieved without any conscious experience of the double steps. Indeed, none of our participants were aware of the double step of the auditory target during the exposure phase of the adaptation condition. Nevertheless, in the backward adaptation exposure, compared to the control exposure where the sound remain at its location, they showed significant adaptive changes in their auditory saccades gain. Therefore, our participants could not consciously anticipate the second step of the sound and saccade directly toward its location. In the literature on visual saccades adaptation, the effect of conscious perception of the double step is still debated. Since in the original McLaughlin's paradigm (McLaughlin, 1967) stepping the visual target occurs while the saccade is in flight, participants are usually unaware of it due to the saccadic

suppression of displacement. However, when the second step is intentionally delayed by 100 ms relative to the saccade's offset, allowing participants to consciously perceive it, a significant adaptation of visual saccades was shown to occur, even though to a lesser extent (Fujita et al., 2002). Furthermore, backward adaptation of visual saccades can also take place even when the participants are informed previously about the occurrence of the double-step, and irrespective of whether they were instructed to ignore it and keep their gaze onto the primary location of the saccade target or to re-fixate the displaced target location at the end of the primary saccade (Heins et al., 2019). These two studies indicate that the participant's awareness of the double step of the tactile stimulations in Study 1 does not rule out the implication of an adaptive process but might have reduced its effect, consistent with the fact that tactile saccade backward adaptation was lower than the adaptation of visual saccades. However, the story doesn't end here. After the adaptation of tactile and auditory saccades, we were able to see a strong generalization of the gain decrease to non-adapted tactile and auditory saccades, respectively, as well as a partial but significant transfer to visual saccades. This spatial generalization and this cross-modal transfer are again difficult to explain as a strategic modification of non-adapted saccades and rather provide additional support for a genuine adaptation mechanism.

In contrast to the visual-to-auditory and the visual-to-tactile transfer of backward adaptation, both the auditory-to-visual and the tactile-to-visual transfers of backward adaptation were only partial. This suggests that saccadic adaptation might be, at least to some degree, sensory-specific. The brain may use different pathways or sensorimotor processes when saccades are directed toward visual compared to non-visual stimuli. The adaptation of reactive non-visual saccades appears to involve, in addition to a motor functional locus of adaptation common for all modalities, other functional sensory-specific loci(us) upstream of the final motor command.

Auditory and tactile saccades are less accurate than visual saccades (Blanke & Grüsser, 2001; Yao & Peck, 1997). During the exposure to the double-step stimulations, adaptation mechanisms might target a set of different non-visual saccades with close but varying vectors, which might result in reduced adaptation efficiency. Thus, when the transfer of non-visual saccadic adaptation to visual saccades is tested, the transfer would be partial due to the differences between the visual saccades vector and those of the adapted non-visual saccades. Nevertheless, if this is the case, it also should entail a partial visual-to-tactile and visual-to-auditory transfer of adaptation. In contrast, our results showed that the transfer of backward adaptation of visual reactive saccades to non-visual ones was complete. We noted in Chapter 3 of the introduction that it is possible to induce backward adaptation for a saccade of a certain amplitude and simultaneously perform forward adaptation of a saccade with a different amplitude but in the same direction (Semmlow et al., 1987). The effect of adaptation to saccades with intermediate amplitudes was seen to reflect a linear summation of the effects produced by both the forward and the backward adaptations at the intermediate location. Based on those findings, we may, therefore, suggest that the transfer of non-visual backward adaptation to visual saccades reflects the effect of a radial summation of multiple dispersed and adapted tactile or auditory

saccades. In this case, the transfer of adaptation should not differ between Experiments 1 and 2 in both of our studies unless it is affected by the presence of different functional loci of adaptations.

Of course, one might wonder why our saccades are adapted differently when aiming at visual versus non-visual targets. One possible functional explanation is that visual information plays a dominant role in guiding and calibrating saccadic eye movements. The visual system provides the most precise and reliable spatial information for the saccadic system, as the latter primary function is to localize visual stimuli. As a result, when adaptation occurs in response to visual targets, it establishes a robust motor recalibration that can be generalized to other sensory modalities like touch and audition. Visual dominance in sensory processing is well-documented in perception. For example, when a combination of auditory and visual or tactile and visual targets are presented simultaneously at relatively close locations, the perception of auditory and tactile targets is biased toward the visual target if the latter provides clear information about its location (Alais et al., 2010). In addition, the dominance of vision and its essential role in shaping the perception from other senses can be seen in the deficits in auditory localization in children with visual impairment compared to normal-sighted children (Cappagli & Gori, 2016). The brain may treat visual information as a primary reference frame for visuospatial orientation and saccade motor control, meaning that when visual saccades are adapted, the recalibration is considered globally useful and applicable across other modalities. In contrast, when saccades are adapted to tactile or auditory targets, the adaptation may be more modality-specific because tactile and auditory inputs are not typically the primary source of information for guiding eye movements.

In Chapter 3, we described that the brain can adapt saccades differently depending on the context in which saccades are performed. The 3-D location (Chaturvedi & van Gisbergen, 1997) and flickering (Herman et al., 2009) of the visual target, the rank of the adapted saccade in a sequence of saccades (Azadi & McPeck, 2022), as well as the initial eye/head positions (Aboukhalil et al., 2004; Alahyane & Pélisson, 2004) have all been recognized as contextual factors used by the saccadic system when facing competing training. It might also be possible that when non-visual saccades are adapted, the brain associates the new motor output with that specific context (the sensory modality), and the oculomotor system might, therefore, not fully apply the learned adaptation to visual saccades because the latter corresponds to a different context.

A second question that can be asked regarding the adaptation of non-visual saccades is: what does the brain rely on to generate an error signal that drives this kind of adaptation in the absence of post-saccadic visual feedback? Indeed, this latter is commonly accepted in the literature to constitute a critical component of error processing. According to the retinal error hypothesis, the error information used by adaptation is the distance between the fovea and the location of the post-saccadic visual target on the retina (Noto & Robinson, 2001; Shafer et al., 2000). According to the predictive sensory error hypothesis, the error represents the mismatch between the actual post-saccadic visual error, as just defined, and the predicted post-saccadic visual error elaborated prior to the saccade onset (Bahcall &

Kowler, 2000; Collins & Wallman, 2012), while the postdictive motor error hypothesis suggests that the error signal represents the difference between the motor commands vector and the post-saccadic visual error postdicted back to pre-saccadic space by the oculomotor efference copy (Masselink & Lappe, 2021). Both of the experiments summarized in this section were performed in a completely dark room. Hence, participants had no visual information about the location of the tactile or auditory stimulations. Yet, a significant backward adaptation of such non-visual saccades occurred. In the following, we suggest different potential explanations for such adaptation. First, the brain might rely on previous visual experience to guide adaptation when there is no direct visual feedback available. If the participants have previously learned to associate certain non-visual targets with specific visual stimuli, the brain could use those learned associations to drive saccadic adaptation. While this can be possible in the first study, where the participants saw the location of their hands before the beginning of the experiment, this is highly unlikely in the second study, as participants had no clue about the nature of the experimental setup prior to and during the experiment. In addition, they were unaware of the presence of a double-step perturbation of the sound in the adaptation conditions. Second, it is possible that under the circumstance of the absence of visual feedback, saccadic adaptation relies on proprioceptive feedback from the eye muscle to estimate the position of the eyes after the saccade and compare it to the perceived location of the final auditory or tactile target. However, the contribution of extraocular muscle signals was previously excluded in the deafferented monkey by Lewis et al. (Lewis et al., 2001). Third, during the adaptation of tactile and auditory saccades, our participants performed secondary saccades, despite we did not analyze them and thus at this point we are unable to say whether they were corrective saccades, those secondary saccades might suggest that the saccadic system has detected some error (despite complete lack of visual information). Contrary to visual perception, auditory perception is not suppressed when the saccade is in flight (L. R. Harris & Lieberman, 1996), which therefore makes auditory information available directly when a backward step of the sound occurs (Study 2). In addition, it was demonstrated that oculomotor centers keep track not only of visual stimuli but also of auditory and audiovisual objects by remapping their eye-centered representations across saccades (Szinte et al., 2020). Furthermore, it was shown that there is a fast bottom-up sensory-induced remapping in PPC, taking into account the relative positions of the eyes and hand (Buchholz et al., 2011). Therefore, these three studies (Buchholz et al., 2011; L. R. Harris & Lieberman, 1996; Szinte et al., 2020) indicate that post-saccadic oculocentric information regarding the tactile and auditory stimuli can be available soon enough to contribute to the error signal processing. Thus, one might suggest that the brain can rely on the discrepancy between the post-saccadically and the pre-saccadically perceived locations of the non-visual target, both of them being in the oculo-centric frame of reference, to compute an error signal. Finally, spatial attention might also contribute to the error processing for non-visual saccades adaptation. For instance, Khan et al. (Khan et al., 2014) presented a visual distractor (either salient or not compared to the saccade's target) close to the saccade target at the time of reactive saccade onset. Despite the saccade target remaining

stationary, the salient distractor was enough to induce backward saccadic adaptation, as evidenced by a progressive decrease of saccadic gain and a significant adaptation after-effect. The authors suggested that the locus of attention drawn toward the distractor can, on its own, act as an error signal for the saccadic adaptation process. A similar proposal was made by Schütz et al. (Schütz et al., 2014), who induced saccadic adaptation via a perceptual task. In addition, McFadden et al. (McFadden et al., 2002) presented a peripheral target to their participants while fixating on a central point. The participants were instructed to remain on fixation; however, at the time of their attentional shift toward the peripheral target, this latter stepped either backward or forward. Spatial attention was measured during their experiment using the so-called line-in-motion task. The authors showed significant backward and forward adaptation (backward adaptation being stronger than forward adaptation) of spatial attention and further revealed that backward adaptation of spatial attention transfers to the saccadic responses measured during post-exposure. Therefore, they suggested that saccades are directed specifically to the locus of attention and that saccadic adaptation could result from either adaptation of attentional shifts or, from saccadic adaptation at the motoric level, or both. In our studies, it can be thus suggested that the displaced non-visual stimuli attracted attention and thereby induced saccade adaptation.

In contrast to the backward steps of the auditory target in the second experiment of Study 2, forward auditory steps did not induce any significant adaptation aftereffect in auditory saccades, despite their progressive and significant gain increase seen during the exposure phase. Compared to visual reactive saccades backward adaptation, the backward adaptation of auditory saccades appears harder to establish when comparing the number of participants who showed significant adaptations for both saccades modalities. In parallel, a slower time course, a lower adaptation aftereffect, and a smaller number of significantly adapted participants are usually observed for forward adaptation compared to backward adaptation of both reactive and voluntary visual saccades (M. Panouillères et al., 2009a). Therefore, we prefer to say that forward adaptation of non-visual saccades is hard to establish rather than that it does not occur. Future work should consider the number of double-step trials (60 in Experiment 2 of Study 2) to verify whether we can achieve stronger gain changes for both forward and backward adaptation of auditory saccades.

Perspectives

In Chapter 4 of this thesis, we reviewed studies showing strong interactions between saccadic eye movements and spatial attention, as well as others revealing a coupling between spatial attention and saccadic adaptation. Nevertheless, the current model investigating the nature of the error signal driving saccadic adaptation does not take into account the role of spatial attention neither in error processing nor for learning or perceptual processes. We think that the role of spatial attention is much more important to consider in future models than ignoring it and classifying it as noise. Indeed, here, the

challenge will be to design an experiment allowing to disentangle between the effects of spatial attention and the random variations classified as noise.

Part 3: The effect of spatial attention on saccadic adaptation

Summary of the results

Study 3, Experiment 1:

In this experiment, we investigated the effect of tactile exogenous spatial attention on the backward adaptation of reactive saccades. Twenty participants performed two experimental sessions, each consisting of 3 phases: pre-exposure, exposure, and post-exposure phases. In the pre- and post-exposure phases, the participants performed simple saccades to visual targets located at 15° to the left or the right of a central fixation point. In the exposure phase, we used a double task (saccades and attention), combining a modified version of the cue-target paradigm to orient exogenous spatial attention and the double-step target paradigm to adapt reactive saccades. After a random fixation, the subjects received a peripheral non-predictive (50% validity) tactile cue on one hand shortly (50 ms) before the appearance of the saccade target and the simultaneous disappearance of the fixation point. Once the saccade onset was detected, the saccade target either stepped 4° toward the fixation point (leftward saccade) or disappeared at the saccade onset (rightward saccade: control). Fifty ms following the saccade offset, a second tactile stimulation was delivered either on the cued hand (valid trials) or the uncued hand (invalid trials). The participants had to discriminate, using foot pedals, the location of the second tactile stimulation (right or left?). The backward adaptation of leftward saccade was either associated systematically with an ipsilateral tactile cue in one session (IPSI) or with a contralateral cue in another session (CONTRA). We calculated the tactile validity index (the difference in discrimination reaction time between invalid and valid trials) for each condition, the saccadic gain change ratio between the pre-exposure and the post-exposure phases (positive values indicate a gain decrease), as well as the slope of gain change during the exposure (negative value indicate a decrease in the gain) for rightward and leftward saccades separately. Indeed, we were able to induce significant adaptation, and we further showed:

1. a significant positive correlation between the gain change ratio and the tactile validity index in the CONTRA session, as well as a significant negative correlation between the slope of gain change and the tactile validity index.
2. no significant correlation in the IPSI session.

Study 3, Experiment 2:

In this experiment, we investigated the effect of tactile endogenous spatial attention on the backward adaptation of voluntary saccades. Each of the 20 participants performed two experimental sessions

(IPSI and CONTRA). An experimental approach similar to Experiment 1 was adopted in this experiment, except that here, both rightward and leftward saccades were adapted. In the exposure phase and after a random fixation, the saccade target appeared in the periphery at 15° either to the left or the right of the fixation point. The participants kept fixating on the central location until the appearance of a go-signal instructing them to perform the saccade. Three hundred and eighty ms before the appearance of the go signal, they received a peripheral predictive (80% validity) tactile cue on both the index and the thumb of one hand. They were instructed to covertly focus their tactile attention on the location of the cue. Once the saccade onset was detected, the visual scene stepped 4° toward the fixation point for both leftward and rightward saccades. Hundred ms following the saccade onset, a second tactile stimulation was delivered either at the index or the thumb finger (50% probability) of the cued hand (valid trials) or the uncued hand (invalid trials). The participants had to discriminate where the second tactile stimulation took place (index or thumb?). The backward adaptation in the exposure phase was systematically associated either with an ipsilateral tactile cue in one session (IPSI) or with a contralateral cue in another session (CONTRA). Our results showed:

1. significant adaptations elicited for both rightward and leftward saccades.
2. significant positive correlations between the gain change ratio and the tactile validity index for both leftward and rightward saccades in the IPSI but not the CONTRA session.
3. a significant negative correlation between the slope of gain change and the tactile validity index for leftward saccades in the IPSI session compared to a significant positive correlation in the CONTRA.
4. a significant negative correlation between the slope of gain change and the tactile validity index for rightward saccades in the CONTRA session compared to a non-significant correlation in the IPSI session.

Discussion III: The effect of spatial attention on saccadic adaptation

In Study 3, we employed an original experimental protocol combining the cue-target paradigm for the orienting of spatial attention and the double-step target paradigm for backward adaptation. In order to avoid any potential interference between visual targets across paradigms, we decided to elicit, through the cue-target paradigm, the orientation of the participant's tactile attention rather than visual attention. Indeed, we intended to orient participants' spatial attention toward or away from the location of the saccade's target at the time of the second step occurrence. To this aim, we leveraged the well-established facilitatory effects occurring across modalities, also known as cross-modal links of attention. Indeed, as recalled in Chapter 4, several previous studies have indicated that cueing a spatial location with a cue in a given modality (for example, tactile) has facilitatory consequences (in case of validly cued positions) also when the target appears in another modality (for example visual).

(Chica et al., 2007; C. Spence et al., 1998, 2000; C. Spence & McGlone, 2001).

In Experiment 1, the analysis of reaction time in the discrimination task showed that we were able to orient tactile spatial locations in certain conditions but not in others. In the successful conditions, our correlation analysis demonstrated that orienting exogenous spatial attention to the opposite location of the saccade's target results in a slower backward adaptation of reactive saccades as well as a smaller adaptation after-effect. Both exogenous spatial attention and the adaptation of reactive saccades implicate the activation of wide cortical networks that overlap at the level of the TPJ (Corbetta & Shulman, 2002; Gerardin et al., 2012). In reactive saccades adaptation, the TPJ was shown to be involved in both the learning process (Gerardin et al., 2012) and the error processing (Guillaume et al., 2018). In spatial attention, the TPJ takes part in the ventral fronto-parietal network and was shown to be implicated in the orienting of exogenous spatial attention as well as stimulus-driven re-orienting irrespective of the stimulus modality (Chica, Bourgeois, et al., 2014; Macaluso, 2010). In parallel to these findings, the ventral fronto-parietal cortex is known to bias the activities of the occipital areas toward the stimulus location indirectly through the dorsal fronto-parietal network (Corbetta et al., 2008; Corbetta & Shulman, 2002). In addition, it was also shown that tactile non-predictive cues boost the occipital visual area contralateral to the stimulus location (Kennett et al., 2001; Macaluso et al., 2000). Based on those studies, one might suggest that exogenous spatial attention directly affects the adaptation of reactive saccades (either the learning mechanism, the error processing, or both), possibly due to shared neuronal substrates or to distinct but interconnected neurons at the level of the TPJ. Another possibility is that exogenous spatial attention has an indirect effect on reactive saccade adaptation through the biasing of neuronal activities in the visual occipital areas, which either disrupts or boosts the post-saccadic visual information involved in error processing. Nevertheless, this does not rule out a possible interaction between the two mechanisms at the level of the subcortical area, such as the SC.

In Experiment 2, our results indicate that, first, orienting endogenous spatial attention toward the location of the saccade target during backward adaptation of voluntary saccades boosts the speed of adaptive gain decrease as well as the adaptation aftereffect. In contrast, orienting endogenous spatial attention to the opposite location of the saccade target results in a slower backward adaptation of voluntary saccades as well as a smaller adaptation after-effect. Here, we can interpret these findings and the possible cause of these effects based on the reasoning we employed in the previous paragraph. The cortical regions involved in the endogenous orienting of spatial attention and those involved in the adaptation of voluntary saccades overlap at the level of the IPS (Corbetta & Shulman, 2002; Gerardin et al., 2012). The IPS was shown to be implicated in both the learning process (Gerardin et al., 2012) as well as the error processing (Guillaume et al., 2018; M. Panouillères et al., 2014b) of voluntary saccades backward adaptation. In spatial attention, the IPS constitutes a part of the dorsal fronto-parietal network, which was shown to be implicated in the orienting of both exogenous and endogenous spatial attention irrespective of the modality of the stimulus (Corbetta et al., 2008;

Macaluso, 2010). The dorsal fronto-parietal network bias directly the visual occipital areas either through the FEF (Moore & Armstrong, 2003) or the IPS (Vossel et al., 2012); therefore, this dorsal network exerts a top-down control on the occipital cortex. This later was shown to provide the dorsal network with sensory information regarding the invalidity between the cue and the target locations either directly (bottom-up influence) (Geng & Mangun, 2009; Ruff et al., 2008) or through the ventral network (Vossel et al., 2012). In addition, it was also shown that tactile predictive cues boost the activity of the visual occipital areas contralateral to the stimulus location (Macaluso et al., 2002b, 2003). Based on these studies, we suggest that endogenous spatial attention may affect the adaptation of voluntary saccades (either the learning mechanism or the error processing, or both) directly due to common neuronal substrates or distinct but interconnected neurons at the level of the IPS. In addition, we also suggest that this effect can be also mediated indirectly through the biasing of neuronal activities in the visual occipital areas which either disrupt or boost the processing of post-saccadic visual information. However, as for the case of exogenous attention and reactive saccades adaptation, the effect of endogenous attention on voluntary saccades adaptation might also be related to interaction at the level of the SC and additionally the FEF (Métais et al., 2022; Moore & Armstrong, 2003).

In both Experiments 1 and 2, the tactile cueing facilitated the discrimination of the tactile target in valid trials compared to invalid ones. However, this effect was not seen in certain conditions. One potential cause for those results would be that using the right foot in a discrimination task might have artificially masked the validity effect (even with the orienting of spatial attention maintained) by speeding up the participants' response to targets presented ipsilaterally to the foot pedal (Lloyd et al., 2010). In addition, our participants discriminated the unseen target location while fixating on its location, which might have an impact on the discrimination reaction time as it has been suggested that discriminating a target is faster when fixating on its location even if the stimulated location is not visible (Honoré et al., 1989). Unfortunately, during the preparation phase of those experiments, our pilot studies did not reveal similar results. Therefore, we weren't able to modify our experimental procedures accordingly. Nevertheless, in potential future studies, it would be recommended to optimize the attentional task to significantly orient spatial attention in all tested conditions.

In Chapter 4, we reviewed the studies that investigated directly or indirectly the effect of attention on saccadic adaptation. For instance, Connolly et al. (A. Connolly et al., 2016) showed that saccadic adaptation is reduced in ADHD patients. Other studies have found that priming attentional focus prior to the adaptation tasks either boosts this later when the focus is wide or reduces it when the focus is relatively narrow (Bock et al., 2017; Borisova & Grigorova, 2015). Khan et al. (Khan et al., 2014) demonstrated that a salient distractor illuminated close to the saccade target results in adaptive changes in saccade amplitude toward the location of the distractor, suggesting that the locus of attention drawn toward the distractor can, on its own, act as an error signal for the saccadic adaptation process. In addition, McFadden et al. (McFadden et al., 2002) showed that it is possible to adapt

spatial attention itself, and this sort of adaptation affects the amplitude of saccades. Finally, Gerardin et al. (Gerardin et al., 2015) showed that high attentional load boosts reactive saccades adaptation compared to low attentional load. Indeed, we are not the first to investigate the effect of attention on the saccadic adaptation. Nevertheless, all of the studies mentioned above examined the effect of attention on the backward adaptation of reactive saccades; therefore, our Study 3 can be considered the first attempt to investigate the effect of attention on voluntary saccades' backward adaptation. In addition, neither of the studies mentioned above examined the effect -on saccadic adaptation- of “**spatial**” orienting of attention, which can be done using the cue-target paradigm.

In summary, our third study showed that exogenous and endogenous spatial attention affect the backward adaptation of reactive and voluntary saccades, respectively. This study brings additional knowledge on the link between spatial attention and saccadic adaptation, which can be added to the relatively small number of studies investigating such coupling between two mechanisms crucial in both perception and actions.

Perspectives

Neither previous studies nor ours have investigated the effect of spatial attention (exogenous or endogenous) on the forward adaptation of saccades (reactive or voluntary). Nevertheless, with further optimization, our experimental protocol can motivate future studies, probably ones including electrophysiological recording or imaging techniques.

Conclusion

There is nothing simple about the human body and, more specifically, the human brain. Its beauty resides in its fine details and complexity, sculptured genetically and epigenetically by the passage of time and the changes in environmental laws and demands. During this long but fun, hard, but rewarding journey, we explored different hypotheses related to the saccadic adaptation mechanism. While this latter was thought to be a relatively simple process restricted to the cerebellum, the increasing amount of research shed light on the complexity and flexibility of this mechanism. In this PhD work, we explored how the adaptation of visual reactive saccades affects saccades performed toward non-visual tactile and auditory targets. Our results indicate a complete transfer of both forward and backward adaptation from visual to non-visual reactive saccades, which argues in favor of a motor functional locus of visual reactive saccades adaptation, common to all saccades modalities. We further investigated whether non-visual saccades can be themselves subject to adaptive changes. We were able to show that the gain of tactile as well as auditory saccades can be reduced using the double-step target paradigm, which consists of creating a mismatch between the saccade landing position and the post-saccadic target location. We provided evidence arguing in favor of a genuine adaptation mechanism being behind the observed changes in non-visual saccades gain and further showed that this kind of adaptation transfers only partially to visual reactive saccades. This, therefore, points to

multiple functional loci for non-visual saccades adaptation, some acting on the motor command while others being modality-specific, probably located upstream of the neural pathway common to all saccades modalities. Additionally, we explored the coupling between spatial attention and saccadic adaptation. Here, we were able to bring additional evidence arguing in favor of a modulatory effect of exogenous spatial attention on reactive saccades adaptation as well as a modulatory effect of endogenous spatial attention on voluntary saccades adaptation.

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