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Strong Rightward Lateralization of the Dorsal Attentional Network in Left-Handers With Right Sighting-Eye: An Evolutionary Advantage

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Abstract: Hemispheric lateralization for spatial attention and its relationships with manual preference strength and eye preference were studied in a sample of 293 healthy individuals balanced for manual preference. Functional magnetic resonance imaging was used to map this large sample while performing visually guided saccadic eye movements. This activated a bilateral distributed cortico-subcortical network in which dorsal and ventral attentional/saccadic pathways elicited rightward asymmetrical activation depending on manual preference strength and sighting eye. While the ventral pathway showed a strong rightward asymmetry irrespective of both manual preference strength and eye preference, the dorsal frontoparietal network showed a robust rightward asymmetry in strongly left-handers, even more pronounced in left-handed subjects with a right sighting-eye. Our findings brings support to the hypothesis that the origin of the rightward hemispheric dominance for spatial attention may have a manipulo-spatial origin neither perceptual nor motor per se but rather reflecting a mechanism by which a spatial context is mapped onto the perceptual and motor activities, including the exploration of the spatial environment with eyes and hands. Within this context, strongly left-handers with a right sighting-eye may benefit from the advantage of having the same right hemispheric control of their dominant hand and visuospatial attention processing. We suggest that this phenomenon explains why left-handed right sighting-eye athletes can outperform their competitors in sporting duels and that the prehistoric and historical constancy of the left-handers ratio over the general population may relate in part on the hemispheric specialization of spatial attention. *Hum Brain Mapp* 36:1151–1164, 2015. © 2014 Wiley Periodicals, Inc.

Key words: hemispheric dominance; spatial attention; handedness; eyedness; fMRI; eye movements; right hemisphere; humans

INTRODUCTION

Hemispheric specialization (HS) is a major characteristic of the human brain organization, with the widely admitted view that the left hemisphere controls language while the right hemisphere is responsible for spatial processing [Herve et al., 2013]. Long-standing behavioral and neuropsychological observations [Corballis, 2003; Hecaen and Sauguet, 1971; Wada and Rasmussen, 1960] as well as neuroimaging studies in healthy subjects [Knecht et al., 2000;

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Pujol et al., 1999; Tzourio et al., 1998] have established manual preference as one explicatory factor of language dominance variability. Actually, left-handers are more variable and, at most, can exhibit right hemisphere dominance for language [Mazoyer et al., 2014]. In return, pioneering neuropsychological studies observed a weaker relation between spatial functions and the right hemisphere in right-handers than that existing between language and the left hemisphere [Bryden et al., 1983; Hecaen et al., 1981]. Surprisingly, very few studies have addressed the issue of the variability of right hemisphere dominance for spatial processing, although understanding HS setting will require knowledge on the determinants of this variability in addition to those of language dominance variability.

The gestural motor theory for the evolution of brain lateralization proposed that left HS for praxis led to left HS for gesture, which in turn led to left HS for language [Corballis, 2003; Hutsler et al., 2001]. The causal complementary scenario suggested that the contralateral right hemisphere has then inherited visuospatial functions by default [Hellige, 1990]. A “perceptive” hypothesis suggested that spatial HS would arise from prenatally auditory and vestibular asymmetries promoting right-sided motor dominance and a right hemispheric superiority in most visuospatial functions [Previc, 1991]. One may also mention another hypothesis, based on split-brain data, which proposed that the right spatial HS would not depend on the perceptive sphere, but rather on the manipulo-spatial coordination [Allen, 1983; LeDoux et al., 1977] giving a more important role to action.

One way to explore these different scenarios is to study the hemispheric variability of spatial networks, in particular in relation with motor lateralization. To date, neuroimaging studies comparing hemispheric dominance for spatial attention elicited by the execution of a landmark task in both right-handers and left-handers did not evidence any incidence of manual preference on the lateralization of spatial attentional networks [Badzakova-Trajkov et al., 2010; Floel et al., 2005; Powell et al., 2012].

Actually, although manual preference is the best-known asymmetry in the motor domain [Serrien et al., 2006], there is also a sighting ocular dominance [Coren 1993; Porac and Coren, 1976]. Such eye preference does not strictly follow manual preference as 80% of RH have a right sighting dominant eye while 60% of LH have a left sighting dominant eye [Bourassa et al., 1996], which might be due to the fact that eye movements are at the interface between perception and action. The question of a potential role of eye preference in HS for eye movements and shifts of spatial attention has been recently reappraised with psychometric studies suggesting that the brain may pay more attention to information arriving via the dominant eye [Shneur and Hochstein, 2006; Shneur and Hochstein, 2008]. A recent psychometric study described an ocular dominance effect on saccadic parameters such as gain and velocity peak in both right- and left-handed subjects [Vergilino-Perez et al., 2012]. Regardless of the manual preference, saccades

directed in the ipsilateral direction relative to the dominant eye sometimes had larger amplitudes and definitively had faster peak velocities, suggesting that eye dominance is the main factor in the left-right asymmetry in such saccade parameters. Another psychometric study recently demonstrated an impact of the eye dominance on neural mechanisms involved in converting visual input into motor commands, strongly depending on the manual preference of participants [Chaumillon et al., 2014].

Investigating the relationships between manual preference (action) and eye preference (perception) with the hemispheric lateralization of attentional networks has never been completed in neuroimaging and could help elucidating the factors explaining the variability of HS for spatial processing in adults.

Visually guided saccadic (VGS) eye movement is an adequate task for such questioning. First, because VGS are supported by a bilateral cortico-subcortical network (review in [McDowell et al., 2008]) reliably activated by both overt (i.e., VGS) and covert shifts of spatial attention [Beauchamp et al., 2001; Corbetta et al., 1998; de Haan et al., 2008; Nobre et al., 2000]. Second, because functional asymmetries in VGS described in right-handers, with a rightward lateralization of a saccadic/attentional network and a leftward asymmetry of a proper saccadic motor system may be potentially explained by eye preference [Petit et al., 2009].

Taking into account both motor lateralization and sighting eye dominance within the spatial-motoric framework, we examined how the hemispheric lateralization of networks supporting overt shift of spatial attention relates to both manual and eye preferences. We thus studied the functional asymmetries of a VGS task in 293 healthy subjects belonging to the BIL&GIN, a database dedicated to the study of HS, including manual and eye preference assessments. The large number of LH in this database (about 50%) offered the possibility to address the question of hand/eye preference interaction on spatial attention networks that, to our knowledge, has never been addressed due to the low prevalence of LH (10%) and left eyed individuals (30–35%, [Bourassa et al., 1996]) in the general population.

MATERIALS AND METHODS

Participants

Data from 293 individuals balanced for sex (145 women) were extracted from the BIL&GIN database (Brain Imaging of Lateralization studied by the Groupe d’Imagerie Neurofonctionnelle). All participants have been documented about manual, verbal, numerical and spatial skills, structural features, and neural networks for spatial, motor, language and number processing functions [Petit et al., 2012]. All subjects had normal or corrected-to-normal vision, and gave written informed consent to participate in the study,

TABLE I. Distribution of manual preference and sighting ocular dominance (OD) among the 293 subjects

	sLH	MH	sRH	Total
LE	72 (30)	38 (21)	13 (11)	123 (62)
RE	26 (14)	60 (30)	84 (39)	170 (83)
Total	98 (44)	98 (51)	97 (50)	293 (145)

sLH: strongly left-handers [−100; −55]; MH: mixed-handers [−54; +99]; RH: strongly right-handers [+100]. LE, RE: left and right preferred sighting eye, respectively. Number of women in parentheses.

which was approved by our local ethics committee. The mean age of the group was 25 (SD: 6 years, range 18–57 years) and the mean level of education was 15 years (SD: 2 years, range 11–20 years) of schooling since primary school.

Manual and Eye Preference Categories

Different measures could have been used to estimate the manual preference such as the conventional assessment of the self-reported hand used for writing, the manual preference strength, the relative hand skill, or performance to a reaching task. None of these different measures has emerged as clearly superior to the others regarding their correlation with cerebral dominance for language [Groen et al., 2013] and at present we are not aware of equivalent data for spatial attention. Since our large cohort of 293 subjects allowed sufficient amount of subjects in every group, we preferentially categorized our subject with their manual preference strength. We will also describe the prevalence of self-reported manual preference for comparison with the literature.

Manual preference strength

The degree of manual preference was quantified using the score at the Edinburgh inventory [Oldfield, 1971]. In this study, we used only 9 of the 10 items dealing with the subject-preferred hand for manipulating objects and tools (dropping the “broom” item). Values ranged from −100 for strong left-manual preference to +100 for strong right-manual preference. Due to the U-shape of its distribution, manual preference strength (MPS) was transformed as an ordinal variable using thresholds close to the first and second terciles of MPS distribution. The boundaries of the subsequent three categories were [−100, −55], [−54, +99], and [+100]. An individual was considered to be strongly left-handed (sLH), mixed-handed (MH), or strongly right-handed (sRH) depending of his Edinburgh score (ES). Ninety-eight subjects were classified as sLH (mean $ES \pm SD$; -88 ± 14 ; 44 females), 98 subjects were classified as MH (mean ES of $+27 \pm 54$; 51 females), and 97 subjects

as sRH (50 females). In the MH group, 46 subjects considered themselves as right-handers and 52 as left-handers.

Self-reported manual preference

Participants were asked to report whether they considered themselves as right- or left-handed: 142 declared themselves as right-hander (70 women, 72 men) and 151 left-handers (72 women, 79 men). Each individual declaring himself as a right-hander used its right hand for writing. For left-handers, 146 used the left hand for writing, 2 used indifferently the left or right hand, and 3 used the right hand (converted left-handers) for writing.

Eye preference

The sighting-dominant eye was evaluated for each participant using a variation of the hole-in-the-card test [Durand and Gould, 1910]. First, the participant was asked to extend his arms in front of him and to form a diamond-like frame using the thumb and index finger of both hands, replacing the card’s hole to sight in. He was then requested to stare through this frame at a specific object located at distance. Without moving his hands, the participant had then to look at the object using only one eye, the right and then the left. The preferred sighting eye is that for which vision is the same as it is when looking with both eyes opened. Note that using both hands to form a diamond-like frame avoids any bias due to a sighting measure using a single hand. Among 293 participants, 170 subjects had a right sighting-eye (RE) and 123 had a left sighting-eye (LE).

We, therefore, defined six different groups of subjects depending of both manual and eye preferences (Table I): strongly left-handers with right sighting-eye (sLH/RE) or left sighting-eye (sLH/LE), mixed-handers with right sighting-eye (MH/RE) or left sighting-eye (sLH/LE), and strongly right-handers with right sighting-eye (sRH/RE) or with left sighting-eye (sRH/LE).

fMRI Scanning of Visually Guided Saccades

The 293 subjects participated in the functional scanning session during which they performed a VGS task. The paradigm randomly alternated four 16-s blocks of saccadic eye movements with four 16-s blocks of central fixation crosshair. The subjects were instructed to move their eyes toward a white visual dot that jumped randomly for 16 s to different eccentric positions along the horizontal axis, with a frequency of 1.25 Hz. The dot (0.4°) was first displayed at the primary central eye position and the number of left and right saccades was equated with an average amplitude in both directions of 6.5° (range, $3-10^\circ$). During the central fixation, the subjects were asked to continuously fixate the cross at the center of the screen. The position of the right eye was monitored during the MR scanning procedure through the use of an infrared eye

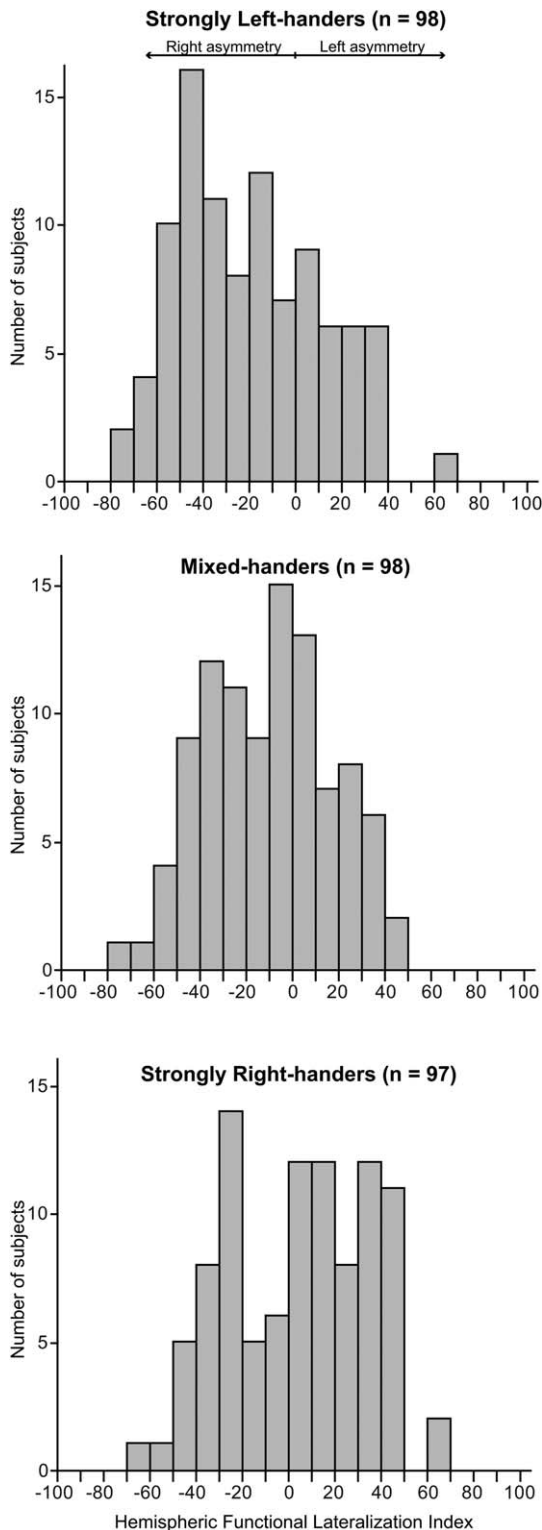


Figure 1.

Histogram distribution of the hemispheric functional lateralization index (HFLI) for VGS in strongly left-handers (top panel), mixed-handers (middle panel), and strongly right-handers (bottom panel).

tracking video system composed of a headcoil-mount 60 Hz-eyetracker camera (Mag Design and Engineering, Redwood City; www.magconcept.com) and a recording unit (iViewX™ MRI-SV™, SensoMotoric Instruments, Berlin, Germany; www.smi.de). Eye tracking data were analyzed using BeGaze™ (SMI Experiment Suite 360™, SensoMotoric Instruments) in a subsample of 174 subjects (69 sLH including 31 women; 53 sRH including 30 women; and 53 MH including 27 women).

Image Data Acquisition and Processing

MRI was performed using a Philips Achieva 3 Tesla scanner. Whole brain functional volumes were acquired with a Bold-fMRI T_2^* -weighted echo-planar sequence (TR = 2 s; TE = 35 ms; flip angle = 80° ; 31 axial slices; $3.75 \times 3.75 \times 3.75 \text{ mm}^3$ isotropic voxel size). The first four volumes of each sequence were discarded to allow for stabilization of the MR signal. Prior to functional acquisition, both high-resolution 3D T1-weighted and T_2^* -weighted multislice (T_2^*MS) volumes were acquired.

Preprocessing was based on Statistical Parametric Mapping subroutines (SPM5; <http://www.fil.ion.ucl.ac.uk/spm>). Anatomical T1-weighted volumes were spatially normalized by aligning individual anatomical volumes to specific cerebral tissue templates built from the T1 images of 80 right-handed subjects (40 men) acquired with the same scanner and acquisition parameters. Spatial normalization parameters were set to their SPM5 default values, providing for each subject a 3D, spatially normalized deformation field of T1 images into the Montreal Neurological Institute (MNI) reference space. Each functional run was corrected for slice timing and motion and registered onto the T_2^*MS volume. Combining the T_2^*MS to T1-weighted registration parameters and the spatial normalization parameters, functional images were resampled into the $2 \times 2 \times 2 \text{ mm}^3$ template space and spatially smoothed (Gaussian 6 mm full width at half maximum filter). For each subject, the effects of interest were modeled by boxcar functions computed with paradigm timing and convolved with a standard hemodynamic response function (SPM5). Finally, the effect of interests-related contrast maps (VGS minus Fixation) was calculated.

Hemispheric Functional Lateralality Indices

The index of functional lateralization for the VGS task was assessed using Wilke and Lidzba's method [Wilke and Lidzba, 2007; Wilke and Schmithorst, 2006], which provides threshold-free and robust estimates of hemispheric functional lateralality indices (HFLI). Each individual HFLI was computed with a bootstrap algorithm from the individual VGS minus Fixation t -map thresholded at $t = 0$ (positive t -map) with a lower bootstrap sample of five voxels and higher sample size of 1000 voxels, with a resample ratio of $k = 0.25$. We reported the weighted HFLI

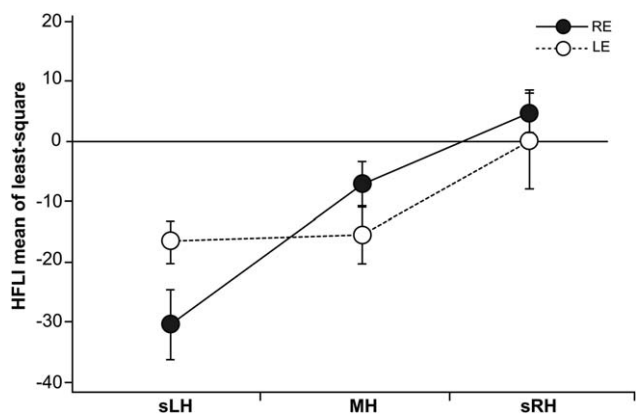


Figure 2.

Plot of mean hemispheric functional lateralization indices for VGS as function of both manual preference strength (sLH, MH, sRH) and eye preference (RE, LE) revealing the MPS × eye preference interaction. Errors bars denote standard error. sLH/RE subjects were significantly more rightward asymmetrical than any other group of subjects (see text for statistical *P* values).

mean that was calculated within the anatomical template mask used for the fMRI data normalization, including both gray and white matters and excluding the cerebellum. It yielded values from -100 for exclusive right activation to +100 for exclusive left activation.

Statistical Analyses

Eye preference distribution according to MPS

We will describe the distribution of eye preference among the 293 subjects in relation with their manual preference strength, and then perform nominal logistic regressions to test the congruency of eye and hand preferences across our sample of subjects. We will also report the distribution of the eye preference according to the self-reported manual preference.

Effects of MPS and eye preference on the HFLI of VGS

As shown in Figure 1, the HFLI values for VGS in sLH and sRH groups were not normally distributed (Shapiro-Wilk test, sLH: $P = 0.016$, sRH: $P = 0.012$). We, therefore, used a purely nonparametric statistical approach [Anderson, 2001a; McArdle and Anderson, 2001] with an analysis of variance experimental design using permutation methods [Anderson and Braak, 2003; Anderson, 2001b]. To test whether MPS or eye preference were related to hemispheric functional asymmetries for spatial attention, we ran a permutational analysis of variance (PERMANOVA) on HFLIs derived from the VGS task with MPS, eye preference and their interaction as between-subject factors. Educational level, age, and sex were included as covariates

of interest. This PERMANOVA was performed with 10,000 permutations of residuals under a full model with Monte Carlo tests, Type 1 sums of squares and fixed effects sum to zero options, using the PERMANOVA+ add-on package for PRIMER software (PRIMER-E Ltd, Devon, UK, version 6, <http://www.primer-e.com>).

Regional voxel-based functional analysis

To identify the brain regions that underlie the interaction between MPS and eye preference observed at the hemispheric level (HFLIs), we performed a voxel-based functional analysis of the BOLD signal in SPM with a $3 \times 2 \times 2$ full-factorial design with MPS, eye preference and asymmetry as factors of interest. Hemispheric asymmetries were obtained by comparing BOLD values of one hemisphere from those of the other hemisphere for each participant. To do so, left/right flipped VGS maps were computed, resulting in individual BOLD and flipped-BOLD maps for the asymmetry factor of interest). The anatomical location of the activation foci was inferred using the in-house automatic anatomical labeling software [Tzourio-Mazoyer et al., 2002].

1. We will describe the average map generated to assess the mean level of activation during VGS in each MPS group as well as the most consistent asymmetrical activation, both at $P < 0.001$ corrected for family-wise error (FWE) for multiple comparisons.
2. We will also perform a conjunction analysis of the average asymmetry maps of the six groups, using a $P < 0.001$ threshold (uncorrected), to question what are the common asymmetrical regions of the VGS networks whatever the manual preference strength and eye preference.
3. The MPS × eye preference interaction observed at the HFLI level will be tested by comparing the average asymmetry map of one group with the average asymmetrical map of all other five groups, thresholded at $P < 0.001$ uncorrected (inclusively masked by the first item of the subtraction, set at $P < 0.05$ uncorrected). For example, the average asymmetry map of the sLH/RE will be compared to the average asymmetry map of the five remaining groups.

RESULTS

Eye Preference Distribution According to MPS

The prevalence of eye preference differs between the three MPS groups (Table I). In the sRH group ($n = 97$, 50 women), 86.6% showed a right eye preference (sRH/RE) and 13.4% a left one (sRH/LE). In the sLH group ($n = 98$, 44 women), 73.5% showed a left sighting-eye (sLH/LE) and 26.5% a right one (sLH/RE). In the MH group ($n = 98$, 51 women), 61.2% showed a right eye preference (MH/RE) and 38.8% a left one (MH/LE).

A nominal logistic regression revealed a highly significant difference of eye preference distribution between the

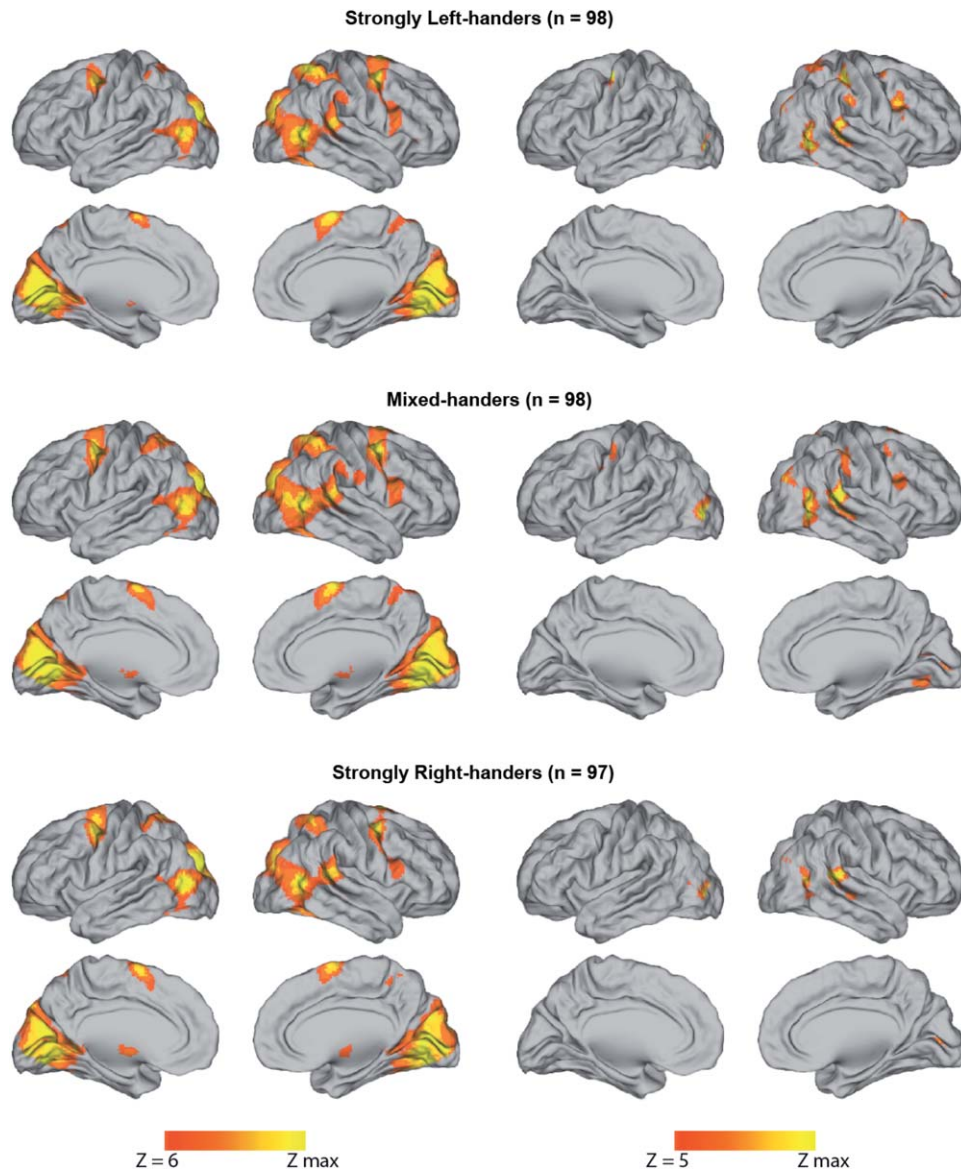


Figure 3.

Statistical parametric map of functional activation (left part) and asymmetries (right part) observed during visually guided saccades according to manual preference strength, illustrated at $P < 0.001$ corrected for family-wise error.

three groups ($X^2(2) = 77.9$, $P < 0.0001$). The sRH/RE and sLH/LE groups were the most frequent and corresponded to individuals having a congruent eye-hand preference. Interestingly, the prevalence of crossed eye-hand preference was more than twice for sLH than for sRH (Table I). Neither age nor level of education effects were observed between the six groups (mean age range [24.9–27.7 years]; $P = 0.78$; mean education range [14.7–16.0 years]; $P = 0.41$).

The prevalence of eye preference differs also between the two groups of self-reported manual preference ($X^2(1) = 64.0$, $P < 0.0001$). In the right-handers, 80.9% showed a right eye

preference and 19.1% a left one. In the left-handers, 64.2% showed a left sighting-eye and 35.8% a right one.

Saccadic Eye Movements During fMRI

Our experimental design was set up with an equal number of visual dot positions with an average amplitude in both direction of 6.5° (range $3^\circ - 10^\circ$). The participants performed leftward and rightward VGS with a mean amplitude of $5.9^\circ \pm 0.9^\circ$ (\pm SD, $N = 177$, range $3.2^\circ - 8.4^\circ$) and $6.0^\circ \pm 1.0^\circ$

TABLE II. MNI coordinates and maximum T-scores for brain regions revealing significant activation to the execution of visually guided saccades compared with central fixation for each MPS group

Functional region	Left hemisphere				Right hemisphere			
	<i>x</i>	<i>y</i>	<i>z</i>	<i>T</i> -score	<i>x</i>	<i>y</i>	<i>z</i>	<i>T</i> -score
sLH Group								
Sup. fr./Precentral gyrus (med-FEF)	-26	-4	52	11.0	28	-4	54	15.5
Mid. fr./Precentral gyrus (lat-FEF)	-44	-6	50	13.5	40	-4	52	13.7
Inf. fr. Gyrus (pars opercularis)					54	8	38	10.9
Medial Sup. fr. gyrus (SEF)	-2	-2	64	13.1	6	0	66	13.8
Intraparietal sulcus (PEF)	-28	-50	54	9.4	26	-54	58	14.7
Temporoparietal junction (TPJ)	-50	-38	24	8.8	60	-36	16	12.1
Temporo-occipital junction (MT/V5)	-44	-72	8	12.6	46	-60	8	16.1
Mid. occipital gyrus	-28	-78	24	14.0	30	-78	26	18.8
Calcarine fissure (posterior part, V1p)	-14	-80	-8	15.1	14	-88	0	19.5
Lingual gyrus	-14	-66	0	13.4	12	-78	-8	17.4
Putamen/Pallidum	-22	8	6	8.7	22	6	8	11.0
Thalamus	-6	-22	-6	7.3	8	-20	-6	9.4
MH Group								
Sup. fr./Precentral gyrus (med-FEF)	-26	-4	52	15.6	26	-4	52	18.8
Mid. fr./Precentral gyrus (lat-FEF)	-42	-6	50	18.6	40	-2	52	18.5
Inf. fr. Gyrus (pars opercularis)					52	6	36	14.7
Medial Sup. fr. gyrus (SEF)	0	-2	66	16.8	6	0	66	16.5
Intraparietal sulcus (PEF)	-28	-52	54	14.7	20	-58	56	16.3
Temporoparietal junction (TPJ)	-48	-36	22	9.0	62	-34	22	13.6
Temporo-occipital junction (MT/V5)	-46	-74	6	15.1	46	-60	8	18.6
Mid. occipital gyrus	-28	-80	24	19.0	28	-78	24	20.8
Calcarine fissure (posterior part, V1p)	-10	-88	0	16.7	14	-88	0	22.5
Lingual gyrus	-10	-78	-6	18.5	12	-74	-8	21.6
Putamen/Pallidum	-22	-8	6	11.0	22	-4	10	10.8
Thalamus	-6	-24	-8	9.9	6	-24	-8	11.4
sRH Group								
Sup. fr./Precentral gyrus (med-FEF)	-26	-4	54	11.3	28	-2	52	12.8
Mid. fr./Precentral gyrus (lat-FEF)	-46	-6	50	13.6	36	-4	50	12.6
Inf. fr. Gyrus (pars opercularis)					52	6	36	9.0
Medial Sup. fr. gyrus (SEF)	-2	0	62	12.2	2	0	66	12.1
Intraparietal sulcus (PEF)	-24	-54	58	10.1	28	-52	56	11.0
Temporoparietal junction (TPJ)	-50	-38	28	6.8	62	-36	16	11.7
Temporo-occipital junction (MT/V5)	-46	-74	8	12.7	48	-64	10	14.2
Mid. occipital gyrus	-26	-82	22	13.6	32	-70	26	14.8
Calcarine fissure (posterior part, V1p)	-12	-62	0	12.4	16	-88	0	16.0
Lingual gyrus	-12	-76	-8	13.5	14	-78	-8	17.3
Putamen/Pallidum	-22	-10	6	10.0	22	-6	8	9.3
Thalamus	-4	-24	-12	8.7	8	-22	-6	9.3

T-score > 5.8, *P* < 0.001, corrected for family-wise error.

(range 3.4° – 9.3°), respectively. We found no effect of MPS, eye preference, MPS × eye preference interaction, age, sex, or educational level on the subjects' mean amplitude of saccades in both directions (ANOVA, all *P* values > 0.05).

VGS HFLI Analysis

VGS HFLI distribution according to MPS

The sample distributions of HFLI values for VGS within the three MPS groups are shown in Figure 1. For the sLH

and MH groups, mean HFLI were significantly rightward lateralized (sLH: -20.0 ± 31.4 ; (*t*₉₇) = -6.3; *P* < 0.0001; MH: -10.3 ± 27.7 ; (*t*₉₇) = -3.7; *P* = 0.0004). For the sRH group, mean HFLI was positive (3.8 ± 30.0) but the difference to 0 was not significant (*t*₉₆) = 1.2; *P* = 0.2).

Note also that the HFLI values for VGS in sLH and sRH groups were not normally distributed (Shapiro-Wilk test, sLH: *P* = 0.016, sRH: *P* = 0.012). We, therefore, applied a nonparametric statistical approach to estimate the effects of MPS and eye preference on the HS for spatial attention.

TABLE III. Cortical clusters showing significant asymmetrical activation for the execution of visually guided saccades compared with central fixation for each MPS group

Functional region	Left hemisphere				Right hemisphere			
	x	y	z	T-score	x	y	z	T-score
sLH Group								
Mid. fr./Precentral gyrus (lat-FEF)					32	-2	56	6.8
Inf. fr. Gyrus (pars opercularis)					40	8	32	8.6
Intraparietal sulcus (PEF)					50	-30	50	10.0
Temporoparietal junction (TPJ)					48	-36	8	9.1
					60	-36	14	8.7
Temporo-occipital junction (MT/V5)					44	-58	2	10.1
Mid. occipital gyrus					34	-72	28	10.6
Calcarine fissure (posterior part, V1p)					16	-88	2	10.2
Post. Precentral.Rolando sulcus (MSEF)	-42	-14	54	7.4				
MH Group								
Mid. fr./Precentral gyrus (lat-FEF)					38	2	50	6.6
Inf. fr. Gyrus (pars opercularis)					46	8	32	9.5
Intraparietal sulcus (PEF)					50	-30	50	8.6
Temporoparietal junction (TPJ)					48	-38	10	11.0
					60	-38	14	11.9
Temporo-occipital junction (MT/V5)					42	-58	8	10.6
Mid. occipital gyrus					34	-70	26	13.7
Calcarine fissure (posterior part, V1p)					18	-88	4	11.9
Post. Precentral.Rolando sulcus (MSEF)	-38	-14	50	7.8				
sRH Group								
Mid. fr./Precentral gyrus (lat-FEF)								
Inf. fr. Gyrus (pars opercularis)								
Intraparietal sulcus (PEF)								
Temporoparietal junction (TPJ)					50	-40	12	9.0
					64	-34	16	8.1
Temporo-occipital junction (MT/V5)					46	-62	12	7.7
Mid. occipital gyrus					34	-68	24	10.6
Calcarine fissure (posterior part, V1p)					18	-88	2	9.2
Post. Precentral.Rolando sulcus (MSEF)								

T-score > 5.8, $P < 0.001$, corrected for family-wise error.

Effects of MPS and Eye Preference

The PERMANOVA HFLI values returned a MPS \times eye preference interaction (pseudo- $F = 3.13$; $P = 0.043$, Fig. 2). Pair-wise post hoc permutational tests demonstrated that this interaction was explained by the largest rightward functional asymmetry detected in the sLH/RE group as compared with the other groups (sLH/RE vs. sLH/LE: $t = 2.0$, $P = 0.04$; vs. MH/RE: $t = 4.0$, $P = 0.0002$; vs. MH/LE: $t = 1.8$, $P = 0.02$; vs. sRH/RE: $t = 5.5$, $P = 0.0001$; vs. sRH/LE, $t = 3.2$, $P = 0.001$).

This PERMANOVA of HFLI values also revealed a significant main effect of MPS (pseudo- $F = 16.1$, $P = 0.0001$). For the main MPS effect, sLH (-20.0 ± 31.4 , $N = 98$) showed a larger rightward hemispheric asymmetry for VGS than MH (-10.3 ± 27.7 , $N = 98$, post hoc permutational test $t = 2.3$, $P = 0.02$) and sRH (3.8 ± 30.0 , $N = 97$; $t = 5.5$, $P = 0.0001$). MH also showed a larger rightward

asymmetry than sRH ($t = 3.4$, $P = 0.0006$). Finally, no effect of sex ($P = 0.09$), age ($P = 0.44$), or educational level ($P = 0.29$) was observed.

Regional VGS Activations in the Three MPS Groups

Whatever the manual preference strength, the performance of VGS activated a bilateral distributed cortico-subcortical network (left part of Fig. 3, Table II). The activations in the frontal lobe were located along the precentral gyrus including both medial and lateral FEF, and extending down into the pars opercularis of the inferior frontal gyrus in the right hemisphere. A medial superior frontal activation was also observed corresponding to the supplementary eye fields (SEF). The parietal activation ran along either side of the intraparietal sulcus (IPS) and corresponded to the parietal eye fields. The activation in the

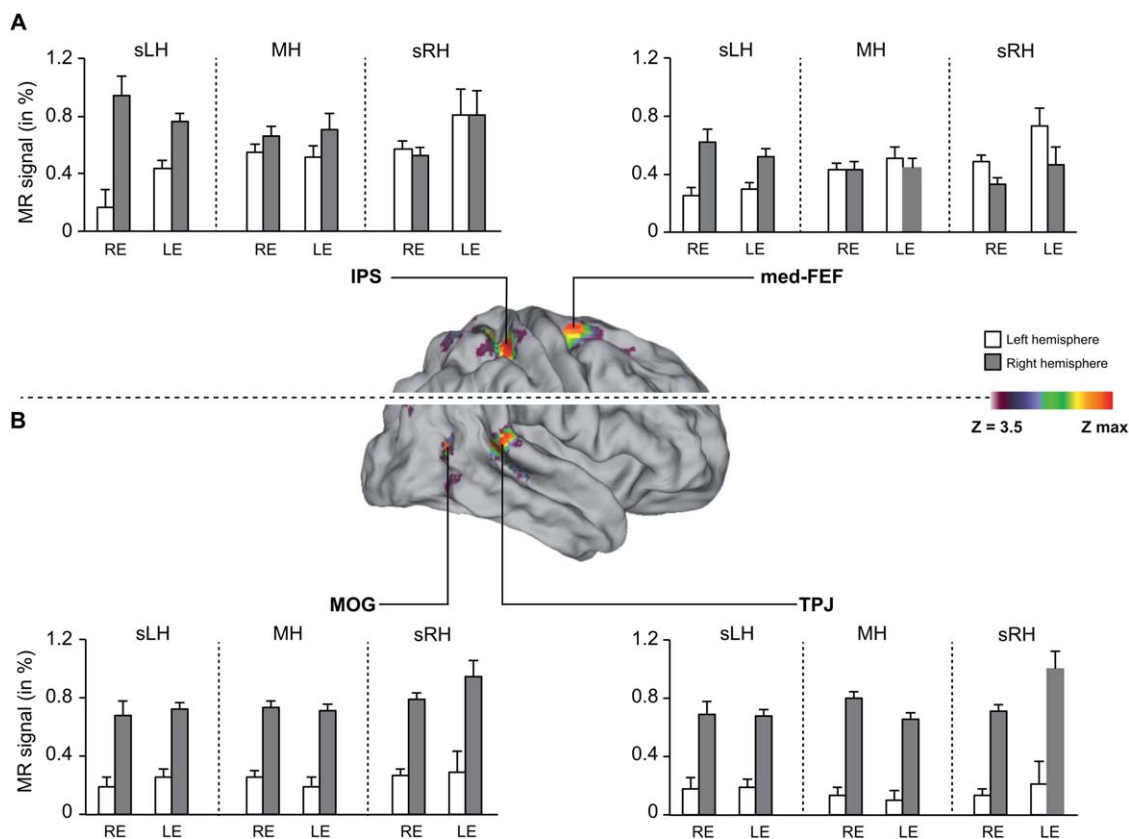


Figure 4.

A. Rightward activations specific to sLH/RE. BOLD signal variations were extracted for both left and right hemispheres for each group and each cluster and presented as histograms. Errors bars denote SD. IPS: Intraparietal sulcus; med-FEF: medial FEF. **B.** Rightward asymmetrical activations common to any manual and eye preference group. MOG: Middle occipital gyrus, TPJ: Temporo-parietal junction.

temporal lobe included the posterior part of both superior and middle temporal gyri extending up to the supramarginal gyrus and corresponded to the temporoparietal junction (TPJ). The occipital activation encompassed the calcarine fissure corresponding to the primary visual area (V1) and extended to both ventral and dorsal extrastriate pathways, including the temporo-occipital junction corresponding to the motion-sensitive MT/V5 area and middle occipital gyri (MOG). Finally, bilateral subcortical activations were observed in the putamen and the thalamus.

Regional rightward asymmetrical activations (Right part of Fig. 3, Table III) were observed irrespective of manual preference strength in TPJ, MOG, MT/V5, and medially in the posterior part of the calcarine sulcus (V1p). Additional rightward asymmetries were observed in the lateral FEF, the pars opercularis of the inferior frontal gyrus, and the anterior part of the IPS for sLH and MH groups. These two groups also elicited leftward asymmetrical activations in the periprecentral region consisting in a cluster

encompassing the precentral gyrus along the Rolando sulcus as part of the motor strip eye field (MSEF).

Regional Asymmetrical VGS Activation Independent of MPS and Eye Preference

The conjunction analysis of the asymmetrical maps of the six groups of subjects revealed two common asymmetrical clusters of activation located in the right hemisphere (Fig. 4B), which correspond to the TPJ and the MOG belonging to the right ventral attentional network [Shulman et al., 2010].

Asymmetrical Brain Regions in sLH/RE Group as Compared to the Other Groups

The comparison of the average functional asymmetry map of the sLH/RE group with the one of all other

subjects revealed two asymmetrical clusters of activation located in the right hemisphere (Fig. 4A), which correspond to the medial FEF and the IPS. They belong to the right dorsal saccadic/attentional network [Anderson et al., 2012; Petit et al., 2009]. In other words, the larger rightward HFLIs measured for the sLH/RE group was due to a stronger rightward asymmetrical activation of the dorsal attentional network. The histograms in Figure 4A show that for each cluster, the group of sLH/RE subjects elicited a significant higher right activation during the VGS performance than in the left counterpart while it led instead to the same magnitude in both hemispheres for the other subjects.

Note that, as for the HFLI effect, only the sLH/RE group stood out from other groups. The other comparisons between the average asymmetry map of one group and the average asymmetrical map of all other subjects did not reveal any specific regions even at the uncorrected threshold of 0.001.

DISCUSSION

In a large sample of healthy individuals balanced for manual preference, the execution of visually guided saccades activated a bilateral distributed cortico-subcortical network in which dorsal and ventral attentional/saccadic pathways elicited rightward asymmetrical activation depending on manual preference strength and sighting eye. Although the ventral pathway showed a strong rightward asymmetry irrespective of both manual and eye preferences, the dorsal frontoparietal network showed a robust rightward asymmetry in strongly left-handers, even more pronounced in left-handed subjects with a right sighting-eye (sLH/RE).

The interaction of these two factors brings support to the hypothesis that the origin of the rightward hemispheric dominance for spatial attention may be spatio-motoric. As early introduced by Ledoux and Gazzaniga [LeDoux et al., 1977], such a manipulo-spatial origin may be neither perceptual nor motor per se but rather reflects a mechanism by which a spatial context is mapped onto the perceptual and motor activities, including the exploration of the spatial environment with eyes and hands.

Before examining in details these results, one may first discuss the distribution of eye preference in our specific cohort of healthy subject balanced for manual preference, and then address the issue of using VGS as a canonical task to study the HS of the spatial attention.

Manual and Eye Preference Relationships

About one third of the general population, including about 10% of left-handers, is left-eye dominant, preferring to use the left eye rather the right eye for monocular sighting tasks [Porac and Coren, 1976]. A higher percentage of left-eye dominant (42%) was observed in this study that is

due to the enrichment of the BIL&GIN database in left-handers (about 50%).

As previously described [McManus et al., 1999], we showed that self-reported manual preference for writing and sighting eye dominance are statistically associated, with right-handers being more likely to be right-eye dominant and left-handers being more likely to be left-eye dominant. A meta-analysis of the literature including 54,087 subjects from 54 set of data has also described that about 57% of left-handers and about 35% of right-handers are left-eye dominant [Bourassa et al., 1996]. Based on the self-reported manual preference, we observed a quite different proportion (64% and 19%) but consistent with a higher number of left eye preference in left-handers than in right-handers. We also revealed for the first time these proportions in relation to manual preference strength balanced among the 293 subjects, showing that about 73% of strongly left-handers, 39% of mix-handers and only 13% of strong-right handers are left-eye dominant.

It is noteworthy that any satisfactory explanation for the relationship between manual and eye preferences has not been yet provided [Annett, 1999; McManus et al., 1999]. Previous and current data presented so far fits with what has been called a phenotypic model by McManus et al. That is, an individual who is right-handed for writing, and also for throwing, is more likely to be right-eyed to the same extent that an individual who is left-handed for writing and throwing is more likely to be left-eyed. This makes it even more interesting in studying incongruent subjects with crossed eye/hand preference.

Visually Guided Saccades: A Reliable Task to Study Spatial Attention Networks

One may also note that this study allows describing for the first time the VGS-related activation in a large cohort of 293 healthy subjects. For each MPS group, the execution of VGS (range 3°–10°) activated a large set of cortical and subcortical areas (left part of Fig. 3, Table II) that previous functional neuroimaging studies agreed in describing as involved in numerous saccadic eye movements and covert shifts of spatial attention (for reviews see [Anderson et al., 2012; Corbetta et al., 2008; Corbetta and Shulman, 2002; McDowell et al., 2008; Petit et al., 2009]). We also observed that, in both sLH and MH groups, VGS-related activation of such a cortico-subcortical network elicited rightward asymmetries in both dorsal and ventral saccadic/attentional networks and leftward asymmetries in the saccadic motor system (MSEF; right part of Fig. 3 and Table III). Note that the strong right-handers elicited a lesser regional rightward asymmetry, restricted to the TPJ and occipital areas (MOG, MT/V5, V1p). This was consistent with the fact that, at the global level of HFLI values' distribution, strong right-handers were not asymmetrical.

We were also concerned by the fact that the use of a VGS task was adequate for studying how both manual

and eye preferences relate to the HS for spatial attention. It is well admitted that both overt (with eye movements) and covert spatial shifts of attention elicit activation in the same frontoparietal network with more robust eye-movement related BOLD signal changes compared with attention-related activation [Beauchamp et al., 2001; de Haan et al., 2008]. This is why the recent studies dealing with right-hemispheric dominance for spatial attention chose a VGS task to localize the dorsal attentional network (e.g., [Duecker et al., 2013; Szczepanski and Kastner, 2013; Szczepanski et al., 2013]).

Manual Lateralization and HS of Spatial Attention

Our findings are the first evidence that the variability in the hemispheric dominance for overt spatial attention relates to manual preference strength. The measure of each HFLI for VGS represents the individual variation in the degree to which the execution of visually guided saccades is right or left lateralized at the hemispheric level. A rightward-lateralized HFLI indicates that the right hemisphere, in line with its dominance for spatial processing, primarily drives the VGS-related functional activation. This is the case for sLH and MH subjects showing rightward hemispheric lateralization for VGS (Fig. 2) and accordingly for spatial attention. On the contrary, sRH subjects are rather distributed equivalently between rightward- and leftward-hemispheric lateralization in line with previous neuropsychological studies showing that the relation between spatial functions and the right hemisphere is weaker than that existing between language and the left hemisphere [Bryden et al., 1983; Hecaen et al., 1981]. Previous neuroimaging studies did not evidence any incidence of manual preference on the lateralization of spatial attentional networks [Badzakova-Trajkov et al., 2010; Floel et al., 2005; Powell et al., 2012] neither of manual preference strength [Tzourio-Mazoyer et al., 2010]. But, these studies used a landmark task, which requires subjects to judge whether premarked lines are correctly bisected, to mimic the line bisection task used to diagnose the attentional deficits of patient with unilateral spatial neglect [Corbetta and Shulman, 2011]. Performing the landmark task involves not only processes related to spatial attention but also processes related to perceptual judgment and decision-making. Depending on the choice of the control condition, some of the activations related to the performance of the landmark task may not be specific to the spatial attention processes and may influence the measure of the hemispheric asymmetry when considering the effect of manual lateralization in these previous studies. As a matter of fact, Badzakova-Trajkov et al. [2010] and Powell et al. [2012] described that, for the landmark task, significant activations unrelated to manual preference were observed mostly in the right hemisphere in the MOG and in cortical areas straddling the Sylvian fissure: the inferior parietal cortex, the TPJ as well as the inferior frontal cortex, namely

along the ventral attentional network [Corbetta et al., 2008]. Interestingly, both MOG and TPJ rightward activation were also observed in this study for the VGS task with no impact of manual lateralization. Every previous fMRI-related description of the right hemisphere asymmetry along the ventral attentional network has concerned right-handed subjects (e.g., [Arrington et al., 2000; Corbetta et al., 2000; Downar et al., 2000; Macaluso et al., 2002; Petit et al., 2009; Shulman et al., 2007; Shulman et al., 2010]). Our results demonstrate that this consistent rightward asymmetry of the ventral attentional network also concerns both sLH and MH individuals (Fig. 4B).

The impact of manual preference strength on the hemispheric lateralization of spatial attention was not due either to functional asymmetries in motor areas but was observed within the cortical regions (med-FEF, IPS) constituting the human dorsal attentional network [Anderson et al., 2012; Corbetta et al., 1998; de Haan et al., 2008; McDowell et al., 2008; Perry and Zeki, 2000; Petit and Beauchamp, 2003; Petit et al., 2009]. Corbetta and Shulman previously proposed that these frontoparietal regions constituted a dorsal network for the control of spatial and featural attention and stimulus-response mapping [Corbetta and Shulman, 2002]. Subsequent work demonstrated that at rest, these regions show highly correlated activity [Fox et al., 2006; He et al., 2007] consistent with the notion that they represent a separate functional-anatomical network analogous to sensory and motor systems, with their own external effectors, the eyes.

Previous studies testing for hemispheric asymmetries in the dorsal network during spatial selective attention and target detection [Shulman et al., 2009; Shulman et al., 2010; Szczepanski and Kastner, 2013] found little evidence of right hemisphere dominance while this latter has been observed during covert visuospatial orienting [Siman-Tov et al., 2007] and visually guided saccades [Anderson et al., 2012; Petit et al., 2009]. Such discrepancies may be due to the fact that all these previous studies were performed in right-handed individuals, which we have shown to be divided equivalently between rightward- and leftward-hemispheric lateralization. Depending on the prevalence of such hemispheric lateralization in a given group of right-handers, one may observe or not a rightward hemispheric dominance.

The Manipulo-Spatial Hypothesis Supported by the HS of the Dorsal Attentional Network in Strong Left-Handers With Right Sighting-Eye

Our study is the first to address the question of the HS of spatial attention in a large group of strongly left-handers and to show that it relies on a robust rightward asymmetry of the dorsal attentional network. The interaction of manual and eye preferences brings support to the hypothesis that the origin of the rightward hemispheric dominance for spatial attention may be of manipulo-

spatial nature. As early introduced by Ledoux and Gazzaniga [LeDoux et al., 1977], such a manipulo-spatial origin may be neither perceptual nor motor per se but rather reflects a mechanism by which a spatial context is mapped onto the perceptual and motor activities, including the exploration of the spatial environment with eyes and hands. Within this context, strongly left-handers with a right sighting-dominant eye may benefit from the advantage of having the same right hemispheric control of their dominant hand and visuospatial attention processing.

It has been proposed that eye dominance is predominantly controlled through the ipsilateral occipital cortex [Erdogan et al., 2002; Shima et al., 2010]. As the responding hand is connected via its primary motor area in the contralateral hemisphere [Serrien et al., 2006], the functional connection between visual input and motor output would involve only one hemisphere for subjects presenting crossed hand-eye laterality. It does not require interhemispheric transfers of information that are relatively time consuming [Corballis, 2002]. In the case of the sLH/RE subjects, it corresponds to the right hemisphere dominant for spatial attention through the dorsal network. We believe that this phenomenon explains why left-handed right sighting dominant eye athletes can outperform their competitors.

As compared to their prevalence in the general population, top-level international left-handed athletes are indeed overrepresented in most of interactive sports in which two or more athletes play or fight each other directly (e.g., fencing, tennis, table tennis, boxing...) but not in non-interactive or individual sports (e.g., golf or swimming) [Grouios et al., 2000]. More interestingly, among high-level left-handed athletes those with a right sighting dominant eye become very efficient in conditions of high spatial and temporal uncertainty, if the time allowed to respond is very short like in fencing [Azemar et al., 2008]. In laboratory conditions, experimental tasks with spatiotemporal uncertainty, for example, Posner's cueing paradigm, have confirmed a visuo-motor advantage in athlete and non-athlete individuals having crossed hand-eye laterality [Nougier et al., 1990]. Hand responding as fast was not the preferred hand of the subject, but that being on the side opposite to the dominant eye. Thus, subjects with right eye dominance showed shorter reaction time with their left hand, and vice versa, in covert spatial attention [Azemar, 2003; Nougier et al., 1990]. In the same line, a recent psychometric study described a significant advantage in manual reaction time in response to a lateralized visual target, whatever the stimulated hemifield, for the left-hand in left-handers with right dominant eye [Chaumillon et al., 2014]. Our results suggest that the dorsal attentional network would be the neural basis of such an advantage at least in the right hemisphere of sLH/RE subjects.

The Evolutionary Advantage of Left-Handed Individuals

The percentage of left-handers (about 10%–15%) in mankind has apparently not changed since the Neolithic

[Coren and Porac, 1977] and such a persistence has always been puzzling [Raymond et al., 1996; Yeo and Gangestad, 1993], as left manual preference is partially heritable [Medland et al., 2009] and appears to be associated with reduced fitness (reviewed in [Yeo and Gangestad, 1993]). This requires that left-handers have some advantages in some situations, which have prevailed in time, and in all cultures, to explain the archaeological and current ratio of left manual preference. It has been proposed that left-handers have a frequency advantage when they engage in fighting because they usually interact with right-handers who are more numerous, and are therefore more accustomed to encountering other right-handers [Raymond et al., 1996]. Previous psychometric studies with left-handed/right-eyed athletes have shown that such an advantage in sporting duels was related to both manual and eye preferences [Azemar et al., 2008]. We suggest that the constancy of the left-handers ratio over the general population relates in part on the HS of spatial attention. Left-handers have been taken advantage to be more frequently rightward lateralized for spatial attention, even more with a right-sighting eye, because they were faster to react under uncertain spatial and temporal situations by mainly using intrahemispheric processing.

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REFERENCES

- Allen M (1983): Models of hemispheric specialization. *Psychol Bull* 93:73–104.
- Anderson EJ, Jones DK, O’Gorman RL, Leemans A, Catani M, Husain M (2012): Cortical network for gaze control in humans revealed using multimodal MRI. *Cereb Cortex* 22:765–75.
- Anderson M, Braak CT (2003): Permutation tests for multifactorial analysis of variance. *J Stat Comput Simul* 73:85–113.
- Anderson MJ (2001a): A new method for non-parametric multivariate analysis of variance. *Austral Ecol* 26:32–46.
- Anderson MJ (2001b): Permutation tests for univariate or multivariate analysis of variance and regression. *Can J Fish Aquat. Sci* 58:626–639.
- Annett M (1999): Eye dominance in families predicted by the right shift theory. *Laterality* 4:167–172.
- Arrington CM, Carr TH, Mayer AR, Rao SM (2000): Neural mechanisms of visual attention: object-based selection of a region in space. *J Cogn Neurosci* 12:106–117.
- Azemar G (2003): *L’homme asymétrique*. Gauchers et droitiers face à face. Paris: CNRS Editions. 324 p.
- Azemar G, Stein JF, Ripoll H (2008): Effects of ocular dominance on eye-hand coordination in sporting duels. *Sci Sports* 23:263–277.
- Badzakova-Trajkov G, Haberling IS, Roberts RP, Corballis MC (2010): Cerebral asymmetries: Complementary and independent processes. *PLoS One* 5:e9682.
- Beauchamp MS, Petit L, Ellmore TM, Ingeholm J, Haxby JV (2001): A parametric fMRI study of overt and covert shifts of visuospatial attention. *Neuroimage* 14:310–321.

- Bourassa DC, McManus IC, Bryden MP (1996): Handedness and Eye-dominance: A meta-analysis of their relationship. *Laterality* 1:5–34.
- Bryden MP, Hecaen H, DeAgostini M (1983): Patterns of cerebral organization. *Brain Lang* 20:249–262.
- Chaumillon R, Blouin J, Guillaume A (2014): Eye dominance influences triggering action: The Poffenberger paradigm revisited. *Cortex* 58:86–98.
- Corballis MC (2002): Hemispheric interactions in simple reaction time. *Neuropsychologia* 40:423–434.
- Corballis MC (2003): From mouth to hand: Gesture, speech, and the evolution of right-handedness. *Behav Brain Sci* 26:199–208.
- Corbetta M, Shulman GL (2002): Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 3:201–215.
- Corbetta M, Shulman GL (2011): Spatial neglect and attention networks. *Annu Rev Neurosci* 34:569–599.
- Corbetta M, Akbudak E, Conturo TE, Drury HA, Linenweber MR, Ollinger JM, Petersen SE, Raichle ME, Snyder AZ, Van Essen DC, Shulman GL (1998): A common cortical network for attention and eye movements. *Neuron* 21:761–768.
- Corbetta M, Kincade JM, Ollinger JM, McAvoy MP, Shulman GL (2000): Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nat Neurosci* 3:292–297.
- Corbetta M, Patel G, Shulman GL (2008): The reorienting system of the human brain: From environment to theory of mind. *Neuron* 58:306.
- Coren S (1993): The lateral preference inventory for measurement of handedness, footedness, eyedness, and earedness: Norms for young adults. *Bull Psychon Soc* 31:1–3.
- Coren S, Porac C (1977): Fifty centuries of right-handedness: The historical record. *Science* 198:631–632.
- de Haan B, Morgan PS, Rorden C (2008): Covert orienting of attention and overt eye movements activate identical brain regions. *Brain Res* 1204:102.
- Downar J, Crawley AP, Mikulis DJ, Davis KD (2000): A multimodal cortical network for the detection of changes in the sensory environment. *Nat Neurosci* 3:277–283.
- Duecker F, Formisano E, Sack AT (2013): Hemispheric differences in the voluntary control of spatial attention: Direct evidence for a right-hemispheric dominance within frontal cortex. *J Cogn Neurosci* 25:1332–1342.
- Durand AC, Gould GM (1910): A method of determining ocular dominance. *J Am Med Assoc* 55:369–370.
- Erdogan AR, Ozdikici M, Aydin MD, Aktas O, Dane S (2002): Right and left visual cortex areas in healthy subjects with right- and left-eye dominance. *Int J Neurosci* 112:517–523.
- Floel A, Jansen A, Deppe M, Kanowski M, Konrad C, Sommer J, Knecht S (2005): Atypical hemispheric dominance for attention: Functional MRI topography. *J Cereb Blood Flow Metab* 25: 1197–1208.
- Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME (2006): Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proc Natl Acad Sci USA* 103:10046–10051.
- Groen MA, Whitehouse AJO, Badcock NA, Bishop DVM (2013): Associations between handedness and cerebral lateralisation for language: A comparison of three measures in children. *PLoS One* 8:e64876.
- Grouios G, Tsorbatzoudis H, Alexandris K, Barkoukis V (2000): Do left-handed competitors have an innate superiority in sports? *Percept Mot Skills* 90:1273–1282.
- He BJ, Snyder AZ, Vincent JL, Epstein A, Shulman GL, Corbetta M (2007): Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. *Neuron* 53:905.
- Hecaen H, Sauguet J (1971): Cerebral dominance in left-handed subjects. *Cortex* 7:19–48.
- Hecaen H, De Agostini M, Monzon-Montes A (1981): Cerebral organization in left-handers. *Brain Lang* 12:261–284.
- Hellige JB (1990): Hemispheric asymmetry. *Annu Rev Psychol* 41: 55–80.
- Herve PY, Zago L, Petit L, Mazoyer B, Tzourio-Mazoyer N (2013): Revisiting human hemispheric specialization with neuroimaging. *Trends Cogn Sci* 17:69–80.
- Hutsler JJ, Gillepsie ME, Gazzaniga MS (2001): The evolution of hemispheric specialization. In: Dulbecco R, Baltimore D, Jacob F, Levi-Montalcini R, editors. *Frontiers of Life*. Treccani: Academic Press. pp 37–49.
- Knecht S, Drager B, Deppe M, Bobe L, Lohmann H, Floel A, Ringelstein EB, Henningsen H (2000): Handedness and hemispheric language dominance in healthy humans. *Brain* 123(Pt 12):2512–2518.
- LeDoux JE, Wilson DH, Gazzaniga MS (1977): Manipulo-spatial aspects of cerebral lateralization: Clues to the origin of lateralization. *Neuropsychologia* 15:743–750.
- Macaluso E, Frith CD, Driver J (2002): Supramodal effects of covert spatial orienting triggered by visual or tactile events. *J Cogn Neurosci* 14:389–401.
- Mazoyer B, Zago L, Jobard G, Crivello F, Joliot M, Percey G, Mellet E, Petit L, Tzourio-Mazoyer N (2014): Gaussian mixture modeling of hemispheric lateralization for language in a large sample of healthy individuals balanced for handedness. *PLoS One* 9:e101165.
- McArdle BH, Anderson MJ (2001): Fitting multivariate models to community data: A comment on distance-based redundancy analysis. *Ecology* 82:290–297.
- McDowell JE, Dyckman KA, Austin BP, Clementz BA (2008): Neurophysiology and neuroanatomy of reflexive and volitional saccades: Evidence from studies of humans. *Brain Cogn* 68: 255–271.
- McManus IC, Porac C, Bryden MP, Boucher R (1999): Eye-dominance, writing hand, and throwing hand. *Laterality* 4:173–192.
- Medland SE, Duffy DL, Wright MJ, Geffen GM, Hay DA, Levy F, van-Beijsterveldt CEM, Willemsen G, Townsend GC, White V, Hewitt AW, Mackey DA, Bailey JM, Slutske WS, Nyholt DR, Treloar SA, Martin NG, Boomsma DI (2009): Genetic influences on handedness: Data from 25,732 Australian and Dutch twin families. *Neuropsychologia* 47:330–337.
- Nobre AC, Gitelman DR, Dias EC, Mesulam MM (2000): Covert visual spatial orienting and saccades: Overlapping neural systems. *Neuroimage* 11:210–216.
- Nougier V, Stein JF, Azemar G (1990): Covert orienting of attention and motor preparation processes as a factor of success in fencing. *J Hum Mov Stud* 19:251–272.
- Oldfield RC (1971): The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 9:97–113.
- Perry RJ, Zeki S (2000): The neurology of saccades and covert shifts in spatial attention: An event-related fMRI study. *Brain* 123(Pt 11):2273–2288.
- Petit L, Beauchamp MS (2003): Neural basis of visually guided head movements studied with fMRI. *J Neurophysiol* 89:2516–2527.
- Petit L, Zago L, Mellet E, Vigneau M, Andersson F, Mazoyer B, Tzourio-Mazoyer N (2009): Functional asymmetries revealed in visually guided saccades: An fMRI study. *J Neurophysiol* 102: 2994–3003.

- Petit L, Crivello F, Mellet E, Jobard G, Zago L, Joliot M, Percey G, Mazoyer B, Tzourio-Mazoyer N (2012): BIL&GIN: A database for the study of hemispheric specialization. Beijing, China.
- Porac C, Coren S (1976): The dominant eye. *Psychol Bull* 83:880–897.
- Powell JL, Kemp GJ, Garcia-Finaña M (2012): Association between language and spatial laterality and cognitive ability: An fMRI study. *NeuroImage* 59:1818–1829.
- Previc FH (1991): A general theory concerning the prenatal origins of cerebral lateralization in humans. *Psychol Rev* 98:299–334.
- Pujol J, Deus J, Losilla JM, Capdevila A (1999): Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology* 52:1038–1043.
- Raymond M, Pontier D, Dufour AB, Moller AP (1996): Frequency-dependent maintenance of left handedness in humans. *Proc Biol Sci* 263:1627–1633.
- Serrien DJ, Ivry RB, Swinnen SP (2006): Dynamics of hemispheric specialization and integration in the context of motor control. *Nat Rev Neurosci* 7:160–166.
- Shima H, Hasegawa M, Tachibana O, Nomura M, Yamashita J, Ozaki Y, Kawai J, Higuchi M, Kado H (2010): Ocular dominance affects magnitude of dipole moment: an MEG study. *Neuroreport* 21:817–821.
- Shneur E, Hochstein S (2006): Eye dominance effects in feature search. *Vision Res* 46:4258–4269.
- Shneur E, Hochstein S (2008): Eye dominance effects in conjunction search. *Vision Res* 48:1592–1602.
- Shulman GL, Astafiev SV, McAvoy MP, d'Avossa G, Corbetta M (2007): Right TPJ deactivation during visual search: Functional significance and support for a filter hypothesis. *Cereb Cortex* 17:2625–2633.
- Shulman GL, Astafiev SV, Franke D, Pope DLW, Snyder AZ, McAvoy MP, Corbetta M (2009): Interaction of stimulus-driven reorienting and expectation in ventral and dorsal frontoparietal and basal ganglia-cortical networks. *J Neurosci* 29:4392–4407.
- Shulman GL, Pope DL, Astafiev SV, McAvoy MP, Snyder AZ, Corbetta M (2010): Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. *J Neurosci* 30:3640–3651.
- Siman-Tov T, Mendelsohn A, Schonberg T, Avidan G, Podlipsky I, Pessoa L, Gadoth N, Ungerleider LG, Hendler T (2007): Bi-hemispheric leftward bias in a visuospatial attention-related network. *J Neurosci* 27:11271–11278.
- Szczepanski SM, Kastner S (2013): Shifting attentional priorities: Control of spatial attention through hemispheric competition. *J Neurosci* 33:5411–5421.
- Szczepanski SM, Pinsk MA, Douglas MM, Kastner S, Saalman YB (2013): Functional and structural architecture of the human dorsal frontoparietal attention network. *Proc Natl Acad Sci USA* 110:15806–15811.
- Tzourio N, Crivello F, Mellet E, Nkanga-Ngila B, Mazoyer B (1998): Functional anatomy of dominance for speech comprehension in left handers vs right handers. *Neuroimage* 8:1–16.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15:273–289.
- Tzourio-Mazoyer N, Petit L, Razafimandimby A, Crivello F, Zago L, Jobard G, Joliot M, Mellet E, Mazoyer B (2010): Left hemisphere lateralization for language in right-handers is controlled in part by familial sinistrality, manual preference strength and head size. *J Neurosci* 30:13314–13318.
- Vergilino-Perez D, Fayel A, Lemoine C, Senot P, Vergne J, Dore-Mazars K (2012): Are there any left-right asymmetries in saccade parameters? Examination of latency, gain, and peak velocity. *Invest Ophthalmol Vis Sci* 53:3340–3348.
- Wada J, Rasmussen T (1960): Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. *J Neurosurg* 17:266–282.
- Wilke M, Lidzba K (2007): LI-tool: A new toolbox to assess lateralization in functional MR-data. *J Neurosci Methods* 163:128–136.
- Wilke M, Schmithorst VJ (2006): A combined bootstrap/histogram analysis approach for computing a lateralization index from neuroimaging data. *NeuroImage* 33:522–530.
- Yeo R, Gangestad S (1993): Developmental origins of variation in human hand preference. *Genetica* 89:281–296.