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The neural correlates of limb apraxia: An anatomical likelihood estimation meta-analysis of lesion-symptom mapping studies in brain-damaged patients

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ABSTRACT

Limb apraxia is a motor disorder frequently observed following a stroke. Apraxic deficits are classically assessed with four tasks: *tool use*, *pantomime of tool use*, *imitation*, and *gesture understanding*. These tasks are supported by several cognitive processes represented in a left-lateralized brain network including inferior frontal gyrus, inferior parietal lobe (IPL), and lateral occipito-temporal cortex (LOTc). For the past twenty years, voxel-wise lesion symptom mapping (VLSM) studies have been used to unravel the neural correlates associated with apraxia, but none of them has proposed a comprehensive view of the topic. In the present work, we proposed to fill this gap by performing a systematic Anatomic Likelihood Estimation meta-analysis of VLSM studies which included tasks traditionally used to assess apraxia. We found that the IPL was crucial for all the tasks. Moreover, lesions within the LOTc were more associated with imitation deficits than tool use or pantomime, confirming its important role in higher visual processing. Our results questioned traditional neurocognitive models on apraxia and may have important clinical implications.

1. Introduction

Apraxia is a disorder affecting voluntary skilled and learnt movement, which cannot be attributed to sensorimotor or comprehensive deficits (de Renzi et al., 1989). Several forms of apraxia have been described in the literature, particularly limb apraxia that was first described by Liepmann (1908, 1920). As reported in a recent review of the literature (Gowda and Kolton Schneider, 2023), limb apraxia is a frequent deficit observed in various neurological disorders, as in neurodegenerative diseases (90%), sclerosis (25%), left stroke (50–80% of patients), and right stroke (30–50% of patients). Limb apraxia is

traditionally explored with four tasks: familiar tool use, pantomime of tool use, imitation, and gesture understanding. Neuroimaging and neuropsychological studies have revealed that these tasks are calling upon several neuro-cognitive processes distributed in a left-lateralized brain network, encompassing three critical hubs, namely, the inferior frontal gyrus (IFG), the inferior parietal lobule (IPL) and the lateral occipital temporal cortex (LOTc; Ishibashi et al., 2016; Johnson-Frey et al., 2003; Lesourd et al., 2021; Osiurak et al., 2021; Reynaud et al., 2016). The development of recent neuroimaging techniques, as voxel-lesion-symptom mapping (VLSM; Bates et al., 2003), has allowed the scientific community working on apraxia to better map the function

Abbreviations: SPL, Superior parietal lobe; IPL, Inferior Parietal Lobule; IPS, Intraparietal sulcus; SMG, Supramarginal gyrus; ASMG, anterior Supramarginal gyrus; AIP, Anterior Intraparietal area; MTG, Middle Temporal Gyrus; PMTG, posterior Middle Temporal Gyrus; STG, Superior temporal lobe; STS, Superior temporal sulcus; PSTS, posterior Superior temporal sulcus; IFG, Inferior frontal gyrus; MFG, Middle frontal gyrus; LOTc, Lateral occipito-temporal cortex; VLSM, voxel-wise lesion symptom mapping; ML imitation, Imitation of meaningless gestures; MF imitation, Imitation of meaningful gestures.

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of these critical brain regions with the human ability to produce and to understand actions (e.g., Achilles et al., 2019; Buxbaum and Kalénine, 2010; Martin, Dressing, et al., 2016; Martin et al., 2015; Martin, Nitschke, et al., 2016; Tarhan et al., 2015). If several studies have tempted to review the works on VLSM on related fields (e.g., action perception and understanding; Urgesi et al., 2014), to our knowledge, there is no systematic work trying to integrate the scientific production of these past two decades on VLSM and limb apraxia. However, a better understanding of the brain regions involved in apraxia would not only increase our theoretical knowledge of the field, but would also improve the efficiency and accuracy of apraxia diagnosis and could ultimately allow the development of strategies to compensate for apraxic deficits.

We proposed in the present paper to fill this gap by conducting a systematic review of VLSM studies associated with familiar tool use, pantomime of tool use, imitation, and gesture understanding tasks and to discuss these results in the framework of the 3-pathways neuro-cognitive model of actions (Binkofski and Buxbaum, 2013). We will briefly present the clinical tasks usually proposed to assess apraxic deficits, the cognitive processes known to be involved in each task, and the brain networks that are engaged in these tasks/processes.

1.1. Clinical tasks assessing limb apraxia

1.1.1. Tool use

To assess the ability to use tools, participants are asked to perform different types of tool use tasks, and particularly single and real tool use (Table 1). Single tool use consists in appropriately use an isolate familiar tool, without any context or associated object (e.g., use a hammer by moving it up and down to simulate the pounding of a nail), while real tool use, consists in using a familiar tool with its typical associated object (e.g., using a hammer with a nail). The ability to use tools can be explored with familiar tools or with novel tools (e.g., mechanical problem-solving tests; Goldenberg and Hagmann, 1998; Jarry et al., 2013; Lesourd et al., 2016; Ochipa et al., 1989; Osiurak, 2013). Tool use skills are often impacted in limb apraxia (for review see Baumard et al., 2014). Patients affected may have difficulties in: (1) performing the gesture adapted to the tool, or/and (2) selecting the appropriate tool,

Table 1
Glossary of Apraxia's assessment tasks.

	Description
Tool use	Participants have to use a tool (e.g., hammer, screwdriver).
Real tool use	Participants have to use a tool with a contextual object (e.g., use a hammer with a nail).
Single tool use	Participants have to grasp a tool and show how to use it without contextual object.
Novel tool use	Participants have to use an unknown tool, designed for the experiment.
Pantomime of tool use	Participants have to simulate the use of a tool without holding it in hand.
Visual modality	Participants have to simulate the use of a tool presented in the picture, without holding it in hand.
Verbal modality	Participants have to simulate the use of a tool presented by verbal instruction, without holding it in hand.
Imitation	Participants have to imitate gestures performed by the experimenter.
Meaningful imitation	The experimenter performs a meaningful symbolic gesture, participants have to imitate this gesture.
Meaningless imitation	The experimenter performs a meaningless gesture, participants have to imitate this gesture.
Transitive imitation	The experimenter performs a pantomime of tool use (without holding the tool in hand), participants have to imitate this gesture.
Intransitive imitation	The experimenter performs a non-tool-related gesture, participants have to imitate this gesture.
Hand imitation	Participants have to imitate hand postures.
Finger imitation	Participants have to imitate finger configurations.

or/and (3) grasping the tool and orienting it correctly.

1.1.2. Pantomime of tool use

Instead of tool use tasks, the pantomime of tool use task consists in performing a transitive gesture without holding the tool in hand (Table 1). Patients have to simulate an object-related-gesture as if they were holding it in hand (e.g., “up and down hand movement” to simulate a hammer pounding a nail in a wall). Pantomime of tool use can be proposed visually (e.g., picture of a hammer) or/and on verbal command (e.g., “Show me how to use a hammer”). To facilitate the reading, for the rest of this paper we will use the term *pantomime* to refer to the pantomime of tool use.

1.1.3. Imitation

Imitation tasks consist in reproducing a gesture presented either by an experimenter or depicted in a picture. Gestures can be either meaningless (ML) or meaningful (MF) (Table 1). A first dissociation has been found between MF and ML gestures during imitation, confirming the importance of studying them independently (Bartolo et al., 2001; Tessari et al., 2007). A second dissociation has been found in ML gestures between hand postures and finger configurations. The first one requires imitating a hand position relative to a body part (e.g., hand on the nose; see for example Goldenberg, 1999), while the second one requires reproducing specific fingers configurations. MF imitation can be divided into two different tasks depending on whether the gesture involved the use of a tool (transitive) or not (intransitive). MF intransitive imitation assesses the ability to reproduce a stored gesture that do not represent the use of a tool (i.e., communicative gesture, e.g., index finger on the lips to request silence) while MF transitive imitation consists in imitating an object-related-gesture (Table 1).

1.1.4. Gesture understanding

In these tasks, participants are required to examine a gesture over several experimental variations and have to judge whether the gesture is correct to perform a given action. For instance, in the recognition of tool manipulation task (Baumard et al., 2016; Jarry et al., 2013; Lesourd, Osiurak, et al., 2017), several pictures of a hand holding a tool are proposed and one picture must be selected according to the best/correct way to hold the tool in order to use it. In other tasks, participants are asked to judge whether two tools have the same manipulation or not, or the same way to be held in hand for subsequent use (for review see Lesourd et al., 2021).

1.2. Cognitive processes involved in the assessment of apraxia

Tool use, pantomime, imitation, and understanding tasks assess different aspects of limb apraxia and are underlaid by different cognitive processes (Baumard and Le Gall, 2021; see Fig. 1). Among all these cognitive processes, several of them appear to be of first importance, that is, semantic knowledge, manipulation knowledge, mechanical knowledge, body knowledge as well as additional non-specific processes.

1.2.1. Semantic knowledge

Semantic knowledge includes general concepts acquired and abstracted from past experiences. This knowledge contains the purpose and the context of an action. Concerning tool use, semantic knowledge allows selecting which tool is associated with a given recipient (e.g., a nail goes with a hammer), or which is the related function of a given tool (e.g., a hammer is used to pound something). Single tool use and pantomime of tool use tasks place a heavier demand on semantic knowledge since no contextual information is provided in addition to the tool presented. Thus, only semantic knowledge about the tool allows identifying the purpose of the action (Hodges et al., 2000; Osiurak et al., 2008, 2021; Silveri and Ciccarelli, 2009). In contrary, by giving a contextual object associated with the tool, semantic knowledge becomes

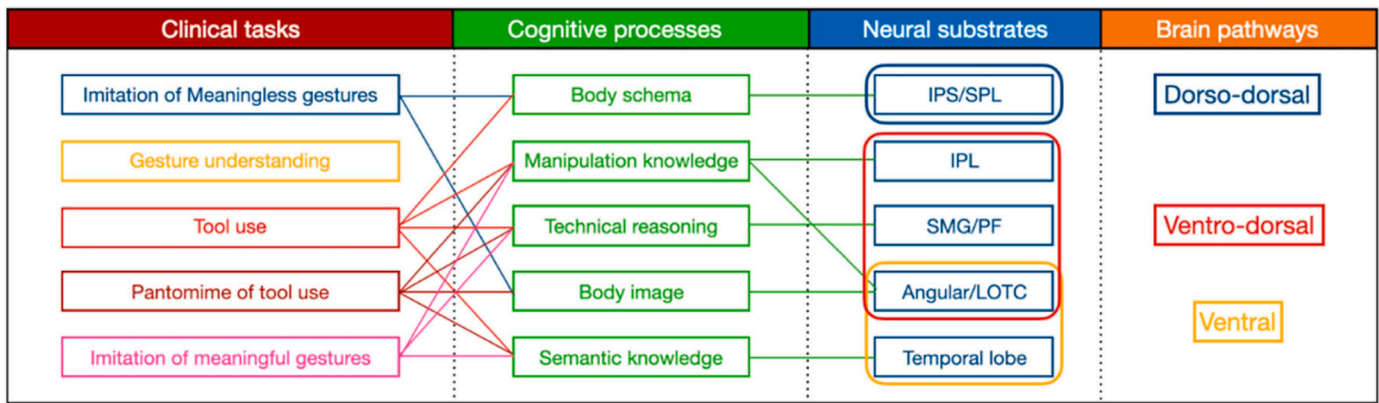


Fig. 1. Correspondence between tasks, processes, neural location, and neural networks (adapted from Baumard and Le Gall, 2021). IPS = intraparietal sulcus; SPL = superior parietal lobe; IPL = inferior parietal lobe; SMG/PF = area PF of the supramarginal gyrus; Angular = angular gyrus; LOTC = lateral occipital temporal cortex.

less necessary. This is the case for real tool use which may depend more on mechanical knowledge (Goldenberg and Spatt, 2009; Hodges et al., 2000; Osiurak et al., 2008). Semantic knowledge is also involved in both transitive and intransitive MF imitation (Mengotti et al., 2013), and finally, gesture understanding tasks are also sustained by semantic knowledge of action (Baumard et al., 2016; Jarry et al., 2013).

1.2.2. Manipulation knowledge

Manipulation knowledge, also known as gesture engrams, contains manipulation aspects of meaningful gestures. Manipulation knowledge is tool-hand centered as it contains information about how to manipulate tools and is “thought to contain the features of gestures which are invariant and critical for distinguishing a given gesture from others.” (Buxbaum, 2001, p.452). Therefore, this knowledge is involved in every transitive gesture task: single tool use, familiar tool use, pantomime, and MF transitive, but also in intransitive imitation (Buxbaum and Saffran, 2002; Goldenberg, 2014; Osiurak et al., 2011; Rothi et al., 1991) and in gesture understanding tasks. Manipulation knowledge may be stored in inferior parietal lobe (IPL; Buxbaum, 2001; Buxbaum et al., 2007; Buxbaum, Kyle, et al., 2005; Haaland et al., 2000; van Elk et al., 2014).

1.2.3. Technical reasoning

Technical reasoning is a “causal and analogical reasoning, which is directed towards the physical world” (Osiurak et al., 2008, 2009, 2021), involving spatial reasoning, physical principles, and interactions between objects and tools. Mechanical knowledge is tool-object centered, as it is based on the understanding of opposition existing between physical properties of tools and objects (Osiurak, 2014; Osiurak et al., 2010; Osiurak and Badets, 2016). Technical reasoning is important to perform actions linked with tool use: single tool use, real tool use, pantomime, and MF transitive imitation (Baumard and Le Gall, 2021; Goldenberg and Hagmann, 1998; Lesourd, Baumard, et al., 2017; Lesourd et al., 2019, 2020; Osiurak et al., 2021). The PF area located in the left IPL is thought to support technical reasoning (Federico et al., 2022; Lesourd, Reynaud, et al., 2023; Reynaud et al., 2016, 2019).

1.2.4. Body schema and body image

Two types of representations can be requested to perform gestures, the body image and the body schema. The body image contains lexical-semantic knowledge of the body and knowledge about structural description of body parts (i.e., perceptual, conceptual, and emotional). Body image is involved in performing ML imitation because patients have to identify body parts of the model they have to reproduce (Baumard and Le Gall, 2021; Buxbaum, 2001; de Vignemont, 2010; Osiurak et al., 2021; Schwoebel and Coslett, 2005). Body image is supported by temporal regions (including LOTC; for review see Lingnau and Downing, 2015; Wurm and Caramazza, 2022), as well as the angular gyrus (Dafsari

et al., 2019). The body schema concerns the motor control system, which guides actions to interact with the physical world, permitting to adapt to external constraints, by taking into account spatial relations between body parts. This ability is involved in ML imitation and pantomime of tool use tasks, and may be mainly supported by the intraparietal sulcus and superior parietal lobe (Baumard and Le Gall, 2021; Buxbaum, 2001; de Vignemont, 2010; Osiurak et al., 2021; Schwoebel and Coslett, 2005).

1.2.5. Non-specific cognitive processes

Working memory is far from being specific to apraxic deficits, it is implicated in several dimensions of gesture tasks. We can define working memory as the ability to store information in short-term memory in order to process this information. Although working memory was found to be involved in single tool use (Baumard et al., 2014), pantomime of tool use task (Bartolo et al., 2003; Cubelli et al., 2000), and ML imitation (Bartolo et al., 2003; Rumiati and Tessari, 2002; Toraldo et al., 2001), its exact role is anything but clear. Indeed, several specific cognitive processes for action can be affected by working memory performance. Thus, the implication of working memory on tool use, pantomime, and imitation would be indirect, which might explain why a dysexecutive syndrome does not systematically lead to a deficit in pantomime of tool use task and/or tool use (Osiurak et al., 2021). Other non-specific processes have been found to be involved in apraxia tasks. This is the case for visuo-spatial skills involved in ML imitation (Goldenberg et al., 2009), and language skills involved in pantomime production (Goldenberg et al., 2003).

1.3. The 3-pathway neurocognitive model of action

The neural correlates of apraxia have been studied for over a century which has led to the emergence of several theories on which current models are based. Historically, two distinct pathways of action have been proposed: a dorsal stream and a ventral stream (Goodale and Milner, 1992; Mishkin et al., 1983). More recently, Binkofski and Buxbaum (2013) proposed an anatomical and functional subdivision of the dorsal pathway into a ventro-dorsal pathway (visual extrastriate cortex, inferior angular gyrus, supramarginal gyrus, anterior intraparietal sulcus, and ventral precentral gyrus) and a dorso-dorsal pathway (visual extrastriate cortex, superior angular gyrus, posterior intraparietal sulcus, superior parietal lobe, and dorsal precentral gyrus). While the dorso-dorsal pathway is mainly involved in online monitoring of action (e.g., reaching/grasping; Rossetti et al., 2005; Tunik et al., 2005), the ventro-dorsal pathway underpins the main representations about tool

use (i.e., manipulation and mechanical knowledge; Buxbaum, 2017; Federico et al., 2022; Reynaud et al., 2016). The ventral pathway³ has been associated with both semantic and manipulation knowledge (e.g., Bozeat et al., 2002; Hodges et al., 2000; Lesourd et al., 2021; Lesourd, Reynaud, et al., 2023). Recent advancements in our understanding of the ventral pathway propose the inclusion of a more dorsal segment, which involves brain regions responsible for perceiving biological motion (MT/V5) and extends toward higher sociocognitive functions via the posterior superior temporal sulcus (Pitcher and Ungerleider, 2021; Rounis and Binkofski, 2023). This segment may be of first importance for processing social gestures.

Each task assessing apraxia relies upon several cognitive processes, which are in turn calling upon these three pathways (Fig. 1 and Fig. 2).

1.3.1. Imitation

Imitation consists in performing a gesture by reproducing it from a model. Since gestures can be either meaningful (MF) or meaningless (ML), this task has been studied to better understand the cognitive bases of action meaning. One of the oldest and most studied cognitive models of imitation is the dual-route model, which opposes semantic and non-semantic routes (Cubelli et al., 2000; Gonzalez Rothi et al., 1991). The semantic route retrieves MF gestures from long-term memory while the direct route is involved in the imitation of ML gestures, by converting directly viewed gestures into sensorimotor information. Neuropsychological double dissociation has been found between imitation of MF and ML gestures, confirming the existence of the two routes (Bartolo et al., 2001; Tessari et al., 2007). However, the direct route is not specific to ML gestures, as MF gestures may be processed through this pathway if they are mixed with ML gestures in the same list (Tessari et al., 2007; Tessari and Rumiati, 2004).

The direct route has been associated with a dorso-dorsal stream, a direct pathway of action production and visuo-motor transformation, supported by occipito-parietal junction, intraparietal sulcus, and superior parietal lobule (Fig. 1 and Fig. 2; for a review see Binkofski and Buxbaum, 2013). In a PET study, Peigneux et al. (2004) highlighted the role of bilateral SPL in ML gestures in contrast to MF gestures. Another PET study conducted by Rumiati et al. (2005) found specific involvement of bilateral SPL and the right occipito-parietal junction for ML imitation. Some lesion mapping studies found dorso-dorsal lesions to be associated with ML imitation deficits, specifically the superior angular gyrus/IPS (Hoeren et al., 2014), and SPL lesions (Hoeren et al., 2014; Martin, Nitschke, et al., 2016). Taken together, these data highlight the strong involvement of the dorso-dorsal stream in the imitation of ML gestures. Moreover, the involvement of the dorso-dorsal route (angular gyrus and IPS) has also been found in MF imitation (Achilles et al., 2019), which agrees with the idea that this pathway may support both MF and ML gestures (Tessari et al., 2007; Tessari and Rumiati, 2004).

The indirect route is associated with the ventral stream (Fig. 1 and Fig. 2) which supports semantic and action semantics (for reviews see Lingnau and Downing, 2015; Ralph et al., 2017). This pathway is supported by the posterior and anterior parts of the temporal lobe, and the occipito-temporal junction. Several neuroimaging studies reported specific involvement of bilateral temporal lobe for MF imitation (Peigneux et al., 2004; Rumiati et al., 2005). Lesion mapping studies confirmed the involvement of temporal regions in MF imitation including the LOTC (Achilles et al., 2019; Binder et al., 2017; Buxbaum et al., 2014; Dressing et al., 2018). However, some studies reported that

ML imitation is supported by several parts of the ventral stream, including the LOTC (Buxbaum et al., 2014; Dressing et al., 2021; Hoeren et al., 2014; Martin, Nitschke, et al., 2016). The indirect route can also be associated with the ventro-dorsal stream, which is known to store sensorimotor representations about gestures, and can therefore be the locus of the action lexicon (Buxbaum, 2001; Buxbaum, Kyle, et al., 2005; Buxbaum et al., 2007; Haaland et al., 2000; van Elk et al., 2014). However, once again this pathway, particularly the left inferior parietal lobe (IPL) supports the imitation of both MF and ML gestures (Achilles et al., 2019; Binder et al., 2017; Dressing et al., 2018, 2019; Martin, Nitschke, et al., 2016; Mengotti et al., 2013; Tessari et al., 2021). The left IPL is an integrative hub at the interplay between ventral and dorsal pathways, which store several kinds of representations. Taken together, these data showed that both MF and ML imitation can be supported by ventral, ventro-dorsal and dorso-dorsal pathways, therefore ruling out the clear association between a cognitive pathway (direct or indirect) and a neural pathway.

A recent meta-analysis nevertheless afforded valuable information by showing that deficit of imitation of MF gestures was associated with lesions involving the left IPL and left STG, whereas a deficit of imitation of ML gestures was more distributed in the left hemisphere including posterior part of the temporal lobe as well as IPL (Lesourd et al., 2018). In line with these data, Tessari et al. (2021) showed that deficit of MF imitation was associated with lesions in left IPL and STG, whereas deficit of ML imitation was associated with lesions in both left IPL and posterior left LOTC, depending on the body part to imitate (i.e., hand posture vs finger configuration). Taken together, these data may suggest that the left IPL is critical for both MF and ML imitation whereas posterior temporal regions may rather be critical for ML imitation.

1.3.2. Tool use

The use of an object is calling upon several representations, that is, manipulation knowledge, mechanical knowledge, and semantic knowledge. Nevertheless, several studies pointed out that manipulation and semantic knowledge were not sufficient to explain our ability to use tools (e.g., Baumard et al., 2019; Buxbaum et al., 2007), instead of mechanical knowledge that may play a critical role (Baumard et al., 2016; Goldenberg and Hagmann, 1998; Jarry et al., 2013; Lesourd et al., 2019, 2020; Osiurak et al., 2008). Semantic knowledge is mainly supported by the lateral pathway (Binder and Desai, 2011; Jefferies, 2013; Jefferies et al., 2020; Lesourd et al., 2021; Lesourd, Reynaud, et al., 2023; Ralph et al., 2017) whereas manipulation knowledge is relying upon both lateral and ventro-dorsal pathways (Buxbaum, 2017; Lesourd, Reynaud, et al., 2023) and mechanical knowledge is mainly supported by the ventro-dorsal pathway (IFG and SMG/PF; Federico et al., 2022; Reynaud et al., 2016).

The ventro-dorsal stream, more particularly the IPL and the SMG, has been strongly associated with tool use. Orban and Caruana (2014) proposed a specific action tool execution route connecting MT cluster (i.e., LOTC), MTGt (i.e., pMTG), IPL, aSMG, and premotor cortex, with a specific role of the aSMG, which compiles semantic information from the ventral stream and technical reasoning from the PF area (Osiurak et al., 2008, 2009, 2010, 2021; Osiurak and Badets, 2016; Reynaud et al., 2016, 2019). Other studies have stressed the role of SMG/PF in manipulation knowledge (Andres et al., 2013, 2017; Kleineberg et al., 2022; but see Lesourd et al., 2017 for an alternative explanation). In any case, a lesion occurring along the ventro-dorsal stream commonly leads to tool use impairment (Goldenberg and Spatt, 2009; Martin, Dressing, et al., 2016, 2016; Mengotti et al., 2013; Randerath et al., 2010; Salazar-López et al., 2016; Stoll et al., 2022). Finally, the IFG has been found to be involved in the selection of functional grasp (Randerath et al., 2010), and more generally in the successful of tool use (Finkel et al., 2018; Goldenberg and Spatt, 2009; Martin, Dressing, et al., 2016; Martin et al., 2015; Randerath et al., 2010; Salazar-López et al., 2016; Stoll et al., 2022).

Tool use has also been associated with the dorso-dorsal pathway. The

³ The ventral pathway encompasses the whole temporal lobe, and recent studies have pointed out the functional organization of the lateral temporal lobe (LOTc and pMTG) which can be dissociated with those of the ventral temporal lobe (fusiform gyrus; Wurm and Caramazza, 2022). While these distinctions appear to be of first importance, we will focus only on the lateral part (LOTc and pMTG), as the lesion overlap in VLSM studies did not include ventral part of the temporal lobe (see Section 4.4 for methodological considerations).

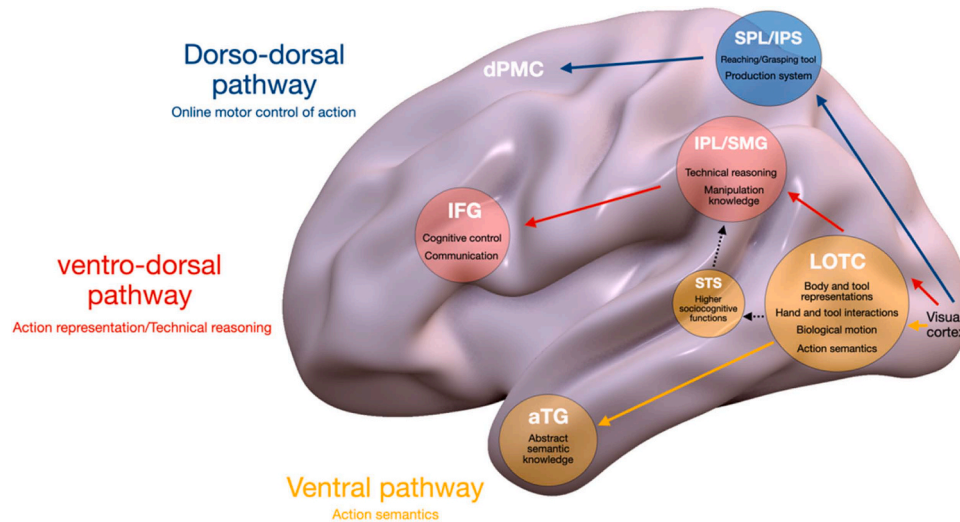


Fig. 2. The 3-pathway neurocognitive model of action. SPL/IPS = superior parietal lobe/intraparietal sulcus; IPL/SMG = inferior parietal lobe/supramarginal gyrus; IFG = inferior frontal gyrus; LOTC = lateral occipital temporal cortex; aTG = anterior temporal gyrus; STS: superior temporal sulcus; dPMC = dorsal premotor cortex.

dorsal part of the parietal lobe has been specifically associated with the egocentric relationship between the body and the object, and in particular the affordance of graspable tools (Buxbaum et al., 2006; Urban and Caruana, 2014; Osiurak, 2013; Osiurak et al., 2010; Randerath et al., 2010; Reynaud et al., 2016). This is in line with body schema capacity localized in SPL/IPS allowing to interact with presented tools. Several lesion mapping studies on tool use reported the involvement of SPL (Buxbaum et al., 2006; Goldenberg and Spatt, 2009; Martin et al., 2015; Randerath et al., 2010; Salazar-López et al., 2016) and superior angular gyrus/IPS (Martin et al., 2015; Randerath et al., 2010; Salazar-López et al., 2016), which suggests a crucial role of the dorso-dorsal route. This role is not just about grasping objects since dorsal regions are involved in isolated tool use execution, grasping excluded (Randerath et al., 2010), which suggest that these regions are not only necessary to reach and grasp a tool, but also to execute the action once the tool in hand.

Traditionally, the ventral pathway has been associated with semantic knowledge, but recent works have stressed its important role in action recognition and action semantics (i.e., LOTC; Buxbaum et al., 2014; Kaléline and Buxbaum, 2016; Lesourd, Afyouni, et al., 2023; Lingnau and Downing, 2015; Wurm et al., 2016, 2017; Wurm and Lingnau, 2015). For instance, lesion mapping studies have highlighted the importance of the LOTC, STG, pTG and aTG (Dovern et al., 2011; Martin, Dressing, et al., 2016; Martin et al., 2015; Salazar-López et al., 2016; Stoll et al., 2022), therefore suggesting a critical role of the ventral stream in tool use.

By focusing in more details on lesion mapping studies, we observed divergent results concerning brain regions required for tool use. While Goldenberg and Spatt (2009) highlighted that both the dorso-dorsal and ventro-dorsal pathways are necessary, other works underline also the importance of the ventral pathway (Dovern et al., 2011; Martin, Dressing, et al., 2016; Martin et al., 2015; Salazar-López et al., 2016). Taken together, these results challenge the critical role of the ventral pathways in tool use.

1.3.3. *Pantomime of tool use*

The pantomime task has been used for many years as a clinical assessment of tool use, with the advantage it does not require the presence of a real tool. It has long been assumed that this task is supported by the activation of gesture engrams, located in the left IPL within the ventro-dorsal stream (Buxbaum, 2001). Neuroimaging has largely confirmed the involvement of IPL in pantomime of tool use task (e.g., Choi et al., 2001; Fridman et al., 2006; Johnson-Frey et al., 2005;

Ohgami et al., 2004; for review see Osiurak et al., 2021). Recent studies have stressed the multidetermined cognitive processes engaged in pantomime, that is, manipulation knowledge, but also communication skills, working memory, and mechanical knowledge. Pantomime is considered by many authors to be a communicative gesture since the only ecological context in which pantomime is used is to transmit information, either to supplement or to replace speech (Finkel et al., 2018; Osiurak et al., 2021). Communicative skills are well known to be processed in IFG but also in temporal regions (Buxbaum et al., 2014; Finkel et al., 2018; Garcea et al., 2020; Osiurak et al., 2021; Tarhan et al., 2015; Weiss et al., 2016).

The dorso-dorsal stream has also been associated with pantomime because of its planning function production system supposed to rely upon the IPS/SPL (e.g., Choi et al., 2001; Fridman et al., 2006; Ohgami et al., 2004; for review see Osiurak et al., 2021). Although the dorso-dorsal stream appears to be identically involved in the motor control process for both pantomime and tool use, this stream was also found to be required for grasping an object. Thus, the absence of grasping during pantomime should result in distinct involvement of the dorso-dorsal stream, which may be more critical for tool use than for pantomime.

Like all meaningful actions, pantomime of tool use recruits semantic representations via the ventral stream. Neuroimaging and lesion mapping studies have shown the importance of semantic representations in pantomime (e.g., Lesourd et al., 2017, 2019), with the involvement of aTG, pTG, LOTC and STG (Buxbaum et al., 2014; Choi et al., 2001; Dressing et al., 2019, 2021; Finkel et al., 2018; Garcea et al., 2020; Hoeren et al., 2014; Johnson-Frey et al., 2005; Manuel et al., 2013; Martin, Nitschke, et al., 2016; Nobusako et al., 2018; Osiurak et al., 2021; Sperber et al., 2019; Tarhan et al., 2015; Watson and Buxbaum, 2015). One may notice that the ventral stream may also support manipulation knowledge mainly in the posterior part of the temporal lobe (LOTC; Buxbaum, 2017; Lesourd et al., 2021; Metzgar et al., 2022).

1.3.4. *Gesture understanding/recognition*

Many paradigms have been developed to explore the neurocognitive bases of gesture recognition or gesture understanding. In these tasks, participants have to make a judgement on a gesture (e.g., kinematics, hand posture, etc.). These kinds of tasks recruit the Action Observation Network, a bilateral brain network engaged during the observation of other's people action. The Action Observation Network encompasses various brain regions such as IFG, IPL, STG, pMTG, and occipito-temporal regions (for reviews see Caspers et al., 2010; Grosbras et al.,

2011; Urgesi et al., 2014). Thus, the Action Observation Network is relying upon ventral and ventro-dorsal streams. Neuroimaging and lesion mapping studies which focused on gesture recognition have confirmed the specific involvement of these two streams, and particularly IFG, IPL, and pMTG/LOTC (e.g., Akinina et al., 2019; Kalénine et al., 2010; Kalénine and Buxbaum, 2016; Lesourd, Afyouni, et al., 2023; Martin, Dressing, et al., 2016; for review see Urgesi et al., 2014). Interestingly, these brain regions are also involved in action production, suggesting similar engagement between understanding and production of gestures (for reviews see Reynaud et al., 2016, 2019). However, Tarhan et al. (2015) showed that action recognition was more affected by pMTG/LOTC lesions, while action production was more affected by IPL and IFG lesions. These results are slightly divergent from those obtained by Caspers et al. (2010), which found that bilateral pMTG, left IPL, and bilateral IFG were more activated in action observation compared to gesture imitation, whereas bilateral IFG, right VOTC, and right IPS were more engaged in the opposite contrast. Although these differences are currently poorly documented, we hypothesized that pMTG/LOTC regions are more critical for action recognition, while IPL appears to be more critical for action production. Finally, IFG appears to be engaged in gesture understanding as well as in action production.

1.4. Objectives and predictions

Many studies and reviews have shown the involvement of specific regions and their functional role in tasks assessing apraxia, but none of them have proposed to review the lesion mapping data on apraxic deficits (but see Urgesi et al., 2014). The aim of this work is to fill this gap by investigating the critical role of the 3 action brain streams in tasks traditionally used to assess apraxic deficits. To clarify and delineate the pathways required when producing and understanding actions successfully, we proposed here, a meta-analysis including data from VLSM studies on tool use, pantomime, imitation, and gesture understanding tasks published during the twenty past years. Based on previous research in neuroimaging and lesion mapping, we formulated the following hypotheses for each of these tasks.

Transitivity of the action has been explored through pantomime and tool use. We assumed a strong involvement of ventro-dorsal and ventral streams in these two tasks. Lesions of the dorso-dorsal stream were also expected to affect both tool use and pantomime, although we expected that tool use would be more affected than pantomime.

We considered imitation according to the meaning of the gesture. We assumed that both meaningful and meaningless imitation should be impacted by lesions occurring in dorso-dorsal and ventro-dorsal streams. Regarding the ventral stream, while we assumed its critical role for both tasks, we proposed that ML imitation would be affected by lesions more posterior (i.e., LOTC) than MF imitation.

Lastly, we predicted that both ventral and ventro-dorsal lesions would affect gesture understanding. Moreover, by comparing gesture understanding and action production, we supposed that lesions in the posterior parts of the lateral stream (i.e., LOTC) would be more likely to affect gesture understanding, while lesions in the IPL would be more associated with action production. The existing literature data did not allow us to formulate a precise hypothesis regarding a preferential disturbance following a lesion in the IFG.

2. Method

2.1. Literature search and selection

We performed a systematic search on the literature following the PRISMA Statement (Page et al., 2021). We followed a two-step method to identify studies of interest: citation searching and databases searching. In the first one, we explored publications from influent groups on apraxia (e.g., Freiburg group, Munich group, MRRI group, etc.) to find papers relevant to our meta-analysis. By this way, we identified 76

papers of interest, which allowed us to refine our searching criteria (see below), and therefore retaining 30 papers. Thus, we selected VLSM studies according to a series of selection criteria:

- (1) Reviews, single case studies, and group studies including less than 15 patients were excluded.
- (2) Studies using voxel-based lesion symptom mapping were included (Kimberg et al., 2007).
- (3) Only patients with left brain-damaged were considered.⁴
- (4) Studies had to investigate one of the four apraxia's tasks: familiar tool use, pantomime, imitation, or gesture understanding tasks.
- (5) Reports had to provide stereotaxic coordinates of lesion peaks or at least overlay lesion plots associated with selective disturbances

In a second step, we sought articles by databases searching. Three databases were used: Web of Science, PubMed, and ScienceDirect. The following keywords were used for production tasks: [“VLSM” OR “voxel-based lesion mapping” OR “voxel wise lesion mapping” OR “voxel lesion symptom mapping”) AND (“Tool use” OR “Pantomime” OR “Imitation” OR “Apraxia” OR “Gesture”)], and the following keywords were used for gesture understanding tasks: [“VLSM” OR “voxel-based lesion mapping” OR “voxel wise lesion mapping” OR “voxel lesion symptom mapping”) AND (“Gesture understanding” OR “Action comprehension” OR “Action perception” OR “Gesture understanding” OR “Gesture comprehension”). These searches resulted in 3994 papers with a last update on 6th December 2022. A first evaluation of these articles was performed by screening title and summary leading to the exclusion of 3872 studies. Of the remaining 129 papers, 32 were finally included in the meta-analyses after detailing screening (see screening criteria above). For a more detailed overview of the selection, see the PRISMA flow diagram (Fig. 3). Tables detailing the literature review step by step are available at <https://osf.io/phwv3/>.

By gathering the 30 papers identified by citations searching, and the 32 papers selected by databases searching, a total of 35 articles were obtained (Table 2). These papers were classified according to the type of tasks reported: 10 studies for the tool use task (Table A1), 16 studies for the pantomime of tool use task (Table A2), 16 studies for the imitation task (Table A3), and 10 studies for the gesture understanding tasks (Table A4). Multiple sub-classifications were used, sorting papers by: (1) transitivity of the action (2) meaning of the action (3) presentation modality (4) body part used for imitation (for more details, see Tables A1-A4). As one study may have used one or several tasks, an overview of the distribution of tasks in the studies examined in the current meta-analysis is provided in supplementary Table S1.

2.2. Data extraction

VLSM studies aim at providing statistical associations between lesions and behavior. These lesions are traditionally presented in stereotaxic coordinates (x, y, z), or as statistical lesion plots. In the first case, we collected directly lesions coordinates of each cluster associated with the task of interest. These coordinates may be the center of mass or activation peak of the cluster, depending of the study. In the second case, when statistical tables were not provided in the original study, we extracted the coordinates directly from available statistical lesion plots. To do so, we used a method described in previous reviews on apraxia (Lesourd et al., 2018; Osiurak et al., 2021; for a similar procedure, see also Niessen et al., 2014). First, from the lesion sites depicted in the overlay plots, we identified the maximum lesion overlap locations for each slice reported. Second, we projected these maximum lesion centers onto the corresponding slice of a MNI standard template brain (Ch2better) provided by MRICron to obtain the corresponding

⁴ Although our first aim was to consider both RBD and LBD patients, we finally focused on LBD patients due to the lack of data for RBD patients.

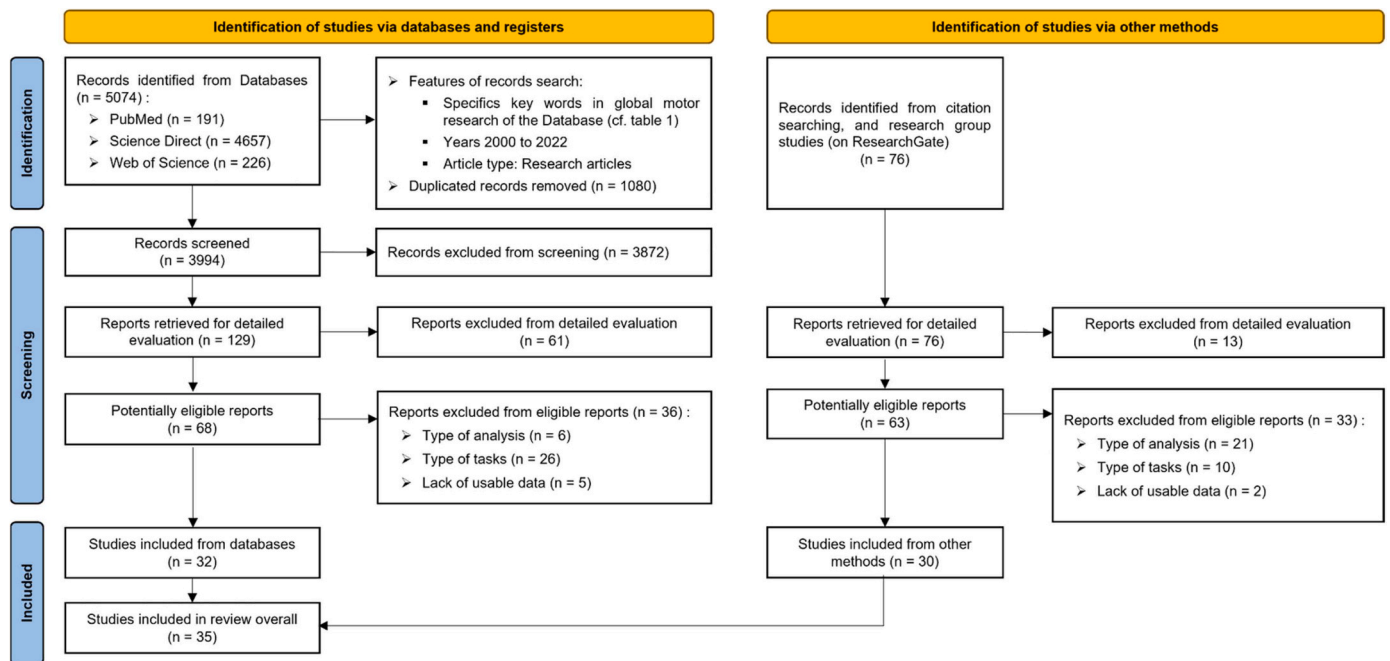


Fig. 3. PRISMA flow diagram for the systematic review of the literature on apraxic tasks (Page et al., 2021). For more details on the different stages of paper inclusion, see the literature review tables available at <https://osf.io/phwv3/>.

Table 2

List of the 35 studies included in the meta-analysis. Papers are sorted by tasks, the same article may appear for several tasks (for more details, see Tables A1, A2, A3 and A4).

Tool use	Pantomime	Imitation	Gesture understanding
Bi et al. (2015)	Achilles et al. (2017)	Buxbaum et al. (2014)	Akinina et al. (2019)
Dovern et al. (2011)	Achilles et al. (2019)	Dovern et al. (2011)	Binder et al. (2017)
Goldenberg and Spatt (2009)	Binder et al. (2017)	Dressing et al. (2019)	Göksun et al. (2015)
Martin et al. (2015)	Buxbaum et al. (2014)	Dressing et al. (2021)	Kalénine et al. (2010)
Martin, Dressing et al. (2016)	Dovern et al. (2011)	Finkel et al. (2018)	Kalénine et al. (2013)
Martin, Nitschke et al. (2016)	Dressing et al. (2018)	Garcea et al. (2020)	Martin, Dressing et al. (2016)
Mengotti et al. (2013)	Dressing et al. (2019)	Goldenberg and Randerath (2015)	Pazzaglia, Smania et al. (2008)
Randerath et al. (2010)	Dressing et al. (2021)	Hoeren et al. (2014)	Pazzaglia, Pizzamiglio et al. (2008)
Salazar-López et al. (2016)	Goldenberg and Randerath (2015)	Manuel et al. (2013)	Pizzamiglio et al. (2019)
Stoll et al. (2022)	Hoeren et al. (2014)	Martin, Nitschke et al. (2016)	Tarhan et al. (2015)
	Martin, Nitschke et al. (2016)	Nobusako et al. (2018)	
	Mengotti et al. (2013)	Pizzamiglio et al. (2019)	
	Nobusako et al. (2018)	Sperber et al. (2019)	
	Pizzamiglio et al. (2019)	Tarhan et al. (2015)	
	Randerath et al. (2018)	Watson and Buxbaum (2015)	
	Stoll et al. (2022)	Weiss et al. (2016)	

coordinates (<https://www.nitrc.org/projects/mricron>). All peak voxel coordinates were either collected or transformed in MNI space. Indeed, if the study reported Talairach coordinates, they were first converted to MNI space using icbm2tal transformation (Lacadie et al., 2008) implemented in a webapp (<https://bioimagesuiteweb.github.io/webapp/mni2tal.html>). The data has been extracted by two researchers, one familiar and one novice with the field. Analyses were performed on both sets of data, and as there was no major difference between the two analyses, we arbitrarily chose to keep one of them. Coordinates retained for each paper can be consulted in supplementary GingerALE data files available at <https://osf.io/phwv3/>. Papers sharing the same participants were considered as a same single experiment to avoid over-interpretation of their results.

2.3. Data analysis

Initially, we planned to use NeuROI software (<https://www.nottingham.ac.uk/research/groups/clinicalneurology/neuroi.aspx>; Tench et al., 2014), which allows to conduct coordinate based random effect size (CBRES; Tench et al., 2017) meta-analysis. However, as effect sizes were not available for about half of the studies selected in the present study,⁵ we conducted our analyses with GingerALE 3.0.2 (<http://www.brainmap.org/ale/>). Activation Likelihood Estimation (ALE) is a voxel-based method that highlights brain regions of significance by pooling coordinates from several neuroimaging experiments (Eickhoff et al., 2009, 2011, 2012; Turkeltaub et al., 2012). Although this method was initially developed for neuroimaging data, ALE algorithm can also be applied with anatomic data such as VBM (DeRamus and Kana, 2015) or more recently with VLSM (Piai and Eikelboom, 2023; Urgesi et al., 2014). In this case, Anatomic likelihood estimation (AnLE; Glahn et al., 2008) pools coordinates of lesion peaks to reveal brain regions that are reliably lesioned across studies. To perform this meta-analysis,

⁵ In case the effect size of the coordinates was not reported, Neuroi software proposes to provide an effect size at Z=1. Using this setting, we found that all the clusters revealed by the analysis were driven by studies that provided real effect sizes.

coordinates of every significant lesion peak for each considered study were collected. The AnLE approach models the anatomical foci from different published reports as Gaussian probability density distribution at a given coordinate and calculates the Modeled Anatomic maps (i.e., the 3D images of each foci group) based on the maximum across each focus's Gaussian. Then, an experimental AnLE map is created from the voxel-wise union of all Modeled Anatomic maps. Differentiation of true concurrence of foci versus random spatial association is performed by testing the experimental AnLE map against AnLE null distribution maps that are generated utilizing a permutation test of randomly generated foci. All foci from a generic contrast are pooled together and the resulting non-parametric p-values are then thresholded at a cluster-level family-wise error (FWE) correction of $p < .05$, with a cluster forming threshold at $p < .001$ and a minimum extent volume of 200 mm^3 . For visualisation, thresholded AnLE maps were mapped on a standardized anatomical MNI-normalized template (Ch2better) using the MRICroGL software (<https://www.nitrc.org/projects/mricrogl/>).

Contrast analyses were conducted and consisted in subtracting two AnLE corrected maps to obtain a z-score contrasted map. GingerALE creates simulated null data to correct for unequal sample sizes by pooling foci and randomly dividing the foci into two groupings that are equal in size to the original data sets. One simulation dataset is subtracted from the other and compared to the true data. This subtraction produces voxel-wise p-value images that show where the true data sit in relation to the distribution of values within that voxel. The p-value images are converted to z-scores. The contrast analysis was then performed on these maps and the results were reported with a p-value threshold set at 0.05 obtained from 10,000 permutations and minimum cluster size set to 50 mm^3 . In addition to contrast analysis, GingerALE offers conjunction analysis by generating a conjunctive ALE map, which combines voxel-wise minimum values from two thresholded ALE maps. This ALE map highlights common voxel clusters shared between the two datasets. We restricted our analysis to clusters larger than 50 mm^3 in size. Significant clusters were overlaid onto a standard brain MNI space and the thresholded z-score maps were visualized on a MNI template provided with MRICroGL (Ch2better).

All analyses performed with GingerALE can be consulted at <https://osf.io/phwv3/>.

3. Results

The following results were obtained in the form of AnLE maps showing lesioned clusters which passed the FWE correction at $p < .05$. Considering that the studies selected from the present meta-analysis only involved left brain-damaged patients, the results involve exclusively lesion clusters located in the left hemisphere. Brain clusters obtained were mapped using MRICroGL (for more details about clusters characteristics, see [Supplementary Tables S6-S12](#)), and labelled with the AAL brain atlas. We noticed that the use of this parcellation can lead to some confusions since some brain regions can be considered part of two different brain streams, for example the angular gyrus, as well as the IPS can be classified in the ventro-dorsal stream for their inferior part, or in the dorso-dorsal stream for their superior part.

3.1. Tool use

AnLE analysis has been conducted on novel tool use and familiar tool use tasks. Other analyses were carried out by separating the familiar tool use depending on whether the tool was used alone (i.e., single tool use) or with the typical recipient (i.e., real tool use). However, due to the lack of available data, only analyses of familiar tool use are presented (for more details about novel, real, and single tool use analyses, see [Supplementary Table S2](#) and [Figure S1](#)). VLSM coordinates of 10 studies on familiar tool use have been collected ([Table A1](#)), regrouping 509 different patients and 158 brain foci. This analysis revealed 4 lesion clusters associated with a deficit of familiar tool use. The brain regions

involved in these clusters were: IFG (triangular, opercular), STG, Heschl gyrus, insula, rolandic operculum, SMG, IPL, postcentral gyrus, and angular gyrus ([Table 3](#) and [Fig. 4a](#)). By looking uncorrected AnLE map thresholded at $p < .001$ we found a 5th cluster located in SPL.

3.2. Pantomime of tool use

Two conditions for the pantomime task were considered, depending on the presentation modality:

- (1) Visual pantomime (i.e., pantomime performed on visual command or on simultaneous visual and verbal command). AnLE analysis has been conducted on 13 VLSM studies ([Table A2](#)) regrouping 688 different patients and 263 brain foci. Results showed 5 lesion clusters associated with visual pantomime impairment, including STG, postcentral gyrus, SMG, IPL, angular gyrus, occipital middle gyrus, MTG, and Heschl gyrus ([Table 3](#) and [Fig. 4b](#)).
- (2) Verbal pantomime (i.e., pantomime performed on verbal command exclusively). AnLE analysis has been conducted on 3 VLSM studies ([Table A2](#)) regrouping 272 different patients and 47 brain foci. Only 1 lesion cluster located in IFG opercular has been linked to a deficit in verbal pantomime ([Table 3](#) and [Fig. 4b](#)).

3.3. Imitation

Imitation tasks have been explored across several factors, i.e., meaning, transitivity, and body part used to reproduce the gesture ([Table A3](#)). However, due to the lack of data, we focused our analyses on the meaning of gestures (for more details about transitivity and body part analyses, see [Supplementary Tables S3-S4](#) and [Figures S2-S3](#)).

- (1) Meaningful imitation (transitive and intransitive). AnLE analysis regrouped 7 VLSM studies, 699 patients, and 141 foci. AnLE map showed 5 lesion clusters associated with a deficit in MF imitation, located in SMG, IPL, STG, postcentral gyrus, insula, and MTG posterior ([Table 4](#) and [Fig. 5a](#)).
- (2) Meaningless imitation. AnLE analysis regrouped 11 VLSM studies, 921 different patients, and 271 foci. AnLE map showed 2 lesion clusters associated with ML imitation, located in the MTG

Table 3
Cerebral lesion clusters associated with a deficit in familiar tool use and pantomime.

Brain regions (AAL)	X	Y	Z	Volume (mm ³)
Familiar tool use				
Insula, Rolandic operculum, STG, Heschl gyrus, IPL, AIP	-39	-28	20	5304
SMG, aSMG/PfT, Postcentral gyrus	-57	-25	30	1840
IFG (opercularis, triangularis)	-41	19	28	1240
Angular gyrus	-42	-67	44	696
Visual pantomime				
IPL, SMG, STG, Postcentral gyrus, MTG	-52	-30	29	9480
STG, Heschl gyrus	-38	-31	7	3472
Angular gyrus, Occipital middle gyrus	-33	-64	27	896
STG	-56	-9	4	864
Verbal pantomime				
IFG opercularis	-51	17	17	592

MNI coordinates and volume (mm³) of lesion clusters obtained from ALE analyses

Abbreviations: MTG=Middle temporal gyrus; STG=Superior temporal gyrus; SMG=Supramarginal gyrus; aSMG = anterior supramarginal gyrus; AIP = anterior intraparietal area; PfT = area PfT; LOTC=Lateral occipito-temporal gyrus; IPL=Inferior parietal lobe; IFG=Inferior frontal gyrus, MFG=Middle frontal gyrus

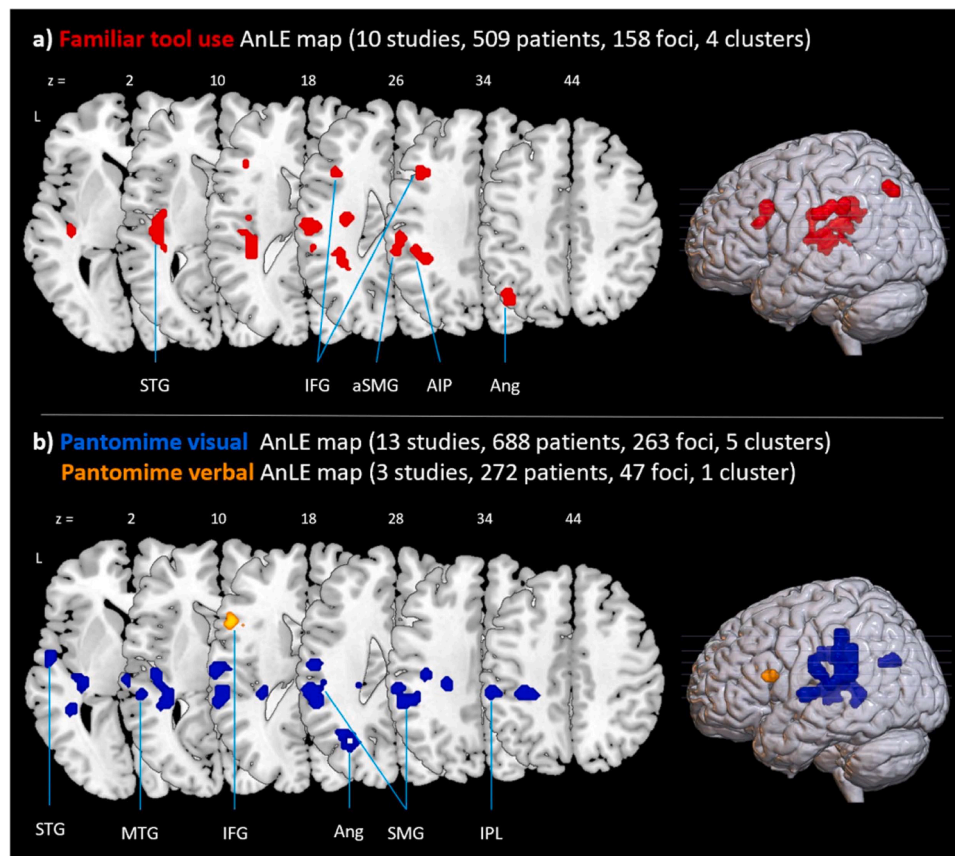


Fig. 4. Neural lesions associated with deficits in familiar tool use and pantomime of tool use. AnLE statistical maps were FWE corrected ($p < .05$) and represented on the MNI standard template Ch2better provided in MRICroGL software. STG = superior temporal gyrus; IFG = inferior frontal gyrus; SMG = supramarginal gyrus; aSMG = anterior supramarginal gyrus; AIP = anterior intraparietal area; Ang = angular gyrus; MTG = middle temporal gyrus; IPL = inferior parietal lobe.

Table 4
Cerebral lesion clusters associated with a deficit in meaningful and meaningless imitation.

Brain regions (AAL)	X	Y	Z	Volume (mm ³)
Meaningful imitation				
SMG, IPL, STG, Postcentral gyrus	-57	-24	30	8144
STG, Insula	-38	-39	20	3400
Postcentral gyrus	-40	-15	34	1400
SMG	-57	-44	29	1000
MTG	-66	-32	4	632
Meaningless imitation				
pMTG, Angular gyrus, SMG, IPL, Postcentral gyrus, Occipital middle gyrus, LOTC	-43	-48	27	16784
Postcentral gyrus	-49	-11	34	1112

MNI coordinates and volume (mm³) of lesion clusters obtained from ALE analyses

Abbreviations: MTG=Middle temporal gyrus; STG=Superior temporal gyrus; SMG=Supramarginal gyrus; LOTC=Lateral occipito-temporal gyrus; IPL=Inferior parietal lobe; IFG=Inferior frontal gyrus, MFG=Middle frontal gyrus

posterior, occipital middle gyrus, angular gyrus, SMG, post-central gyrus, and IPL (Table 4 and Fig. 5b).

3.4. Gesture understanding and action production

Gesture understanding. AnLE analysis has been carried out on 10 VLSM studies regrouping 621 subjects and 236 foci (Table A4). Results showed 6 lesion clusters associated with gesture understanding including IFG (triangularis, opercularis, orbital), MFG, insula, rolandic

operculum, precentral gyrus, MTG posterior, STG, angular gyrus, SMG, and IPL (Table 5 and Fig. 6a).

Action production condition has been studied by regrouping every meaningful production tasks of the meta-analysis (i.e., familiar tool use, pantomime, and MF imitation tasks). AnLE has been conducted with 28 VLSM studies (Tables A1-A3) regrouping 1596 different patients and 623 brain foci. Results showed 5 lesion clusters including IFG (triangularis, opercularis), MFG, SMG, IPL, angular gyrus, MFG, insula, STG, MTG, postcentral gyrus, precentral gyrus, rolandic operculum, occipital middle gyrus, and temporal pole (Table 5 and Fig. 6b).

A contrast analysis has been performed between gesture understanding AnLE map and action production AnLE map regrouping every meaningful production tasks of the meta-analysis (i.e. familiar tool use, pantomime, and MF imitation tasks; See Tables A1-A3). Results showed 4 lesion clusters affecting more gesture understanding than action production, these clusters were located IFG (opercularis, triangularis, orbital), MFG, precentral gyrus, insula, rolandic operculum, and MTG posterior (Table 5 and Fig. 6c). On the other hand, 7 lesions clusters were found to be more associated with action production compared to gesture understanding, these clusters were located in IPL, SMG, STG, postcentral gyrus, precentral gyrus, and rolandic operculum (Table 5 and Fig. 6c).

Finally, a conjunction analysis has been performed between gesture understanding AnLE map and MF action production AnLE map (i.e., familiar tool use, pantomime of tool use, and MF imitation tasks; See Tables A1-A3). Results revealed 7 lesion clusters which commonly affect understanding and production tasks, these clusters are located in IFG (pars opercularis and pars triangularis), SMG, STG, IPL, precentral gyrus, Insula, rolandic operculum, and Heschl gyrus (Table 5 and Fig. 6d).

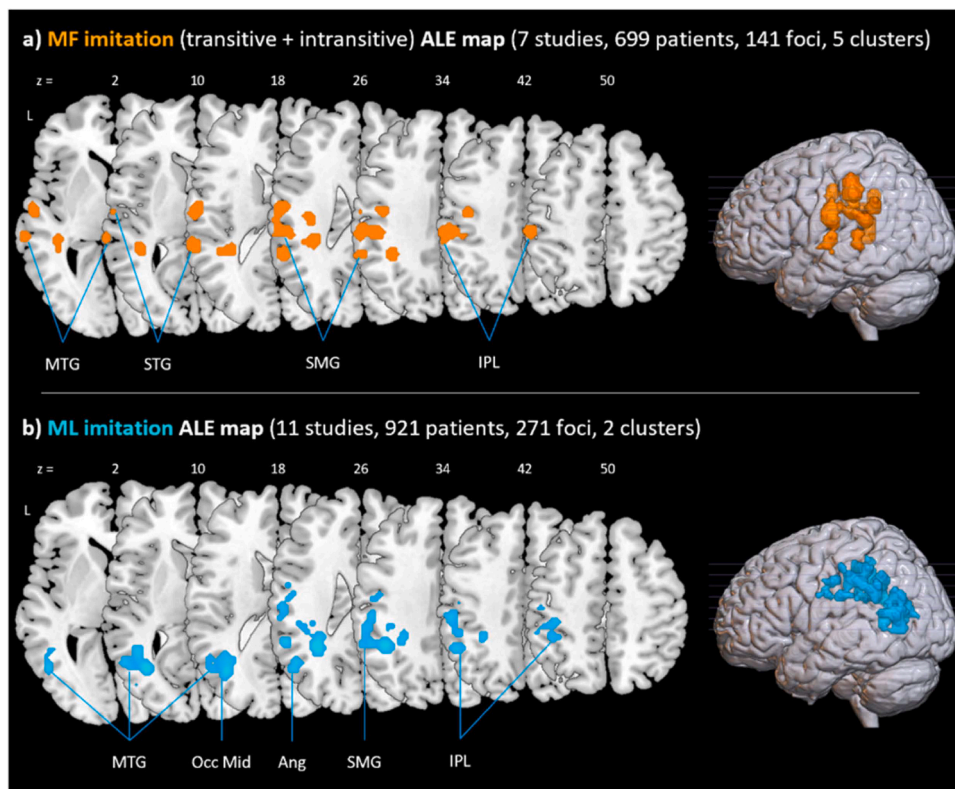


Fig. 5. Neural lesions associated with deficits in imitation of meaningful and meaningless gestures. AnLE statistical maps were FWE corrected ($p < .05$) and represented on the MNI standard template Ch2better provided in MRICroGL software. STG = superior temporal gyrus; SMG = supramarginal gyrus; Ang = angular gyrus; MTG = middle temporal gyrus; IPL = inferior parietal lobe, Occ Mid = occipital middle gyrus.

4. Discussion

In this meta-analysis, we proposed a synthesis of lesion mapping data applied to the main tasks assessing limb apraxia in order to determine the critical role of several brain regions disseminated across the 3 action streams. We identified 35 papers using VLSM on tool use tasks, pantomime, imitation, and gesture understanding tasks. Our AnLE analysis highlighted that deficits in tool use task have been associated with lesions of the ventro-dorsal and the dorso-dorsal, while deficits in pantomime were associated with lesions of the ventro-dorsal and the ventral streams. Lesions associated with an impairment in imitation task depend on the meaning of the gesture, although both MF and ML imitation was affected by lesions in ventro-dorsal and ventral streams, ML imitation was more affected by lesions in the posterior part of the lateral stream (i.e., LOTC) than MF imitation. Finally, deficits in action understanding and action production have been associated with ventro-dorsal pathway, and particularly IFG and IPL, as well as ventral pathway. Moreover, we found that lesions in the posterior part of the ventral stream and in the IFG impaired more action understanding while lesions in the IPL impaired more action production. We will now discuss these results in turn.

4.1. Tool use is more dorsal than pantomime of tool use

By investigating the involvement of the ventro-dorsal stream in pantomime and tool use tasks, we found that this stream was critical for both tasks. In a recent meta-analysis, Osiurak et al. (2021) found similar involvement of the ventro-dorsal stream and highlighted the key role of the SMG/PF area for both pantomime and tool use tasks. According to the reasoning-based approach (Osiurak and Badets, 2016), this brain area is known to support technical reasoning (Federico et al., 2022; Reynaud et al., 2016), therefore, we can assume that both tasks are supported by this ability to understand the physical interactions of

objects with the physical world (Lesourd et al., 2019; Lesourd, Osiurak, et al., 2017). The involvement of the ventro-dorsal stream in pantomime and tool use is also consistent with the manipulation-based approach (Buxbaum, 2001, 2017), which suggests that information about how to manipulate tools is stored in left IPL (Buxbaum, 2001; Buxbaum et al., 2007; Buxbaum, Johnson-Frey, et al., 2005; Haaland et al., 2000; van Elk et al., 2014). Another region of SMG, aSMG/PfT has been proposed by Orban and Curuana (2014) to occupy a central role in information integration within left IPL, as it receives information from SMG/PF area, IPS and ventral stream (see also Reynaud et al., 2016). We suppose that this integrative area aSMG/PfT for tool use could be useful in both pantomime, and tool use tasks, as these tasks both require the integration of several kinds of representations. Finally, ventral part of the angular gyrus has been found to be critical for pantomime, this area has been described to support body representations (Osiurak et al., 2021).

While we found that IFG was critical for tool use, and pantomime of tool use on verbal command, this was not the case for pantomime on visual command, suggesting a differential role of IFG in pantomiming the use of tools. Randerath et al. (2010) found this region to be critical for the selection of functional grasp in tool use, which could explain why we found IFG lesions leading to tool use deficit. This frontal area has also been associated with the communicative aspect of action (Finkel et al., 2018; Goldenberg, 2017), as it includes Broca's area, a key region for language. Since the ecological function of pantomime is to communicate how to use a tool, this gesture should involve IFG in both conditions. Our results are at odds with this hypothesis, as the critical involvement of IFG in pantomime may rather depend on the modality of execution of this kind of gesture, than its communicative aspect *per se*. However, when looking at uncorrected analyses for pantomime on visual presentation, we found a lesion cluster in left IFG. Although we do not consider this analysis to be sufficient to prove that IFG is critical to pantomime on visual presentation, we cannot rule out this possibility. Taken together, these data suggest that the left IFG seems to be more critical when the

Table 5

Cerebral lesion clusters associated with a deficit in gesture understanding and action production.

Brain regions (AAL)	X	Y	Z	Volume (mm3)
Gesture understanding				
MFG, IFG (opercularis, triangularis), Precentral gyrus, Insula, Rolandic operculum	-49	12	22	7128
IFG (opercularis, triangularis, orbital), Insula, Precentral gyrus	-34	18	17	6080
IPL, SMG, STG	-53	-36	33	4192
pMTG, LOTC	-56	-47	4	1808
Insula, Rolandic operculum	-37	-19	15	1336
pMTG, LOTC, Angular gyrus	-46	-66	18	1096
Action Production				
STG, MTG, Insula, Postcentral gyrus, Rolandic operculum, SMG, Angular gyrus, Occipital middle gyrus, IPL, Precentral gyrus	-47	-30	26	47672
IFG (triangularis, opercularis), MFG, Insula, Rolandic operculum, Precentral gyrus	-39	14	24	9656
STG, Temporal Pole, Rolandic operculum	-56	5	-4	1064
Insula, Temporal Pole	-36	5	-10	968
IFG triangularis, Insula	-39	31	5	856
Contrast analysis: Gesture understanding > Action Production				
IFG (opercularis, triangularis, orbital), Insula	-35	18	13	2480
MFG, IFG (opercularis, triangularis), Precentral gyrus	-51	15	34	1808
IFG opercularis, Precentral gyrus, Rolandic operculum, Insula	-48	7	11	920
MTG, LOTC	-54	-48	10	528
Contrast analysis: Action production MF > Gesture understanding				
STG, Rolandic operculum	-37	-31	13	560
SMG, Postcentral gyrus	-49	-26	28	536
Postcentral gyrus, IPL	-31	-34	45	368
Precentral gyrus	-38	-8	49	352
Postcentral gyrus	-64	-15	21	248
IPL	-39	-36	38	88
STG	-63	-38	21	56
Conjunction analysis: Action production MF = Gesture understanding				
SMG, STG, IPL	-54	-35	34	3352
IFG (triangularis, opercularis), Insula	-32	20	20	1176
IFG (triangularis, opercularis), Rolandic operculum, Precentral gyrus, MFG	-48	15	22	936
Insula, Heschl gyrus, STG	-40	-17	7	496
Precentral gyrus	-35	2	34	312
Rolandic operculum, Insula	-38	-27	22	88
Rolandic operculum, Insula	-38	-19	23	88

MNI coordinates and volume (mm³) of lesion clusters obtained from Gesture understanding ALE analyses, and from contrasts between gesture understanding and action production meaningful

Abbreviations: MTG=Middle temporal gyrus; STG=Superior temporal gyrus; SMG=Supramarginal gyrus; LOTC=Lateral occipito-temporal gyrus; IPL=Inferior parietal lobe; IFG=Inferior frontal gyrus, MFG=Middle frontal gyrus

object to be pantomimed is presented verbally (e.g., "Show me how to use a hammer") than visually (e.g., picture of hammer).

Our results showed a critical involvement of the dorso-dorsal stream in tool use but not in pantomime of tool use. We found that tool use was affected by a lesion cluster in the dorsal part of the angular gyrus, and when looking at the tool use uncorrected analyses, we also found a lesion cluster in SPL. The dorso-dorsal stream is known to be involved in tool grasping (Buxbaum et al., 2006; Orban and Caruana, 2014; Osiurak, 2013; Osiurak et al., 2010; Randerath et al., 2010; Reynaud et al., 2016), this ability could be important when using a tool, but less for pantomiming the use of tool, as it does not require to grasp and hold a real tool in hand. Although the dorso-dorsal involvement during a pantomime has been associated with planning function and on-line control of motor actions (for review see Osiurak et al., 2021), our results suggest that pantomime use may not critically rely upon these

abilities.

Finally, we found the ventral stream to be critical for pantomime but not for tool use. These results are in line with the literature on apraxia of tool use which showed that if semantic knowledge represents an advantage in using tools (Lesourd, Osiurak, et al., 2017; Osiurak, 2014), it is neither sufficient nor necessary to use tools (Baumard et al., 2019; Bozeat et al., 2002; Buxbaum et al., 1997; Hodges et al., 2000). We suppose that technical reasoning could compensate the lack of semantic information concerning the action to produce (Goldenberg, 2014; Goldenberg and Hagmann, 1998), notably because holding the tool, and the presence of the contextual recipient can provide cues on how it could be used (Goldenberg and Spatt, 2009). Concerning pantomime, the ventral stream may be important as it includes semantic knowledge about tools but also manipulation knowledge (Lesourd, Reynaud, et al., 2023; for a review see Lesourd et al., 2021), which are both involved in this kind of gesture (Lesourd et al., 2019).

4.2. Imitation and ventral stream: a matter of meaning

We found that the ventro-dorsal pathway is critical for both MF imitation (86% of the studies) and ML imitation (91% of the studies), confirming its major role in imitation, whatever the meaning of gestures. This result is consistent with neuroimaging data (for review see Caspers et al., 2010) and lesion mapping studies (e.g., Buxbaum et al., 2014; Dressing et al., 2018; Hoeren et al., 2014; Mengotti et al., 2013; Tessari et al., 2021; for review see Lesourd et al., 2018). Furthermore, a cTBS study conducted by Vanbellingen et al. (2014) demonstrated that stimulation of the IPL leads to a deficit in both MF and ML imitation, supporting the critical role of this brain area in this task. These data are at odds with the manipulation knowledge theory, which assumes that the left IPL contains aspects of known gestures only (Buxbaum, 2001; Buxbaum et al., 2007; Buxbaum and Saffran, 2000; Goldenberg, 2014; Gonzalez Rothi et al., 1991; Haaland et al., 2000; Osiurak et al., 2021; van Elk et al., 2014).

Our results showed that the ventral stream was involved in both MF and ML imitation tasks. By looking more precisely at the posterior ventral stream, we found an interesting dissociation: ML imitation was affected by more posterior lesions than MF imitation. This result is supported by a complementary AnLE analysis carried out by combining pantomime of tool use task and MF imitation task, to obtain a meaningful gestures condition (Supplementary Figure S4 and Table S5). This analysis showed that these meaningful gestures are sustained by more anterior part of the ventral stream compared to the ML imitation task. This dissociation is in line with a PET study in which Rumiati et al. (2005) highlighted that anterior part of the ventral stream can be associated with MF imitation while the posterior part of the ventral networks can be associated with ML imitation. Therefore, this dissociation suggests that the meaning of action could be processed in the LOTC. More recently, Wurm and Caramazza (2022) proposed a functional gradient in the LOTC, with the posterior LOTC (pLOTC) more specifically involved in concrete/perceptual processes, whereas the anterior LOTC (aLOTC) being more specifically involved in abstract/conceptual processes (Wurm et al., 2017; for review see Wurm and Caramazza, 2022). Taken together, these data indicate the existence of an antero-posterior gradient of the semantic processing in the LOTC, with MF gestures being processed in the anterior part of the LOTC, and ML gestures in the posterior part of the LOTC (Fig. 7). Beyond their semantic characteristics, MF gestures are also considered as expressive or communicative gestures (Bartolo et al., 2019; Ham et al., 2010). Consequently, the processing of these gestures may require the involvement of brain regions associated with social cognition. In the present study, we observed that lesions affecting MF gestures encompass the aLOTC/pSTS region, which is known for its involvement in the processing of dynamic social cues. These findings reinforce the established role of the dorsal LOTC in processing social stimuli, as previously described in several fMRI studies (Lesourd, Afyouni, et al., 2023; Wurm

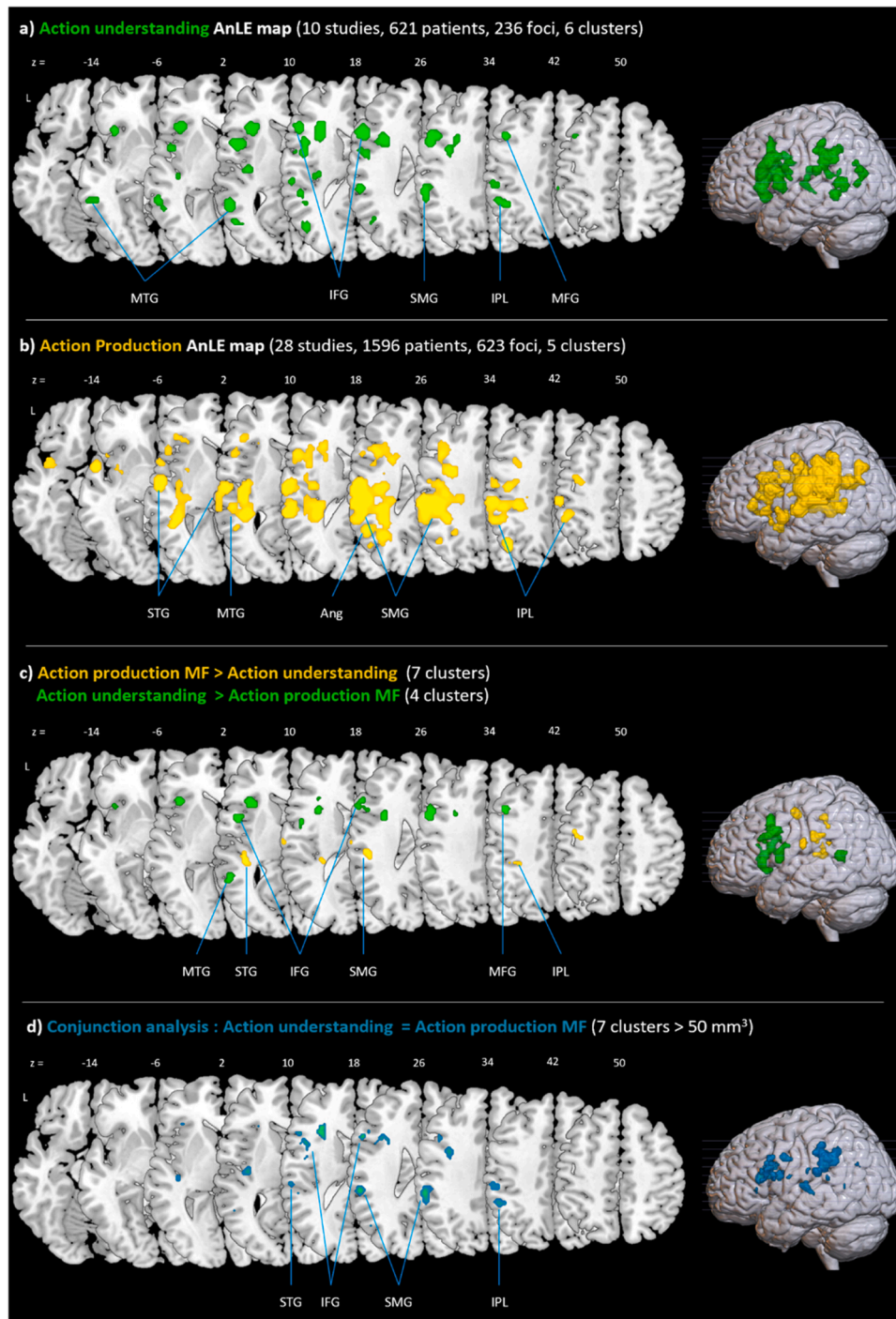


Fig. 6. Neural lesions associated with deficits in gesture understanding and gesture production. For (a) and (b), AnLE statistical maps were FWE corrected ($p < .05$). For (c), contrast analyses have been performed between gesture understanding AnLE map and action production AnLE map, contrasted maps have been obtained from 10,000 permutations, and thresholded at $p < .05$. For (d), a conjunction analysis between the action production and action understanding AnLE maps has been performed to highlight common voxel clusters shared between the two datasets. Results are represented on the MNI standard template Ch2better provided in MRlcroGL software. STG = superior temporal gyrus; IFG = inferior frontal gyrus; SMG = supramarginal gyrus; Ang = angular gyrus; MTG = middle temporal gyrus; IPL = inferior parietal lobe; MFG = middle frontal gyrus.

et al., 2017; Wurm and Caramazza, 2019).

The LOTC is a high-level visual area well known to extract visual characteristics of gestures such as body part, body orientation and action directedness (for review see Lingnau and Downing, 2015; Wurm and Caramazza, 2022). Since LOTC has been found to be a key region in action observation (Urgesi et al., 2014), it is easy to think that this region may be essentially involved in perceptual part of gesture processing.

However, in a fMRI study, Molenberghs et al. (2010) showed higher activation of the LOTC during imitation task compared to action observation task. Thus, the LOTC is thought to play a crucial role in perceiving gestures with the intention to imitate them, but not in their production (Vry et al., 2015). Concerning IPL, its posterior part was found to be involved in the preparation of the action and its anterior part (aSMG) in the execution of the action (Vry et al., 2015). Thus, one may

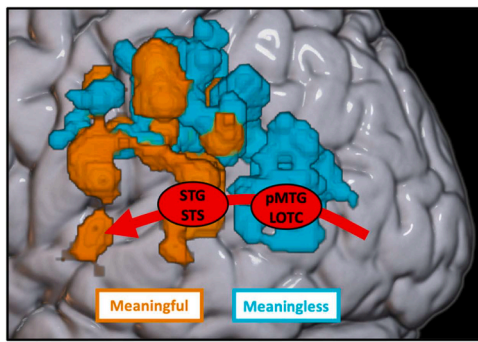


Fig. 7. Anterior-posterior gradient of the meaning of gestures in the posterior temporal lobe. In blue: neural lesions associated with deficit in ML imitation; and in orange: neural lesions associated with deficit in MF gestures. STG = superior temporal gyrus; STS = superior temporal sulcus, pMTG = posterior middle temporal gyrus; LOTC = lateral occipital temporal cortex.

suppose that the decoding of visual information and activation of sensory-motor knowledge would be carried out within posterior LOTC and IPL, respectively, and finally being integrated in aSMG before being transferred to the motor cortex. Further studies are required to explore the dynamical interplay between LOTC and IPL during gesture imitation and gesture understanding.

Although we expected a specific involvement of the dorso-dorsal stream in ML imitation, we did not identify a critical role for this stream in either MF imitation (0% of the studies) or ML imitation (27% of the studies). This finding is at odds with neuroimaging data from healthy subjects which reported a strong involvement of the SPL in ML imitation compared with MF imitation (Peigneux et al., 2004; Rumiati et al., 2005) as well as in lesion studies (e.g., Hoeren et al., 2014). Our analyses concluded that dorso-dorsal pathway does not constitute a critical component of the direct route, therefore challenging the idea that the direct route is underpinned by the dorso-dorsal stream (e.g., 2AS+ model; Buxbaum, 2017). However, this stream has been described to underlain sensory-motor representations of body parts allowing to guide actions online (de Vignemont, 2010; Schwöbel and Coslett, 2005). Thus, our results suggest that (1) this capacity is not necessary in an imitation task, or (2) this capacity can be supported by other brain regions in case of brain injury. We noticed that lesions of the anterior IPS were associated with a deficit in ML imitation, however this part of the IPS is difficult to categorize as it is part of the ventro-dorsal or the dorso-dorsal pathway. An alternative explanation of this unexpected result is that VLSM studies underestimate the involvement of dorsal regions, as middle cerebral artery, traditionally considered in this kind of studies, does not irrigate the dorsal part of parietal regions (for methodological limitations see Section 4.4).

4.3. Understanding and producing: role of ventral and ventro-dorsal streams

Our results showed that LOTC and MTG lesions were associated with a deficit in gesture understanding, suggesting a critical role of the ventral stream. This ventral involvement makes sense given the nature of the understanding tasks, as these tasks required semantic knowledge to be performed successfully. Moreover, the ventral stream is known to decode visual gestures (see Section 4.2) thanks to the LOTC. The LOTC takes part in decoding the visual properties of gestures, and this area is known to process several concrete-to-abstract aspects of gestures such as transitivity and social dimension of gestures (Bluet et al., 2024; Lesourd, Afyouni, et al., 2023; Wurm et al., 2017; Wurm and Caramazza, 2022). Thus, the LOTC may participate in gesture understanding by bringing together basic attributes of gestures to build more abstract representations of these gestures.

We found the ventro-dorsal stream to be critical in gesture

understanding tasks. This finding suggests that the IPL plays a key role in successfully understanding a gesture. This result is far from isolated, as other studies have found an involvement of the IPL in action observation (Caspers et al., 2010; Urgesi et al., 2014). Most of the studies that were included in understanding task were using transitive stimuli, thus, the critical involvement of the IPL could be explained by the importance of tool related actions. More precisely, Kalénine et al. (2013) identified a critical role of the IPL for spatial gesture comprehension, in contrast to semantic gesture recognition. This result supports the hypothesis that IPL is taking part in kinematics/hand posture processing of tool related actions.

The IFG has been found to be critical for action understanding (see for reviews Caspers et al., 2010; Reynaud et al., 2019; Urgesi et al., 2014). The specific role of the IFG in action understanding remains poorly understood, as this region can support many high-level processes. In this work, we included many kinds of different tasks (e.g., explanation, discrimination, matching, etc.; for more details, see Table A4), thus ruling out the possibility to draw firm conclusions about the specific role of IFG in a particular process. The simple fact of passively observing an action seems to imply activation of the IFG, whether this action is transitive (Reynaud et al., 2019) or not (Caspers et al., 2010). However, a critical role of the IFG specific to action observation should have repercussions on imitation tasks, but we did not find such IFG involvement in imitation tasks, suggesting that the IFG is not necessary to action observation ability. Concerning studies implying a discrimination between two pictures/videos (e.g., Martin, Dressing, et al., 2016; Pazzaglia et al., 2008), Moro et al. (2008) found that the IFG was critical to perform body action discrimination, suggesting that the IFG might play a key role in the selection of an appropriate gesture. This is consistent with the work of Kalénine et al. (2013), who found a critical involvement of the IFG in videos showing the outcome of the action, as opposed to videos showing the means of performing the action. This suggests that the IFG is necessary for understanding an action by supporting the action-goal. Another possibility is that some action understanding tasks asked participants to name or explain an action, which required to produce an oral or written response. These language skills are well known to be supported by Broca's area, which is located in the IFG. Therefore, a lesion in the IFG could affect this process. Finally, as described above, most of the included papers on action understanding used transitive gestures, so the involvement of the IFG could be related to the transitivity of the seeing gestures. However, Pazzaglia, Smania et al. (2008) showed a critical involvement of the IFG in a discrimination task for both transitive and intransitive gestures, suggesting that the involvement of the IFG does not depend on transitivity.

Since action understanding and meaningful production seem to be supported by the same brain regions (for reviews see Reynaud et al., 2016, 2019), namely the ventro-dorsal and the ventral streams, we proposed to contrast action understanding with action production in order to identify streams that are preferentially critical for these tasks. In other words, we investigated whether some brain lesions affect one of these tasks more than the other. We found that lesions in IPL affected more action production, whereas lesions in IFG and pMTG affected more action understanding. These results confirm those of Tarhan et al. (2015), who found that IPL was more critical for action production than for action recognition. The IPL is a key area in any production task, we consider that this region supports important abilities required to perform an action such as technical reasoning or manipulation knowledge (Buxbaum, 2001; Buxbaum et al., 2007; Federico et al., 2022; Haaland et al., 2000; Osiurak et al., 2010, 2021; van Elk et al., 2014). Although we have emphasized in the previous section that the technical reasoning could be crucial to better understand an action, the fact remains that the technical reasoning theory has been developed from clinical observations on tool use deficits (Osiurak et al., 2008, 2009, 2010). Therefore, even if action understanding recruits the IPL, this area remains mainly required in production. We found that the IFG played a critical role in meaningful action production tasks (i.e., tool use,

pantomime, and MF imitation). Furthermore, our conjunction analysis revealed that this critical role of the IFG was shared with tasks involving understanding, confirming its important role in both performing and understanding actions (see Caspers et al., 2010 for similar results). However, when examining action production tasks individually, we observed a differential impact of the IFG, suggesting that its involvement is not similar across all tasks. Specifically, our analyses showed no critical involvement of the IFG in either MF imitation or pantomime on visual command, whereas lesions in this area affected performance in the tool use task. This suggests that the IFG may be particularly crucial for grasping selection during tool use tasks, rather than being essential for all production tasks. The contrast analysis supports the non-specificity of IFG in production, as it was critically involved only in action understanding tasks. The literature is quite divided on whether the IFG has a preferential involvement in production or understanding, with some authors attributing a preferential role to production (e.g., Tarhan et al., 2015), while others suggest a role in both production and understanding (Caspers et al., 2010). Our results align with the view that IFG is critical for both action understanding and action production tasks, with nevertheless a preferential involvement of the IFG in action understanding, given its non-specific role in action production.

We also found that lesions in the pMTG/LOTG affected action understanding more than meaningful action production. This result is in line with the literature (Caspers et al., 2010; Tarhan et al., 2015), highlighting a preferential involvement of the LOTG in action understanding rather than in action production. It is not surprising that this visually integrative area is crucial for action understanding as this task is required to successfully decode the perceived action. Furthermore, as discussed above, the LOTG could play a key role in semantic decoding by identifying the meaning of gestures. On the other hand, although we found that meaningful production tasks were supported by the ventral stream, it did not include the LOTG. This result comforts the key role of the LOTG in decoding and processing visual information.

Finally, our findings indicating the critical involvement of STS, IPL, and IFG in both action production and action understanding, are consistent with the mirror neuron theory (Rizzolatti and Craighero, 2004). According to this theory, visual information from occipital regions is processed by the posterior STS neurons providing a visual description of the perceived action. These visual representations are then transmitted to mirror neurons in the IPL, where sensorimotor aspects of gestures are processed. Finally, the action goal is encoded by mirror neurons in the IFG, and the information is translated into motor processes by the premotor cortex (Iacoboni, 2005; Iacoboni and Dapretto, 2006; Iacoboni and Wilson, 2006; Rajmohan and Mohandas, 2007).

4.4. Methodological considerations

The current meta-analysis exclusively included VLSM studies, excluding therefore functional imaging studies. This methodological choice entails that our results do not provide information about the brain areas participating in apraxia's tasks, but only regions critically involved in performing these tasks. This consideration may partly explain why some brain regions well known to be involved in certain tasks, are not found in our analyses. We assume that these regions are not critical for the execution of a gesture, since when damaged, the correctness of task execution is not affected. Thus, lesion mapping studies provide complementary information to functional imaging. This integrative perspective has been proposed in some recent meta-analyses (Lesourd et al., 2018; Niessen et al., 2014; Osiurak et al., 2021) which have demonstrated the relevance of the meta-analysis applied to lesion data.

However, lesion mapping data suffer from some limitations due to the lesion overlap. Lesion mapping studies consist in associating structural brain lesions with behavioral data. For this purpose, stroke patients with attested brain lesions are recruited. Strokes are most of the time

caused by a vascular accident in the middle cerebral artery (Nogles and Galuska, 2023), which supplies the temporal and parietal lobes at the level of the Sylvian fissure. Patients with stroke present therefore brain lesions mainly located in the vicinity of this artery (i.e., the ventral part of the parietal lobe, the dorsal part of the temporal lobe, and the inferior part of the frontal lobe). Lesion overlap plots provided by lesion mapping studies confirm this lesion distribution, with most patients suffering from lesions close to the Sylvian fissure, while few of them have a lesion in the dorsal part of the parietal lobe and the ventral part of the temporal lobe. This lack of data in these areas could limit the possibility of significant results, therefore underestimating their role in the functions screened here. For example, this consideration could explain why dorso-dorsal stream was not found to be critical in ML imitation, whereas most of neurocognitive models have identified this stream to support this task (e.g., 2AS+ model; Buxbaum, 2017). Therefore, our global lack of results regarding the dorso-dorsal stream must be considered in the light of this limitation.

Another limitation could stem from the insufficient data in certain conditions, which might have prevented the identification of significant clusters. For example, while we confirmed that impairment of ML hand imitation is linked to lesions in left IPL, we did not report involvement of the left IFG, particularly for ML finger imitation. This finding contrasts with previous studies (Achilles et al., 2017, 2019; Goldenberg and Karnath, 2006; Goldenberg and Randerath, 2015). Although some data indicate a moderate role of the left IFG in ML finger imitation (for a review see Lesourd et al., 2018), our study suggests that the left IFG might not be as crucial for ML finger imitation as the IPL is for ML hand imitation. However, the limited data available in the ML finger imitation condition ($n = 4$ studies) may explain why no significant clusters were identified in the left IFG for ML finger imitation and therefore call for further elaboration.

Apraxia is frequently observed after a lesion to the left hemisphere rather than to the right hemisphere. Thus, the neurocognitive models of action are based on the left hemisphere. However, recent works showed that right brain lesions can also lead to apraxia, this lobe could therefore be important for action processing (e.g., Dressing et al., 2020). Although we had initially planned to examine VLSM papers focusing on both right and left regions, we did not find enough data to perform analyses with right brain lesions. Thus, by focusing on the left hemisphere, we had to disregard the right hemisphere in action processing.

Our data extraction was realized in two ways: (1) VLSM studies providing coordinates of the lesion cluster centers given in tables, and (2) VLSM studies providing only brain plots with damaged regions. For the latter, we determined the lesion cluster centers through manual estimation using the CH2better niftii map on MRICron (Lesourd et al., 2018). This method allowed us to include many additional VLSM papers in our meta-analysis, allowing us to perform analyses that would not have been possible due to lack of data. However, it is possible that the coordinates we have extracted in this way are slightly different from those initially obtained, but not reported.

5. Conclusion and perspectives

This research provides a deeper understanding of the neural networks involved in skilled gesture performance by investigating apraxia's tasks with AnLE meta-analysis focusing on VLSM studies. Our results provided new considerations about the 3 pathways of action model, by identifying the critical regions involved in tool use, pantomime, imitation, and action understanding. One of the main results of the present study was the crucial role of the IPL in each of these tasks, suggesting a key role of this region to successfully produce and understand a gesture. Another main result is that the LOTG plays a key role in processing meaningless gestures which led us to propose an antero-posterior gradient of meaning in the posterior ventral stream with the LOTG involved in decoding new meaningless gestures, and the pMTG involved in the semantic treatment of meaningful gestures.

All these results have important outcomes for future neurocognitive models of apraxia, as well as for clinical considerations. A significant implication of our findings for clinicians is that apraxic deficits may arise from lesions beyond the parietal lobe. While the parietal lobe remains crucial for generating skilled voluntary gestures, lesions in the LOTC and/or the IFG can also lead to apraxic deficits, further increasing the risk of developing persistent apraxic deficits (Kusch et al., 2018; Pazzaglia and Galli, 2019). While our study reviewed the primary structures associated with apraxic deficits, further research is necessary to fully comprehend the brain networks implicated in specific apraxic deficits (e.g., Garcea et al., 2020; Rosenzopf et al., 2022). Furthermore, in the realm of remediation, identifying the affected brain networks in patients could allow for the recruitment of intact action networks to compensate for deficits, for example the understanding of the interplay between the left and right hemispheres will be crucial for future apraxia treatments (Watson et al., 2019). Future research could leverage innovative techniques such as Transcranial Magnetic Stimulation (TMS) or Transcranial Direct Current Stimulation (tDCS) to target impaired structures in order to diagnose the presence of specific apraxic deficits (for a discussion see Rounis and Binkofski, 2023) or to improve apraxic deficits by targeting spared brain regions (Pastore-Wapp et al., 2022).

Appendix A

Table A1
Studies using VLSM on tool use task included in the meta-analysis.

Studies	Task	Number of foci	Type of data	n	Type of injury	Damaged hemisphere	Mean age (range)	Disease	Mean days post-stroke (range)
Bi et al. (2015)	Single familiar tool use	6	Extracted from VLSM plots	86	Stroke = 76; Traumatic brain injuries = 12	Bilateral = 35; LBD = 33; RBD = 18	45 (19–76)	Aphasia=74	180 (30–2580)
Dovern et al. (2011)	Single familiar tool use	11	Extracted from VLSM plots	43	Stroke	LBD	(21–77)	Apraxia=14	Apraxic: 367 (16–1209) Non-apraxic: 315 (27–1506)
Goldenberg and Spatt (2009)	Real familiar tool use Novel tool use	19 16	Extracted from VLSM plots	38	Stroke (Ischaemic=23; Bleeding =15)	LBD	54,1 (18–73)	Aphasia=38	Ischaemic: 66,5 (21–182); Bleeding: 161,7 (28–700)
Martin et al. (2015)	Real familiar tool use	22	Extracted from VLSM plots	136 ¹	Stroke	LBD	65 (36–85)	Aphasia=69	5,1 (1–10)
Martin, Dressing, et al. (2016)	Real familiar tool use	41	Extracted from VLSM plots	98 ¹	Stroke	LBD	65,4 (21,9–85,8)	Aphasia=52	4,4 (± 2 days)
Martin, Nitschke, et al. (2016)	Real familiar tool use	18	Extracted from VLSM plots	36	Stroke	LBD	59,7 (31–77)	n.m.	933 (180–2730)
Mengotti et al. (2013)	Single familiar tool use	4	Collected on VLSM table	57	Stroke	LBD	64.05	Aphasia=27	174,9 (15–2310)
Randerath et al. (2010)	Single familiar tool use	12	Collected on VLSM table	42	Stroke	LBD	57	Aphasia=42	93
Salazar-López et al. (2016)	Real familiar tool use Novel tool use	18 25	Collected on VLSM table	31	Stroke	LBD	58,3 ²	Aphasia=23 at least ³	127 ²
Stoll et al. (2022)	Real familiar tool use Novel tool use	20 27	Extracted from VLSM plots	58	Stroke	LBD	59,71 (30–79)	Aphasia=36	82,93 (18–857)

1: 58 subjects from Martin et al., (2015) - 2: Mean age and mean time post-stroke are based on the 31 patients mentioned above, plus 19 right brain damaged patients - 3: AAT test was used on 26 of the 31 patients, and detected aphasia in 23 of them. Abbreviations: RBD=Right brain damaged; LBD=Left brain damaged; n.m.= not mentioned

Authors contributions

M.M., M.L., and F.O. designed the research question. M.M. performed the literature review, M.M and A.S. extracted data from papers, and M.M analyzed the data. M.M. and M.L. wrote the manuscript. M.M., M.L., and F.O. reviewed and edited the manuscript. M.L. and F.O. supervised each step of the research.

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Declaration of Competing Interest

The authors declare that they have no competing interests.

Data Availability

Data are available at <https://osf.io/phwv3/>.

Table A2
Studies using VLSM on pantomime of tool use task included in the meta-analysis.

Auteurs	Task	Presentation modalities	Stimuli	NB of foci	Type of data	n	Type of injury	Damaged hemisphere	Mean age (range)	Disease	Mean days post-stroke (range)
Buxbaum et al. (2014)	Pantomime performance	Visual	Real tool	5	Collected on VLSM table	71	Stroke	LBD	58 (35–80)	n.m.	1477,2 (60–9570)
Dovern et al. (2011)	Pantomime performance	Visual + Verbal	Tool pictures + Verbal instructions	6	Extracted from VLSM plots	43	Stroke	LBD	52,6 (21–77)	Apraxia=14	334,5 (16–1506)
Dressing et al. (2019)	Pantomime performance	Visual	Tool pictures	8	Extracted from VLSM plots	48	Stroke (acute stage)	LBD	63,31 (21–79)	Apraxia=17	4,5 (1–9)
Dressing et al. (2021)	Pantomime production	Visual	Tool pictures	3	Collected on VLSM table	90	Stroke (chronic stage)	LBD	64,46 (22–87)	n.m.	429 (120–1980)
Finkel et al. (2018)	Pantomime Body-Part-Object	Visual + Verbal	Tool pictures + Verbal instructions	33	Extracted from VLSM plots	67	Stroke	LBD	56,1 (26–82)	Apraxia=49 Aphasia=42	399,3 (21–3480)
	Transitive No-Body-Part-Object	Visual + Verbal	Tool pictures + Verbal instructions	54							
Garcea et al. (2020)	Pantomime performance	Visual	Tool pictures	20	Collected on VLSM table	57	Stroke	LBD	56 (31–80)	n.m.	1215 (120–5520)
Goldenberg and Randerath (2015)	Pantomime performance	Visual + Verbal	Tool pictures + Verbal instructions	14	Extracted from VLSM plots	96 ¹	Stroke	LBD	56,9 (26–83)	Aphasia=90	93,1 (21–406)
Hoeren et al. (2014)	Pantomime performance	Visual	Tool pictures	20	Extracted from VLSM plots	96	Stroke (acute stage)	LBD	63 (26–85)	Aphasia=35	5,3 (2–10)
Manuel et al. (2013)	Pantomime Configural/Spatial	Verbal	Verbal instructions	21	Extracted from VLSM plots	42	Stroke	LBD	60,5 (16–89) ²	Aphasia=38 on 84 LBD patients	16,1 (±48,3) ²
	Pantomime Body-Part-Object	Verbal	Verbal instructions	6							
Martin, Nitschke, et al. (2016)	Pantomime performance	Visual	Tool pictures	31	Extracted from VLSM plots	36	Stroke (chronic stage)	LBD	60	n.m.	>180
Nobusako et al. (2018)	Pantomime performance	Verbal	Verbal instructions	17	Collected on VLSM table	19	Stroke	LBD	67,5e	Apraxia=7e Pseudo-apraxia=6 ³	237,5 (15–1126) ³
Pizzamiglio et al. (2019)	Pantomime performance	Verbal	Verbal instructions	3	Collected on VLSM table	211	Stroke	LBD=202 Bilateral=9	72,39 (27–94) ⁴	n.m.	24,3 (1–93) ⁴
Sperber et al. (2019)	Pantomime performance	Visual + Verbal	Tool pictures + Verbal instructions	14	Extracted from VLSM plots	130 ¹	Stroke	LBD	56,5 (26–83)	Aphasia=124	101,7
Tarhan et al. (2015)	Pantomime performance	Visual + Verbal	Tool pictures + Verbal instructions	9	Collected on VLSM table	131	Stroke	LBD	57,8	n.m.	1233
Watson and Buxbaum (2015)	Pantomime performance	Visual	Tool pictures	30	Extracted from VLSM plots	31	Stroke	LBD	57 (31–76)	n.m.	>180
Weiss et al. (2016)	Pantomime performance	Visual	Tool pictures	11	Extracted from VLSM plots	49	Stroke (acute stage)	LBD	65,9 (34–87)	Apraxia=27 Aphasia=37	6,53 (2–20)

1: Studies sharing 90 patients: Goldenberg et Randerath 2015; Sperber et al., (2019) - 2: Mean age and mean time post-stroke are based on initial 150 patients - 3: Mean age and mean time post-stroke are based on initial 22 patients - 4: Mean age and mean time post-stroke are based on initial 387 patients. Abbreviations: RBD=Right brain damaged; LBD=Left brain damaged; n.m.= not mentioned

Table A3
Studies using VLSM on imitation tasks included in the meta-analysis.

Auteurs	Meaning	Transitivity	Body part (Hand/Finger)	Number of foci	Type of data	n	Type of injury	Damaged hemisphere	Mean age (range)	Disease	Mean days post-stroke (range)
Achilles et al. (2017)	ML	Intransitive	Hand	46	Extracted from VLSM plots	257 ¹	Stroke	LBD	56	n.m.	231
	ML	Intransitive	Finger	18							
Achilles et al. (2019)	ML and MF	Intransitive	Hand	23	Extracted from VLSM plots	291 ¹	Stroke	LBD	57	n.m.	270 (<1–3810)
	ML and MF	Intransitive	Finger	11							
	ML	Intransitive	Finger	19							
Binder et al. (2017)	MF	Intransitive	Finger	24	Extracted from VLSM plots	38	Stroke	LBD	60,8 (30–80) ²	Apraxia=18 Aphasia=26	15,7 ²
	MF	Intransitive	Hand and finger	49							
Buxbaum et al. (2014)	MF	Transitive	Hand and finger	2	Collected on VLSM table	71	Stroke	LBD	58 (35–80)	n.m.	1477,2 (60–9570)
	ML	Intransitive	Hand and finger	6							
Dovern et al. (2011)	ML	Intransitive	Hand	11	Extracted from VLSM plots	43	Stroke	LBD	52,6 (21–77) ³	Apraxia=14	334,5 (16–1506) ³
	ML	Intransitive	Finger	10							
Dressing et al. (2018)	MF	Transitive and Intransitive	Hand and finger	29	Extracted from VLSM plots	156 ⁴	Stroke (acute stage)	LBD	64,3 (21,9–85,6)	Aphasia=81	4,9 (1–10)
	MF	Transitive	Hand and finger	26							
	MF	Intransitive	Hand and finger	20							
Dressing et al. (2019)	MF	Transitive	Hand and finger	7	Collected on VLSM table	48	Stroke (acute stage)	LBD	63,31 (21–79)	Apraxia=17	4,5 (1–9)
Dressing et al. (2021)	ML	Intransitive	Hand and finger	4	Collected on VLSM table	90 ⁴	Stroke (chronic stage)	LBD	64,46 (22–87)	n.m.	429 (120–1980)
Goldenberg and Randerath (2015)	ML	Intransitive	Hand	36	Extracted from VLSM plots	96	Stroke	LBD	56,9 (26–83)	Aphasia=90	93,1 (21–406)
	ML	Intransitive	Finger	15							
Hoeren et al. (2014)	ML	Intransitive	Hand	17	Extracted from VLSM plots	96 ⁴	Stroke (acute stage)	LBD	63 (26–85)	Aphasia=35	5,3 (2–10)
	ML	Intransitive	Finger	9							
	ML	Intransitive	Hand and finger	20							
Martin, Nitschke, et al. (2016)	MF	Transitive	Hand and finger	26	Extracted from VLSM plots	36	Stroke (chronic stage)	LBD	60	n.m.	>180
	ML	Intransitive	Hand and finger	44							
Mengotti et al. (2013)	ML	Intransitive	Hand	26	Collected on VLSM table	57	Stroke	LBD	64,05	Aphasia=27	174,9 (15–2310)
	MF	Intransitive	Hand and finger	4							
Nobusako et al. (2018)	ML and MF	Transitive and Intransitive	NA	14	Collected on VLSM table	19	Stroke	LBD	67,5 ⁵	Apraxia=7 ⁵ Pseudo-apraxia=6 ⁵	237,5 (15–1126) ⁵
Pizzamiglio et al. (2019)	ML	Intransitive	Hand and finger	3	Collected on VLSM table	211	Stroke	LBD=202 Bilateral=9	72,39 (27–94) ⁶	n.m.	24,3 (1–93) ⁶
Randerath et al. (2018)	ML	Intransitive	Hand	14	Extracted from VLSM plots	17	Stroke	LBD	65	n.m.	702 (15–3480)
Stoll et al. (2022)	ML	Intransitive	Hand	25	Extracted from VLSM plots	58	Stroke	LBD	59,71 (30–79)	Aphasia=36	82,93 (18–857)

1: Studies sharing 190 patients: Achilles et al., (2017); Achilles et al., (2019) - 2: Mean age and mean time post-stroke are based on initial 44 patients - 3: Mean age and mean time post-stroke are based on initial 48 patients - 4: Studies sharing the same patients: Hoeren et al., (2014); Dressing and al., 2018, 2021–5: Mean age and mean time post-stroke are based on initial 22 patients - 6: Mean age and mean time post-stroke are based on initial 387 patients. Abbreviations: ML=Meaningless; MF=Meaningful; RBD=Right brain damaged; LBD=Left brain damaged; n.m.= not mentioned

Table A4
Studies using VLSM on gesture understanding tasks included in the meta-analysis.

Auteurs	Task specificity	Transitivity	Presentation modality	NB of foci	Type of data	n	Type of injury	Damaged hemisphere	Mean age (range)	Disease	Mean days post-stroke (range)
Akinina et al. (2019)	Action naming	Transitive and intransitive	Action picture	14	Extracted from VLSM plots	40	Stroke	LBD	51,65 (33–78)	Aphasia=38	746,4 (90–4380)
Binder et al. (2017)	Association of an action picture with a contextual object	Intransitive gesture + tool picture	Action picture and contextual picture	44	Extracted from VLSM plots	41	Stroke	LBD	60,8 (30–80)a	Apraxia=18 Aphasia=26 (Both=14)	15,7a
Göksun et al. (2015)	Naming path of motion	Intransitive	Action video clips	12	Extracted from VLSM plots	16	Stroke (chronic stage)	LBD	64,69 (37–79)	n.m.	4065 (1500–6300)
Kalénine et al. (2010)	Naming manner of motion	Intransitive	Action video clips	6	Extracted from VLSM plots	43	Stroke	LBD	56,16 (41–74)	n.m.	n.m.
Kalénine et al. (2010)	Recognition of accurate spatial gestures	Transitive	Action video clips	29	Extracted from VLSM plots	43	Stroke	LBD	56,16 (41–74)	n.m.	n.m.
Kalénine et al. (2010)	Recognition of semantic gestures	Transitive	Action video clips	29	Extracted from VLSM plots	43	Stroke	LBD	56,16 (41–74)	n.m.	n.m.
Kalénine et al. (2013)	Comprehension of the means to perform a specific action	Transitive	Action video clips	13	Extracted from VLSM plots	23	Stroke (chronic stage)	LBD	59,48 (33–75)	n.m.	2160
Kalénine et al. (2013)	Comprehension of the outcome of a specific action	Transitive	Action video clips	3	Extracted from VLSM plots	23	Stroke (chronic stage)	LBD	59,48 (33–75)	n.m.	2160
Martin, Dressing, et al. (2016)	Discrimination of correct/incorrect tool-related actions	Transitive	Video clips	43	Extracted from VLSM plots	98	Stroke	LBD	65,4 (21,9–85,8)	Aphasia=52	4,4 (± 2)
Pazzaglia, Smania, et al. (2008)	Discrimination of correct/incorrect tool-related actions	Transitive Intransitive	Video clips Video clips	12 15	Extracted from VLSM plots	33	Stroke	LBD	63,7	Apraxia=21	57,7 (± 29)
Pazzaglia, Pizzamaglio, et al. (2008)	Discrimination of action pictures matching with a sound	Transitive and Intransitive	Action pictures	11	Extracted from VLSM plots	28	Stroke	LBD	58,33 (25–79)	Apraxia=21	n.m.
Pizzamaglio et al. (2019)	Action recognition	Transitive and intransitive	Gestures performed by the experimenter	1	Collected on VLSM table	211	Stroke	LBD=202 Bi=9	72,39 (27–94)b	n.m.	24,3 (1–93) b
Tarhan et al. (2015)	Recognition of semantic gestures	Transitive	Action video clips	4	Collected on VLSM table	131	Stroke (chronic stage)	LBD	57,8	n.m.	1353

1: Based on initial 44 patients - 2: Studies sharing patients: Kalénine et al., (2010); Tarhan et al., (2015) - 3: Mean age and mean time post-stroke are based on initial 387 patients. Abbreviations: RBD=Right brain damaged; LBD=Left brain damaged; n.m.= not mentioned

Supplementary analysis

Supplementary analysis associated with this article can be found in the online version at [doi:10.1016/j.neubiorev.2024.105720](https://doi.org/10.1016/j.neubiorev.2024.105720).

References

- Achilles, E.I.S., Ballweg, C.S., Niessen, E., Kusch, M., Ant, J.M., Fink, G.R., Weiss, P.H., 2019. Neural correlates of differential finger gesture imitation deficits in left hemisphere stroke. *NeuroImage. Clin.* 23, 101915. <https://doi.org/10.1016/j.nicl.2019.101915>.
- Achilles, E.I.S., Weiss, P.H., Fink, G.R., Binder, E., Price, C.J., Hope, T.M.H., 2017. Using multi-level Bayesian lesion-symptom mapping to probe the body-part-specificity of gesture imitation skills. *NeuroImage* 161, 94–103. <https://doi.org/10.1016/j.neuroimage.2017.08.036>.
- Akinina, Yu, Dragoy, O., Ivanova, M.V., Iskra, E.V., Soloukhina, O.A., Petryshevsky, A.G., Fedina, O.N., Turken, A.U., Shklovsky, V.M., Dronkers, N.F., 2019. Grey and white matter substrates of action naming. *Neuropsychologia* 131, 249–265. <https://doi.org/10.1016/j.neuropsychologia.2019.05.015>.
- Andres, M., Pelgrims, B., Olivier, E., 2013. Distinct contribution of the parietal and temporal cortex to hand configuration and contextual judgements about tools. *Cortex* 49 (8), 2097–2105. <https://doi.org/10.1016/j.cortex.2012.11.013>.
- Andres, M., Pelgrims, B., Olivier, E., Vannuscors, G., 2017. The left supramarginal gyrus contributes to finger positioning for object use: A neuronavigated transcranial magnetic stimulation study. *Eur. J. Neurosci.* 46 (12), 2835–2843. <https://doi.org/10.1111/ejn.13763>.
- Bartolo, A., Claisse, C., Gallo, F., Ott, L., Sampaio, A., Nandrino, J.-L., 2019. Gestures convey different physiological responses when performed toward and away from the body. *Sci. Rep.* 9 (1), 12862. <https://doi.org/10.1038/s41598-019-49318-3>.
- Bartolo, A., Cubelli, R., Della Sala, S., Drei, S., 2003. Pantomimes are special gestures which rely on working memory. *Brain Cogn.* 53 (3), 483–494. [https://doi.org/10.1016/S0278-2626\(03\)00209-4](https://doi.org/10.1016/S0278-2626(03)00209-4).
- Bartolo, A., Cubelli, R., Sala, S.D., Drei, S., Marchetti, C., 2001. Double Dissociation between Meaningful and Meaningless Gesture Reproduction in Apraxia. *Cortex* 37 (5), 696–699. [https://doi.org/10.1016/S0010-9452\(08\)70617-8](https://doi.org/10.1016/S0010-9452(08)70617-8).

- Bates, E., Wilson, S.M., Saygin, A.P., Dick, F., Sereno, M.I., Knight, R.T., Dronkers, N.F., 2003. Voxel-based lesion-symptom mapping. *Nat. Neurosci.* 6 (5), 448–450. <https://doi.org/10.1038/nn1050>.
- Baumard, J., Le Gall, D., 2021. The challenge of apraxia: Toward an operational definition? *Cortex* 141, 66–80. <https://doi.org/10.1016/j.cortex.2021.04.001>.
- Baumard, J., Lesourd, M., Jarry, C., Merck, C., Etcharry-Bouyx, F., Chauviré, V., Belliard, S., Moreaud, O., Croisile, B., Osiurak, F., Le Gall, D., 2016. Tool use disorders in neurodegenerative diseases: Roles of semantic memory and technical reasoning. *Cortex* 82, 119–132. <https://doi.org/10.1016/j.cortex.2016.06.007>.
- Baumard, J., Lesourd, M., Remigereau, C., Merck, C., Jarry, C., Etcharry-Bouyx, F., Chauviré, V., Belliard, S., Moreaud, O., Osiurak, F., Le Gall, D., 2019. The – weak – role of memory in tool use: Evidence from neurodegenerative diseases. *Neuropsychologia* 129, 117–132. <https://doi.org/10.1016/j.neuropsychologia.2019.03.008>.
- Baumard, J., Osiurak, F., Lesourd, M., Le Gall, D., 2014. Tool use disorders after left brain damage. *Front. Psychol.* 5. <https://www.frontiersin.org/articles/10.3389/fpsyg.2014.00473>.
- Bi, Y., Han, Z., Zhong, S., Ma, Y., Gong, G., Huang, R., Song, L., Fang, Y., He, Y., Caramazza, A., 2015. The White Matter Structural Network Underlying Human Tool Use and Tool Understanding. *J. Neurosci.* 35 (17), 6822–6835. <https://doi.org/10.1523/JNEUROSCI.3709-14.2015>.
- Binder, J.R., Desai, R.H., 2011. The neurobiology of semantic memory. *Trends Cogn. Sci.* 15 (11), 527–536. <https://doi.org/10.1016/j.tics.2011.10.001>.
- Binder, E., Dovern, A., Hesse, M.D., Ebke, M., Karbe, H., Saliger, J., Fink, G.R., Weiss, P.H., 2017. Lesion evidence for a human mirror neuron system. *Cortex* 90, 125–137. <https://doi.org/10.1016/j.cortex.2017.02.008>.
- Binkofski, F., Buxbaum, L.J., 2013. Two action systems in the human brain. *Brain Lang.* 127 (2), 222–229. <https://doi.org/10.1016/j.bandl.2012.07.007>.
- Bluet, A., Reynaud, E., Federico, G., Bryche, C., Lesourd, M., Fournel, A., Lamberton, F., Ibarrola, D., Rossetti, Y., Osiurak, F., 2024. The technical-reasoning network is recruited when people observe others make or teach how to make tools. *fMRI Study* 2024, 03.21.586121. <https://doi.org/10.1101/2024.03.21.586121>.
- Bozeat, S., Ralph, M.A.L., Patterson, K., Hodges, J.R., 2002. When objects lose their meaning: What happens to their use? *Cogn., Affect., Behav. Neurosci.* 2 (3), 236–251. <https://doi.org/10.3758/CABN.2.3.236>.
- Buxbaum, L.J., 2001. Ideomotor Apraxia: A Call to Action. *Neurocase* 7 (6), 445–458. <https://doi.org/10.1093/neucas/7.6.445>.
- Buxbaum, L.J., 2017. Learning, remembering, and predicting how to use tools: Distributed neurocognitive mechanisms. *Psychol. Rev.* 124 (3), 346–360. <https://doi.org/10.1037/rev0000051>.
- Buxbaum, L.J., Johnson-Frey, S.H., Bartlett-Williams, M., 2005. Deficient internal models for planning hand-object interactions in apraxia. *Neuropsychologia* 43 (6), 917–929. <https://doi.org/10.1016/j.neuropsychologia.2004.09.006>.
- Buxbaum, L.J., Kalénine, S., 2010. Action knowledge, visuomotor activation, and embodiment in the two action systems. *Ann. N. Y. Acad. Sci.* 1191, 201–218. <https://doi.org/10.1111/j.1749-6632.2010.05447.x>.
- Buxbaum, L.J., Kyle, K.M., Menon, R., 2005. On beyond mirror neurons: Internal representations subserving imitation and recognition of skilled object-related actions in humans. *Cogn. Brain Res.* 25 (1), 226–239. <https://doi.org/10.1016/j.cogbrainres.2005.05.014>.
- Buxbaum, L.J., Kyle, K., Grossman, M., Coslett, B., 2007. Left Inferior Parietal Representations for Skilled Hand-Object Interactions: Evidence from Stroke and Corticobasal Degeneration. *Cortex* 43 (3), 411–423. [https://doi.org/10.1016/S0010-9452\(08\)70466-0](https://doi.org/10.1016/S0010-9452(08)70466-0).
- Buxbaum, L.J., Kyle, K.M., Tang, K., Detre, J.A., 2006. Neural substrates of knowledge of hand postures for object grasping and functional object use: Evidence from fMRI. *Brain Res.* 1117 (1), 175–185. <https://doi.org/10.1016/j.brainres.2006.08.010>.
- Buxbaum, L.J., Saffran, E.M., 2002. Knowledge of object manipulation and object function: Dissociations in apraxic and nonapraxic subjects. *Brain Lang.* 82 (2), 179–199. [https://doi.org/10.1016/S0093-934X\(02\)00014-7](https://doi.org/10.1016/S0093-934X(02)00014-7).
- Buxbaum, L.J., Schwartz, M.F., Carew, T.G., 1997. The role of semantic memory in object use. *Cogn. Neuropsychol.* 14, 219–254. <https://doi.org/10.1080/026432997381565>.
- Buxbaum, L.J., Shapiro, A.D., Coslett, H.B., 2014. Critical brain regions for tool-related and imitative actions: A componential analysis. *Brain* 137 (7), 1971–1985. <https://doi.org/10.1093/brain/awu111>.
- Caspers, S., Zilles, K., Laird, A.R., Eickhoff, S.B., 2010. ALE meta-analysis of action observation and imitation in the human brain. *NeuroImage* 50 (3), 1148–1167. <https://doi.org/10.1016/j.neuroimage.2009.12.112>.
- Choi, S., Na, D.L., Kang, E., Lee, K., Lee, S., Na, D., 2001. Functional magnetic resonance imaging during pantomiming tool-use gestures. *Exp. Brain Res.* 139 (3), 311–317. <https://doi.org/10.1007/s002210100777>.
- Cubelli, R., Marchetti, C., Boscolo, G., Della Sala, S., 2000. Cognition in Action: Testing a Model of Limb Apraxia. *Brain Cogn.* 44 (2), 144–165. <https://doi.org/10.1006/brcg.2000.1226>.
- Dafsari, H.S., Dovern, A., Fink, G.R., Weiss, P.H., 2019. Deficient body structural description contributes to apraxic end-position errors in imitation. *Neuropsychologia* 133, 107150. <https://doi.org/10.1016/j.neuropsychologia.2019.107150>.
- DeRamus, T.P., Kana, R.K., 2015. Anatomical likelihood estimation meta-analysis of grey and white matter anomalies in autism spectrum disorders. *NeuroImage: Clin.* 7, 525–536. <https://doi.org/10.1016/j.nicl.2014.11.004>.
- Dovern, A., Fink, G.R., Saliger, J., Karbe, H., Koch, I., Weiss, P.H., 2011. Apraxia Impairs Intentional Retrieval of Incidentally Acquired Motor Knowledge. *J. Neurosci.* 31 (22), 8102–8108. <https://doi.org/10.1523/JNEUROSCI.6585-10.2011>.
- Dressing, A., Kaller, C.P., Martin, M., Nitschke, K., Kiemmerer, D., Beume, L.-A., Schmidt, C.S.M., Musso, M., Urbach, H., Rijntjes, M., Weiller, C., 2021. Anatomical correlates of recovery in apraxia: A longitudinal lesion-mapping study in stroke patients. *Cortex* 142, 104–121. <https://doi.org/10.1016/j.cortex.2021.06.001>.
- Dressing, A., Kaller, C.P., Nitschke, K., Beume, L.-A., Kiemmerer, D., Schmidt, C.S.M., Bormann, T., Umarova, R.M., Egger, K., Rijntjes, M., Weiller, C., Martin, M., 2019. Neural correlates of acute apraxia: Evidence from lesion data and functional MRI in stroke patients. *Cortex* 120, 1–21. <https://doi.org/10.1016/j.cortex.2019.05.005>.
- Dressing, A., Martin, M., Beume, L.-A., Kiemmerer, D., Urbach, H., Kaller, C.P., Weiller, C., Rijntjes, M., 2020. The correlation between apraxia and neglect in the right hemisphere: A voxel-based lesion-symptom mapping study in 138 acute stroke patients. *Cortex* 132, 166–179. <https://doi.org/10.1016/j.cortex.2020.07.017>.
- Dressing, A., Nitschke, K., Kiemmerer, D., Bormann, T., Beume, L., Schmidt, C.S.M., Ludwig, V.M., Mader, I., Willmes, K., Rijntjes, M., Kaller, C.P., Weiller, C., Martin, M., 2018. Distinct Contributions of Dorsal and Ventral Streams to Imitation of Tool-Use and Communicative Gestures. *Cereb. Cortex* 28 (2), 474–492. <https://doi.org/10.1093/cercor/bhw383>.
- Eickhoff, S.B., Bzdok, D., Laird, A.R., Roski, C., Caspers, S., Zilles, K., Fox, P.T., 2011. Co-activation patterns distinguish cortical modules, their connectivity and functional differentiation. *NeuroImage* 57 (3), 938–949. <https://doi.org/10.1016/j.neuroimage.2011.05.021>.
- Eickhoff, S.B., Bzdok, D., Laird, A.R., Kurth, F., Fox, P.T., 2012. Activation likelihood estimation meta-analysis revisited. *NeuroImage* 59 (3), 2349–2361. <https://doi.org/10.1016/j.neuroimage.2011.09.017>.
- Eickhoff, S.B., Laird, A.R., Grefkes, C., Wang, L.E., Zilles, K., Fox, P.T., 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. *Hum. Brain Mapp.* 30 (9), 2907–2926. <https://doi.org/10.1002/hbm.20718>.
- van Elk, M., van Schie, H., Bekkering, H., 2014. Action semantics: A unifying conceptual framework for the selective use of multimodal and modality-specific object knowledge. *Phys. Life Rev.* 11 (2), 220–250. <https://doi.org/10.1016/j.plrev.2013.11.005>.
- Federico, G., Reynaud, E., Navarro, J., Lesourd, M., Gaujoux, V., Lamberton, F., Ibarrola, D., Cavaliere, C., Alfano, V., Aiello, M., Salvatore, M., Seguin, P., Schnebelen, D., Brandimonte, M.A., Rossetti, Y., Osiurak, F., 2022. The cortical thickness of the area PF of the left inferior parietal cortex mediates technical-reasoning skills. *Article 1. Sci. Rep.* 12 (1) <https://doi.org/10.1038/s41598-022-15587-8>.
- Finkel, L., Hogrefe, K., Frey, S.H., Goldenberg, G., Randerath, J., 2018. It takes two to pantomime: Communication meets motor cognition. *NeuroImage: Clin.* 19, 1008–1017. <https://doi.org/10.1016/j.nicl.2018.06.019>.
- Fridman, E.A., Immisch, I., Hanakawa, T., Bohlhalter, S., Waldvogel, D., Kansaku, K., Wheaton, L., Wu, T., Hallett, M., 2006. The role of the dorsal stream for gesture production. *NeuroImage* 29 (2), 417–428. <https://doi.org/10.1016/j.neuroimage.2005.07.026>.
- Garcea, F.E., Greene, C., Grafton, S.T., Buxbaum, L.J., 2020. Structural Disconnection of the Tool Use Network after Left Hemisphere Stroke Predicts Limb Apraxia Severity. *Cereb. Cortex Commun.* 1 (1), tgaa035 <https://doi.org/10.1093/texcom/tgaa035>.
- Glahn, D.C., Laird, A.R., Ellison-Wright, I., Thelen, S.M., Robinson, J.L., Lancaster, J.L., Bullmore, E., Fox, P.T., 2008. Meta-analysis of gray matter anomalies in schizophrenia: Application of anatomic likelihood estimation and network analysis. *Biol. Psychiatry* 64 (9), 774–781. <https://doi.org/10.1016/j.biopsych.2008.03.031>.
- Göksun, T., Lehet, M., Malykhina, K., Chatterjee, A., 2015. Spontaneous gesture and spatial language: Evidence from focal brain injury. *Brain Lang.* 150, 1–13. <https://doi.org/10.1016/j.bandl.2015.07.012>.
- Goldenberg, G., 1999. Matching and imitation of hand and finger postures in patients with damage in the left or right hemispheres. *Neuropsychologia* 37 (5), 559–566. [https://doi.org/10.1016/S0028-3932\(98\)00111-0](https://doi.org/10.1016/S0028-3932(98)00111-0).
- Goldenberg, G., 2014. Apraxia – The cognitive side of motor control. *Cortex* 57, 270–274. <https://doi.org/10.1016/j.cortex.2013.07.016>.
- Goldenberg, G., 2017. Facets of Pantomime. *J. Int. Neuropsychol. Soc.* 23 (2), 121–127. <https://doi.org/10.1017/S1355617716000989>.
- Goldenberg, G., Hagmann, S., 1998. Tool use and mechanical problem solving in apraxia. *Neuropsychologia* 36 (7), 581–589. [https://doi.org/10.1016/S0028-3932\(97\)00165-6](https://doi.org/10.1016/S0028-3932(97)00165-6).
- Goldenberg, G., Hartmann, K., Schlott, I., 2003. Defective pantomime of object use in left brain damage: Apraxia or asymbolia? *Neuropsychologia* 41 (12), 1565–1573. [https://doi.org/10.1016/S0028-3932\(03\)00120-9](https://doi.org/10.1016/S0028-3932(03)00120-9).
- Goldenberg, G., Karnath, H.-O., 2006. The Neural Basis of Imitation is Body Part Specific. *J. Neurosci.* 26 (23), 6282–6287. <https://doi.org/10.1523/JNEUROSCI.0638-06.2006>.
- Goldenberg, G., Münsinger, U., Karnath, H.-O., 2009. Severity of neglect predicts accuracy of imitation in patients with right hemisphere lesions. *Neuropsychologia* 47 (13), 2948–2952. <https://doi.org/10.1016/j.neuropsychologia.2009.06.024>.
- Goldenberg, G., Randerath, J., 2015. Shared neural substrates of apraxia and aphasia. *Neuropsychologia* 75, 40–49. <https://doi.org/10.1016/j.neuropsychologia.2015.05.017>.
- Goldenberg, G., Spatt, J., 2009. The neural basis of tool use. *Brain* 132 (6), 1645–1655. <https://doi.org/10.1093/brain/awp080>.
- Gonzalez Rothi, L.J., Ochipa, C., Heilman, K.M., 1991. A Cognitive Neuropsychological Model of Limb Praxis. *Cogn. Neuropsychol.* 8 (6), 443–458. <https://doi.org/10.1080/02643299108253382>.
- Goodale, M.A., Milner, A.D., 1992. Separate visual pathways for perception and action. *Trends Neurosci.* 15 (1), 20–25. [https://doi.org/10.1016/0166-2236\(92\)90344-8](https://doi.org/10.1016/0166-2236(92)90344-8).
- Gowda, S.N., Kolton Schneider, L., 2023. Apraxia. In *StatPearls*. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK585110/>.

- Grosbras, M., Beaton, S., Eickhoff, S.B., 2011. Brain regions involved in human movement perception: A quantitative voxel-based meta-analysis. *Hum. Brain Mapp.* 33 (2), 431–454. <https://doi.org/10.1002/hbm.21222>.
- Haaland, K.Y., Harrington, D.L., Knight, R.T., 2000. Neural representations of skilled movement. *Brain: A J. Neurol.* 123 (Pt 11), 2306–2313. <https://doi.org/10.1093/brain/123.11.2306>.
- Ham, H.S., Bartolo, A., Corley, M., Swanson, S., Rajendran, G., 2010. Case report: Selective deficit in the production of intransitive gestures in an individual with autism. *Cortex; a J. Devoted Study Nerv. Syst. Behav.* 46 (3), 407–409. <https://doi.org/10.1016/j.cortex.2009.06.005>.
- Hodges, J.R., Bozeat, S., Ralph, M.A.L., Patterson, K., Spatt, J., 2000. The role of conceptual knowledge in object use evidence from semantic dementia. *Brain* 123 (9), 1913–1925. <https://doi.org/10.1093/brain/123.9.1913>.
- Hoeren, M., Kümmerer, D., Bormann, T., Beume, L., Ludwig, V.M., Vry, M.-S., Mader, I., Rijntjes, M., Kaller, C.P., Weiller, C., 2014. Neural bases of imitation and pantomime in acute stroke patients: Distinct streams for praxis. *Brain* 137 (10), 2796–2810. <https://doi.org/10.1093/brain/awu203>.
- Iacoboni, M., 2005. Neural mechanisms of imitation. *Curr. Opin. Neurobiol.* 15 (6), 632–637. <https://doi.org/10.1016/j.conb.2005.10.010>.
- Iacoboni, M., Dapretto, M., 2006. The mirror neuron system and the consequences of its dysfunction. *Nat. Rev. Neurosci.* 7 (12), 942–951. <https://doi.org/10.1038/nrn2024>.
- Iacoboni, M., Wilson, S.M., 2006. Beyond a Single Area: Motor Control and Language Within a Neural Architecture Encompassing Broca's Area. *Cortex* 42 (4), 503–506. [https://doi.org/10.1016/S0010-9452\(08\)70387-3](https://doi.org/10.1016/S0010-9452(08)70387-3).
- Ishibashi, R., Pobric, G., Saito, S., Lambon Ralph, M.A., 2016. The neural network for tool-related cognition: An activation likelihood estimation meta-analysis of 70 neuroimaging contrasts. *Cogn. Neuropsychol.* 33 (3–4), 241–256. <https://doi.org/10.1080/02643294.2016.1188798>.
- Jarry, C., Osiurak, F., Delafuys, D., Chauviré, V., Etcharry-Bouyx, F., Le Gall, D., 2013. Apraxia of tool use: More evidence for the technical reasoning hypothesis. *Cortex* 49 (9), 2322–2333. <https://doi.org/10.1016/j.cortex.2013.02.011>.
- Jefferies, E., 2013. The neural basis of semantic cognition: Converging evidence from neuropsychology, neuroimaging and TMS. *Cortex* 49 (3), 611–625. <https://doi.org/10.1016/j.cortex.2012.10.008>.
- Jefferies, E., Thompson, H., Cornelissen, P., Smallwood, J., 2020. The neurocognitive basis of knowledge about object identity and events: Dissociations reflect opposing effects of semantic coherence and control. *Philos. Trans. R. Soc. B: Biol. Sci.* 375 (1791), 20190300. <https://doi.org/10.1098/rstb.2019.0300>.
- Johnson-Frey, S.H., Maloof, F.R., Newman-Norlund, R., Farrer, C., Inati, S., Grafton, S.T., 2003. Actions or Hand-Object Interactions? Human Inferior Frontal Cortex and Action Observation. *Neuron* 39 (6), 1053–1058. [https://doi.org/10.1016/S0896-6273\(03\)00524-5](https://doi.org/10.1016/S0896-6273(03)00524-5).
- Johnson-Frey, S.H., Newman-Norlund, R., Grafton, S.T., 2005. A Distributed Left Hemisphere Network Active During Planning of Everyday Tool Use Skills. *Cereb. Cortex* 15 (6), 681–695. <https://doi.org/10.1093/cercor/bhh169>.
- Kalénine, S., Buxbaum, L.J., 2016. Thematic knowledge, artifact concepts, and the left posterior temporal lobe: Where action and object semantics converge. *Cortex* 82, 164–178. <https://doi.org/10.1016/j.cortex.2016.06.008>.
- Kalénine, S., Buxbaum, L.J., Coslett, H.B., 2010. Critical brain regions for action recognition: Lesion symptom mapping in left hemisphere stroke. *Brain* 133 (11), 3269–3280. <https://doi.org/10.1093/brain/awq210>.
- Kalénine, S., Shapiró, A.D., Buxbaum, L.J., 2013. Dissociations of action means and outcome processing in left hemisphere stroke. *Neuropsychologia* 51 (7), 1224–1233. <https://doi.org/10.1016/j.neuropsychologia.2013.03.017>.
- Kimberg, D.Y., Coslett, H.B., Schwartz, M.F., 2007. Power Voxel-Based Lesion – Symptom Mapp. 1067–1080.
- Kleineberg, N.N., Tscherpel, C., Fink, G.R., Grefkes, C., Weiss, P.H., 2022. Different facets of object-use pantomime: Online TMS evidence on the role of the supramarginal gyrus. *Cortex* 156, 13–25. <https://doi.org/10.1016/j.cortex.2022.06.018>.
- Kusch, M., Schmidt, C.C., Göden, L., Tscherpel, C., Stahl, J., Saliger, J., Karbe, H., Fink, G.R., Weiss, P.H., 2018. Recovery from apraxic deficits and its neural correlate. *Restor. Neurol. Neurosci.* 36 (6), 669–678. <https://doi.org/10.3233/RNN-180815>.
- Lacadie, C.M., Fulbright, R.K., Constable, R.T., Papademetris, X., 2008. More accurate Talairach coordinates for neuroimaging using nonlinear registration. *NeuroImage* 42, 717–725.
- Lesourd, M., Afyouni, A., Geringswald, F., Cignetti, F., Raoul, L., Sein, J., Nazarian, B., Anton, J.-L., Grosbras, M.-H., 2023. Action Observation Network Activity Related to Object-Directed and Socially-Directed Actions in Adolescents. *J. Neurosci.* 43 (1), 125–141. <https://doi.org/10.1523/JNEUROSCI.1602-20.2022>.
- Lesourd, M., Baumard, J., Jarry, C., Etcharry-Bouyx, F., Belliard, S., Moreaud, O., Croisille, B., Chauviré, V., Granjon, M., Le Gall, D., Osiurak, F., 2016. Mechanical problem-solving strategies in Alzheimer's disease and semantic dementia. *Neuropsychology* 30 (5), 612–623. <https://doi.org/10.1037/neu0000241>.
- Lesourd, M., Baumard, J., Jarry, C., Le Gall, D., Osiurak, F., 2017. A cognitive-based model of tool use in normal aging. *Aging, Neuropsychol., Cogn.* 24 (4), 363–386. <https://doi.org/10.1080/13825585.2016.1218822>.
- Lesourd, M., Budriesi, C., Osiurak, F., Nichelli, P.F., Bartolo, A., 2019. Mechanical knowledge does matter to tool use even when assessed with a non-production task: Evidence from left brain-damaged patients. *J. Neuropsychol.* 13 (2), 198–213. <https://doi.org/10.1111/jnp.12140>.
- Lesourd, M., Naëgelé, B., Jaillard, A., Detante, O., Osiurak, F., 2020. Using tools effectively despite defective hand posture: A single-case study. *Cortex* 129, 406–422. <https://doi.org/10.1016/j.cortex.2020.04.023>.
- Lesourd, M., Osiurak, F., Baumard, J., Bartolo, A., Vanbellingen, T., Reynaud, E., 2018. Cerebral correlates of imitation of intransitive gestures: An integrative review of neuroimaging data and brain lesion studies. *Neurosci. Biobehav. Rev.* 95, 44–60. <https://doi.org/10.1016/j.neubiorev.2018.07.019>.
- Lesourd, M., Osiurak, F., Navarro, J., Reynaud, E., 2017. Involvement of the Left Supramarginal Gyrus in Manipulation Judgment Tasks: Contributions to Theories of Tool Use. *J. Int. Neuropsychol. Soc.* 23 (8), 685–691. <https://doi.org/10.1017/S1355617717000455>.
- Lesourd, M., Reynaud, E., Navarro, J., Gaujoux, V., Faye-Védrières, A., Alexandre, B., Baumard, J., Federico, G., Lamberton, F., Ibarrola, D., Rossetti, Y., Osiurak, F., 2023. Involvement of the posterior tool processing network during explicit retrieval of action tool and semantic tool knowledge: An fMRI study. *Cereb. Cortex*. <https://doi.org/10.1093/cercor/bhac522>.
- Lesourd, M., Servant, M., Baumard, J., Reynaud, E., Ecochard, C., Medjaoui, F.T., Bartolo, A., Osiurak, F., 2021. Semantic and action tool knowledge in the brain: Identifying common and distinct networks. *Neuropsychologia* 159, 107918. <https://doi.org/10.1016/j.neuropsychologia.2021.107918>.
- Liepmann, H., 1908. Drei Aufsätze aus dem Apraxiegebiet. S.Karger AG. <https://doi.org/10.1159/isbn.978-3-318-05375-3>.
- Liepmann, H., 1920. *Aprax. Ergeb. der Gesamt Med. Vol. 1*, 516–543.
- Lingnau, A., Downing, P.E., 2015. The lateral occipitotemporal cortex in action. *Trends Cogn. Sci.* 19 (5), 268–277. <https://doi.org/10.1016/j.tics.2015.03.006>.
- Manuel, A.L., Radman, N., Mesot, D., Chouiter, L., Clarke, S., Annoni, J.-M., Spierer, L., 2013. Inter- and Intra-hemispheric Dissociations in Ideomotor Apraxia: A Large-Scale Lesion-Symptom Mapping Study in Subacute Brain-Damaged Patients. *Cereb. Cortex* 23 (12), 2781–2789. <https://doi.org/10.1093/cercor/bhs280>.
- Martin, M., Beume, L., Kümmerer, D., Schmidt, C.S.M., Bormann, T., Dressing, A., Ludwig, V.M., Umarova, R.M., Mader, I., Rijntjes, M., Kaller, C.P., Weiller, C., 2015. Differential Roles of Ventral and Dorsal Streams for Conceptual and Production-Related Components of Tool Use in Acute Stroke Patients. *Cereb. Cortex* 26 (9), 3754–3771. <https://doi.org/10.1093/cercor/bhv179>.
- Martin, M., Dressing, A., Bormann, T., Schmidt, C.S.M., Kümmerer, D., Beume, L., Saur, D., Mader, I., Rijntjes, M., Kaller, C.P., Weiller, C., 2016. Componential Network for the Recognition of Tool-Associated Actions: Evidence from Voxel-based Lesion-Symptom Mapping in Acute Stroke Patients. *cercor/bhw226v1 Cereb. Cortex*. <https://doi.org/10.1093/cercor/bhw226>.
- Martin, M., Nitschke, K., Beume, L., Dressing, A., Bühler, L.E., Ludwig, V.M., Mader, I., Rijntjes, M., Kaller, C.P., Weiller, C., 2016. Brain activity underlying tool-related and imitative skills after major left hemisphere stroke. *Brain* 139 (5), 1497–1516. <https://doi.org/10.1093/brain/aww035>.
- Mengotti, P., Corradi-Dell'Acqua, C., Negri, G.A.L., Ukmar, M., Pesavento, V., Rumiati, R.I., 2013. Selective imitation impairments differentially interact with language processing. *Brain* 136 (8), 2602–2618. <https://doi.org/10.1093/brain/awt194>.
- Metzgar, R., Stoll, H., Grafton, S.T., Buxbaum, L.J., Garcea, F.E., 2022. Single-case disconnectome lesion-symptom mapping: Identifying two subtypes of limb apraxia. *Neuropsychologia* 170, 108210. <https://doi.org/10.1016/j.neuropsychologia.2022.108210>.
- Mishkin, M., Ungerleider, L.G., Macko, K.A., 1983. Object vision and spatial vision: Two cortical pathways. *Trends Neurosci.* 6, 414–417. [https://doi.org/10.1016/0166-2236\(83\)90190-X](https://doi.org/10.1016/0166-2236(83)90190-X).
- Molenberghs, P., Brander, C., Mattingley, J.B., Cunnington, R., 2010. The role of the superior temporal sulcus and the mirror neuron system in imitation. *Hum. Brain Mapp.* 31 (9), 1316–1326. <https://doi.org/10.1002/hbm.20938>.
- Moro, V., Urgesi, C., Pernigo, S., Lanteri, P., Pazzaglia, M., Aglioti, S.M., 2008. The Neural Basis of Body Form and Body Action Agnosia. *Neuron* 60 (2), 235–246. <https://doi.org/10.1016/j.neuron.2008.09.022>.
- Niessen, E., Fink, G.R., Weiss, P.H., 2014. Apraxia, pantomime and the parietal cortex. *NeuroImage: Clin.* 5, 42–52. <https://doi.org/10.1016/j.nicl.2014.05.017>.
- Nobusako, S., Ishibashi, R., Takamura, Y., Oda, E., Tanigashira, Y., Kouno, M., Tominaga, T., Ishibashi, Y., Okuno, H., Nobusako, K., Zama, T., Osumi, M., Shimada, S., Morioka, S., 2018. Distortion of Visuo-Motor Temporal Integration in Apraxia: Evidence From Delayed Visual Feedback Detection Tasks and Voxel-Based Lesion-Symptom Mapping. *Front. Neurol.* 9, 709. <https://doi.org/10.3389/fneur.2018.00709>.
- Nogles, T.E., Galuska, M.A., 2023. Middle Cerebral Artery Stroke. In *StatPearls*. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK556132/>.
- Ochipa, C., Rothi, L.J., Heilman, K.M., 1989. Ideational apraxia: A deficit in tool selection and use. *Ann. Neurol.* 25 (2), 190–193. <https://doi.org/10.1002/ana.410250214>.
- Ohgami, Y., Matsuo, K., Uchida, N., Nakai, T., 2004. An fMRI study of tool-use gestures: Body part as object and pantomime. *Neuroreport* 15 (12), 1903–1906. <https://doi.org/10.1097/00001756-200408260-00014>.
- Orban, G.A., Caruana, F., 2014. The neural basis of human tool use. *Front. Psychol.* 5. <https://www.frontiersin.org/articles/10.3389/fpsyg.2014.00310>.
- Osiurak, F., 2013. Apraxia of tool use is not a matter of affordances. *Front. Hum. Neurosci.* 7. <https://www.frontiersin.org/articles/10.3389/fnhum.2013.00890>.
- Osiurak, F., 2014. What Neuropsychology Tells us About Human Tool Use? The Four Constraints Theory (4CT): Mechanics, Space, Time, and Effort. *Neuropsychol. Rev.* 24 (2), 88–115. <https://doi.org/10.1007/s11065-014-9260-y>.
- Osiurak, F., Aubin, G., Allain, P., Jarry, C., Richard, I., Le Gall, D., 2008. Object utilization and object usage: A single-case study. *Neurocase* 14 (2), 169–183. <https://doi.org/10.1080/13554790802108372>.
- Osiurak, F., Badets, A., 2016. Tool use and affordance: Manipulation-based versus reasoning-based approaches. *Psychol. Rev.* 123, 534–568. <https://doi.org/10.1037/rev0000027>.

- Osiurak, F., Jarry, C., Le Gall, D., 2010. Grasping the affordances, understanding the reasoning: Toward a dialectical theory of human tool use. *Psychol. Rev.* 117, 517–540. <https://doi.org/10.1037/a0019004>.
- Osiurak, F., Jarry, C., Le Gall, D., 2011. Re-examining the gesture engram hypothesis. New perspectives on apraxia of tool use. *Neuropsychologia* 49 (3), 299–312. <https://doi.org/10.1016/j.neuropsychologia.2010.12.041>.
- Osiurak, F., Jarry, C., Allain, P., Aubin, G., Etcharry-Bouyx, F., Richard, I., Bernard, I., Le Gall, D., 2009. Unusual use of objects after unilateral brain damage: The technical reasoning model. *Cortex; a J. Devoted Study Nerv. Syst. Behav.* 45 (6), 769–783. <https://doi.org/10.1016/j.cortex.2008.06.013>.
- Osiurak, F., Reynaud, E., Baumard, J., Rossetti, Y., Bartolo, A., Lesourd, M., 2021. Pantomime of tool use: Looking beyond apraxia. *Brain Commun.*, fcab263 <https://doi.org/10.1093/braincomms/fcab263>.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., Moher, D., 2021. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 372, n71. <https://doi.org/10.1136/bmj.n71>.
- Pastore-Wapp, M., Gyurkó, D.M., Vanbellingen, T., Lehnick, D., Cazzoli, D., Pflugshaupt, T., Pflugi, S., Nyffeler, T., Walther, S., Bohlhalter, S., 2022. Improved gesturing in left-hemispheric stroke by right inferior parietal theta burst stimulation. *Front. Neurosci.* 16 <https://doi.org/10.3389/fnins.2022.998729>.
- Pazzaglia, M., Galli, G., 2019. Action Observation for Neurorehabilitation in Apraxia. *Front. Neurol.* 10, 309. <https://doi.org/10.3389/fneur.2019.00309>.
- Pazzaglia, M., Pizzamiglio, L., Pes, E., Aglioti, S.M., 2008. The Sound of Actions in Apraxia. *Curr. Biol.* 18 (22), 1766–1772. <https://doi.org/10.1016/j.cub.2008.09.061>.
- Pazzaglia, M., Smania, N., Corato, E., Aglioti, S.M., 2008. Neural Underpinnings of Gesture Discrimination in Patients with Limb Apraxia. *J. Neurosci.* 28 (12), 3030–3041. <https://doi.org/10.1523/JNEUROSCI.5748-07.2008>.
- Peigneux, et al., 2004. Imaging a cognitive model of apraxia. *Neural Substr. gesture-Specif. Cogn. Process.* <https://doi.org/10.1002/hbm.10161>.
- Piai, V., Eikelboom, D., 2023. Brain areas critical for picture naming: A systematic review and meta-analysis of lesion-symptom mapping studies. *Neurobiol. Lang.* 1–48. https://doi.org/10.1162/nol_a.00097.
- Pitcher, D., Ungerleider, L.G., 2021. Evidence for a Third Visual Pathway Specialized for Social Perception. *Trends Cogn. Sci.* 25 (2), 100–110. <https://doi.org/10.1016/j.tics.2020.11.006>.
- Pizzamiglio, G., Zhang, Z., Kolasinski, J., Riddoch, J.M., Passingham, R.E., Mantini, D., Rounis, E., 2019. A Role for the Action Observation Network in Apraxia After Stroke. *Front. Hum. Neurosci.* 13. (<https://www.frontiersin.org/articles/10.3389/fnhum.2019.00422>).
- Rajmohan, V., Mohandas, E., 2007. Mirror neuron system. *Indian J. Psychiatry* 49 (1), 66–69. <https://doi.org/10.4103/0019-5545.31522>.
- Ralph, M.A.L., Jefferies, E., Patterson, K., Rogers, T.T., 2017. The neural and computational bases of semantic cognition. *Nat. Rev. Neurosci.* 18 (1), 42–55. <https://doi.org/10.1038/nrn.2016.150>.
- Randerath, J., Finkel, L., Shigaki, C., Burris, J., Nanda, A., Hwang, P., Frey, S.H., 2018. Does it fit? – Impaired affordance perception after stroke. *Neuropsychologia* 108, 92–102. <https://doi.org/10.1016/j.neuropsychologia.2017.11.031>.
- Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., Hermsdörfer, J., 2010. Different left brain regions are essential for grasping a tool compared with its subsequent use. *NeuroImage* 53 (1), 171–180. <https://doi.org/10.1016/j.neuroimage.2010.06.038>.
- de Renzi, E., Gentilini, M., Barbieri, C., 1989. Auditory neglect. *J. Neurol., Neurosurg. Psychiatry* 52, 613–617. <https://doi.org/10.1136/jnnp.52.5.613>.
- Reynaud, E., Lesourd, M., Navarro, J., Osiurak, F., 2016. On the neurocognitive origins of human tool use: A critical review of neuroimaging data. *Neurosci. Biobehav. Rev.* 64, 421–437. <https://doi.org/10.1016/j.neubiorev.2016.03.009>.
- Reynaud, E., Navarro, J., Lesourd, M., Osiurak, F., 2019. To Watch is to Work: A Review of Neuroimaging Data on Tool Use Observation Network. *Neuropsychol. Rev.* 29 (4), 484–497. <https://doi.org/10.1007/s11065-019-09418-3>.
- Rizzolatti, G., Craighero, L., 2004. The mirror-neuron system. *Annu. Rev. Neurosci.* 27, 169–192. <https://doi.org/10.1146/annurev.neuro.27.070203.144230>.
- Rosenzopf, H., Wiesen, D., Basilakos, A., Yourganov, G., Bonilha, L., Rorden, C., Fridriksson, J., Karnath, H.-O., Sperber, C., 2022. Mapping the human praxis network: An investigation of white matter disconnection in limb apraxia of gesture production. *Brain Commun.* 4 (1), fcac004 <https://doi.org/10.1093/braincomms/fcac004>.
- Rossetti, Y., Revol, P., McIntosh, R., Pisella, L., Rode, G., Danckert, J., Tilikete, C., Dijkerman, H.C., Boisson, D., Vighetto, A., Michel, F., Milner, A.D., 2005. Visually guided reaching: Bilateral posterior parietal lesions cause a switch from fast visuomotor to slow cognitive control. *Neuropsychologia* 43 (2), 162–177. <https://doi.org/10.1016/j.neuropsychologia.2004.11.004>.
- Rothi, L.J., Ochipa, C., Heilman, K.M., 1991. A cognitive neuropsychological model of limb praxis. *Cogn. Neuropsychol.* 8 (6), 443–458. <https://doi.org/10.1080/02643299108253382>.
- Rounis, E., Binkofski, F., 2023. Limb Apraxias: The Influence of Higher Order Perceptual and Semantic Deficits in Motor Recovery After Stroke. *Stroke* 54 (1), 30–43. <https://doi.org/10.1161/STROKEAHA.122.037948>.
- Rumiati, R.I., Tessari, A., 2002. Imitation of novel and well-known actions: The role of short-term memory. *Exp. Brain Res.* 142 (3), 425–433. <https://doi.org/10.1007/s00221-001-0956-x>.
- Rumiati, R.I., Weiss, P.H., Tessari, A., Assmus, A., Zilles, K., Herzog, H., Fink, G.R., 2005. Common and Differential Neural Mechanisms Supporting Imitation of Meaningful and Meaningless Actions. *J. Cogn. Neurosci.* 17 (9), 1420–1431. <https://doi.org/10.1162/0898929054985374>.
- Salazar-López, E., Schwaiger, B.J., Hermsdörfer, J., 2016. Lesion correlates of impairments in actual tool use following unilateral brain damage. *Neuropsychologia* 84, 167–180. <https://doi.org/10.1016/j.neuropsychologia.2016.02.007>.
- Schwoebel, J., Coslett, H.B., 2005. Evidence for Multiple, Distinct Representations of the Human Body. *J. Cogn. Neurosci.* 17 (4), 543–553. <https://doi.org/10.1162/0898929053467587>.
- Silveri, M.C., Ciccarello, N., 2009. Semantic memory in object use. *Neuropsychologia* 47 (12), 2634–2641. <https://doi.org/10.1016/j.neuropsychologia.2009.05.013>.
- Sperber, C., Wiesen, D., Goldenberg, G., Karnath, H.-O., 2019. A network underlying human higher-order motor control: Insights from machine learning-based lesion-behaviour mapping in apraxia of pantomime. *Cortex; a J. Devoted Study Nerv. Syst. Behav.* 121, 308–321. <https://doi.org/10.1016/j.cortex.2019.08.023>.
- Stoll, S.E.M., Finkel, L., Buchmann, I., Hassa, T., Spiteri, S., Liepert, J., Randerath, J., 2022. 100 years after Liepmann–Lesion correlates of diminished selection and application of familiar versus novel tools. *Cortex* 146, 1–23. <https://doi.org/10.1016/j.cortex.2021.10.002>.
- Tarhan, L.Y., Watson, C.E., Buxbaum, L.J., 2015. Shared and Distinct Neuroanatomic Regions Critical for Tool-related Action Production and Recognition: Evidence from 131 Left-hemisphere Stroke Patients. *J. Cogn. Neurosci.* 27 (12), 2491–2511. https://doi.org/10.1162/jocn_a.00876.
- Tench, C.R., Tanasescu, R., Auer, D.P., Cottam, W.J., Constantinescu, C.S., 2014. Coordinate Based Meta-Analysis of Functional Neuroimaging Data Using Activation Likelihood Estimation; Full Width Half Max and Group Comparisons. *PLOS ONE* 9 (9), e106735. <https://doi.org/10.1371/journal.pone.0106735>.
- Tench, C.R., Tanasescu, R., Constantinescu, C.S., Auer, D.P., Cottam, W.J., 2017. Coordinate based random effect size meta-analysis of neuroimaging studies. *NeuroImage* 153, 293–306. <https://doi.org/10.1016/j.neuroimage.2017.04.002>.
- Tessari, A., Canessa, N., Ukmar, M., Rumiati, R.I., 2007. Neuropsychological evidence for a strategic control of multiple routes in imitation. *Brain* 130 (4), 1111–1126. <https://doi.org/10.1093/brain/awm003>.
- Tessari, A., Mengotti, P., Faccioli, L., Tuozzi, G., Boscarato, S., Taricco, M., Rumiati, R.I., 2021. Effect of body-part specificity and meaning in gesture imitation in left hemisphere stroke patients. *Neuropsychologia* 151, 107720. <https://doi.org/10.1016/j.neuropsychologia.2020.107720>.
- Tessari, A., Rumiati, R.I., 2004. The Strategic Control of Multiple Routes in Imitation of Actions. *J. Exp. Psychol.: Hum. Percept. Perform.* 30, 1107–1116. <https://doi.org/10.1037/0096-1523.30.6.1107>.
- Toraldo, A., Reverberi, C., Rumiati, R.I., 2001. Critical Dimensions Affecting Imitation Performance of Patients with Ideomotor Apraxia. *Cortex* 37 (5), 737–740. [https://doi.org/10.1016/S0010-9452\(08\)70628-2](https://doi.org/10.1016/S0010-9452(08)70628-2).
- Tunik, E., Frey, S.H., Grafton, S.T., 2005. Virtual lesions of the anterior intraparietal area disrupt goal-dependent on-line adjustments of grasp. *Nat. Neurosci.* 8 (4), 505–511. <https://doi.org/10.1038/nn1430>.
- Turkeltaub, P.E., Eickhoff, S.B., Laird, A.R., Fox, M., Wiener, M., Fox, P., 2012. Minimizing within-experiment and within-group effects in Activation Likelihood Estimation meta-analyses. *Hum. Brain Mapp.* 33 (1), 1–13. <https://doi.org/10.1002/hbm.21186>.
- Urgesi, C., Candidi, M., Avenanti, A., 2014. Neuroanatomical substrates of action perception and understanding: An anatomic likelihood estimation meta-analysis of lesion-symptom mapping studies in brain injured patients. *Front. Hum. Neurosci.* 8 <https://doi.org/10.3389/fnhum.2014.00344>.
- Vanbellingen, T., Bertschi, M., Nyffeler, T., Cazzoli, D., Wiest, R., Bassetti, C., Kaelin-Lang, A., Müri, R., Bohlhalter, S., 2014. Left posterior parietal theta burst stimulation affects gestural imitation regardless of semantic content. *Clin. Neurophysiol.* 125 (3), 457–462. <https://doi.org/10.1016/j.clinph.2013.07.024>.
- de Vignemont, F., 2010. Body schema and body image—Pros and cons. *Neuropsychologia* 48 (3), 669–680. <https://doi.org/10.1016/j.neuropsychologia.2009.09.022>.
- Vry, M.-S., Tritschler, L.C., Hamzei, F., Rijntjes, M., Kaller, C.P., Hoeren, M., Umarova, R., Glauche, V., Hermsdörfer, J., Goldenberg, G., Hennig, J., Weiller, C., 2015. The ventral fiber pathway for pantomime of object use. *NeuroImage* 106, 252–263. <https://doi.org/10.1016/j.neuroimage.2014.11.002>.
- Watson, C.E., Buxbaum, L.J., 2015. A distributed network critical for selecting among tool-directed actions. *Cortex* 65, 65–82. <https://doi.org/10.1016/j.cortex.2015.01.007>.
- Watson, C.E., Gotts, S.J., Martin, A., Buxbaum, L.J., 2019. Bilateral functional connectivity at rest predicts apraxic symptoms after left hemisphere stroke. *NeuroImage: Clin.* 21, 101526 <https://doi.org/10.1016/j.nicl.2018.08.033>.
- Weiss, P.H., Ubben, S.D., Kaesberg, S., Kalbe, E., Kessler, J., Liebig, T., Fink, G.R., 2016. Where language meets meaningful action: A combined behavior and lesion analysis of aphasia and apraxia. *Brain Struct. Funct.* 221 (1), 563–576. <https://doi.org/10.1007/s00429-014-0925-3>.

- Wurm, M.F., Ariani, G., Greenlee, M.W., Lingnau, A., 2016. Decoding Concrete and Abstract Action Representations During Explicit and Implicit Conceptual Processing. *Cereb. Cortex* 26 (8), 3390–3401. <https://doi.org/10.1093/cercor/bhv169>.
- Wurm, M.F., Caramazza, A., Lingnau, A., 2017. Action Categories in Lateral Occipitotemporal Cortex Are Organized Along Sociality and Transitivity. *J. Neurosci.* 37 (3), 562–575. <https://doi.org/10.1523/JNEUROSCI.1717-16.2016>.
- Wurm, M.F., Caramazza, A., 2019. Lateral occipitotemporal cortex encodes perceptual components of social actions rather than abstract representations of sociality. *NeuroImage* 202, 116153. <https://doi.org/10.1016/j.neuroimage.2019.116153>.
- Wurm, M.F., Caramazza, A., 2022. Two 'what' pathways for action and object recognition. *Trends Cogn. Sci.* 26 (2), 103–116. <https://doi.org/10.1016/j.tics.2021.10.003>.
- Wurm, M.F., Lingnau, A., 2015. Decoding Actions at Different Levels of Abstraction. *J. Neurosci.* 35 (20), 7727–7735. <https://doi.org/10.1523/JNEUROSCI.0188-15.2015>.