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Authors: Mathieu Lesourd, François Osiurak, Josselin
Baumard, Angela Bartolo, Tim Vanbellingen, Emanuelle
Reynaud

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CEREBRAL CORRELATES OF IMITATION OF INTRANSITIVE GESTURES: AN INTEGRATIVE REVIEW OF NEUROIMAGING DATA AND BRAIN LESION STUDIES

Mathieu Lesourd[1,2*], François Osiurak[3,4], Josselin Baumard[5], Angela Bartolo[4,6], Tim Vanbellingen[7,8], and Emanuelle Reynaud[3]

[1] Aix Marseille Univ, CNRS, LNC, Laboratoire de Neurosciences Cognitives, Marseille, France
[2] Aix Marseille Univ, CNRS, Fédération 3C, Marseille, France
[3] Laboratoire d'Etude des Mécanismes Cognitifs (EA 3082), Université Lyon 2, France
[4] Institut Universitaire de France, Paris, France
[5] Normandie Univ, UNIROUEN, CRFDP, Rouen, France
[6] Laboratoire de Sciences Cognitives et Sciences Affectives (CNRS UMR 9193), Université de Lille, France
[7] ARTORG Center for Biomedical Engineering Research, Gerontechnology and Rehabilitation Group, University of Bern, Switzerland
[8] Neurology and Neurorehabilitation Center, Luzerner Kantonsspital, Switzerland

***CORRESPONDING AUTHOR:**

Mathieu Lesourd
Laboratoire de Neurosciences Cognitives (CNRS UMR 7291)
Aix-Marseille Université
3 place Victor Hugo
13003 Marseille
Email: mathieu.lesourd@univ-amu.fr

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Highlights

- Neuroimaging data and brain lesions concerning imitation of gestures are reviewed
- Imitation of intransitive gestures activates a bilateral fronto-parietal network
- More brain areas are involved in meaningless compared to meaningful gestures
- The angular gyrus is particularly important for body part coding
- These results question neuropsychological accounts on apraxia

Abstract

The aim of the present review is to investigate the cerebral correlates, more particularly the role of the parietal lobe, when imitating intransitive gestures, a task highly sensitive to apraxic errors. By providing an integrative review of functional imaging and brain lesion studies, we focused our attention on the meaning of gestures (meaningful and meaningless) and the body parts (finger and hand).

We found that imitation of intransitive gestures is relying upon a bilateral brain network including fronto-parietal areas irrespective of meaning or body parts. Moreover, we observed that while imitation of meaningful and meaningless gestures is predominantly impacted following left parietal lesions, more brain areas are engaged during meaningless gesture imitation. Concerning body parts, whereas imitation of hand postures is relying upon the left parietal lobe (angular gyrus), imitation of finger postures is more likely to be impaired following lesions in the frontal lobe, insula and basal ganglia.

These results question neuropsychological theories on apraxia and open promising avenues for a better understanding of apraxia.

***Keywords**: neuroimaging; brain-damaged patients; imitation; intransitive gestures; hand posture; finger posture; parietal lobe; apraxia*

Anatomical abbreviations

Abbreviations used in the text, tables and figures:

- aSMG: Anterior portion of SMG
- ACC: Anterior Cingulate Cortex
- AG: Angular Gyrus
- BA44: Broca Area (Brodmann Area 44)
- DIPSA: anterior dorsal intraparietal sulcus
- dPMC: dorsal Pre-motor Cortex (BA6)
- IFG: Inferior Frontal Gyrus
- IPL: Inferior Parietal Lobe
- IPS: Intraparietal Sulcus
- ITG: Inferior Temporal Gyrus
- MFG: Middle Frontal Gyrus
- phAIP: putative human homologue of anterior intraparietal area
- PO: Parietal Operculum
- PoG: Post-central Gyrus
- PrG: Pre-central Gyrus
- SFG: Superior Frontal Gyrus
- SMG: Supramarginal Gyrus
- SPL: Superior Parietal Lobe
- TPJ: Temporo-Parietal Junction
- vPMC: ventral Pre-motor Cortex (BA6)

1. Introduction

Apraxia is a motor control disorder which cannot be explained by “elemental” motor deficits nor by general cognitive impairment (De Renzi & Lucchelli, 1988; Heilman & Rothi, 1993). In the field of apraxia, an important distinction has been made between transitive (i.e., object-related) and intransitive actions. For instance, hammering a nail into a wall requires that the user holds a hammer in hand (i.e., actual use of tool). Thus, this action is typically considered as transitive. In contrast, intransitive gestures do not require to hold/manipulate a tool to be performed. Moreover, transitive and intransitive gestures can be either meaningful (MF) or meaningless (ML; see **Table 1**). Apraxic errors may occur for transitive gestures (i.e., actual use of tools and objects and pantomime of tool use) but also for intransitive gestures (i.e., imitation of meaningless gestures) (Goldenberg, 2009). Whereas recent neurocognitive reviews have centered their attention on transitive gestures, namely pantomimes of tool use (Niessen, Fink, & Weiss, 2014) and actual tool use (Ishibashi, Pobric, Saito, & Lambon Ralph, 2016; Reynaud, Lesourd, Navarro, & Osiurak, 2016), there is no available review on imitation of intransitive gestures.

< Insert **Table 1** about here >

1.1. Scope and purpose of the present review

The aim of the present work is twofold. First, to investigate the cerebral correlates of imitation[1] of intransitive gestures, as this task is very sensitive to detect apraxic deficits

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[1] There are several ways of copying behavior and each way to copy others’ actions might serve different functions and reflect distinct underlying processes (Byrne & Russon, 1998). In the neuropsychological assessment of praxis, *emulation* and *true imitation* are often explored. *Emulation* occurs when the observer copies the goal or the products of an action, but not the means used to achieve the goals. *True imitation* involves copying both the means and the goals of the actions performed by the demonstrator. *True imitation* and *emulation* both require that the observer copies the product (e.g., hand posture) but sometimes the means are

(Heath, Roy, Black, & Westwood, 2001). Second, to question neuropsychological theories on apraxia and particularly the involvement of the parietal lobes in imitation (e.g., Goldenberg *vs* Buxbaum account; see for example Chaminade, Meltzoff, & Decety, 2005). By providing an integrative review of functional (i.e., neuroimaging) and structural (i.e., brain lesion) studies, we will focus our attention on: (1) the meaning of gestures (i.e., MF/ML gestures); and (2) the body part specificity (i.e., finger/hand). Studying these two components are motivated by the observation of double dissociations between imitation of MF and ML gestures (Bartolo, Cubelli, Della Sala, Drei, & Marchetti, 2001) and between imitation of finger and hand postures (Goldenberg, 1999).

1.2. Neuropsychological observations

1.2.1. THE MEANING OF INTRANSITIVE GESTURES

Concerning the meaning of gestures, in the clinical assessment, subjects are asked to imitate either MF (e.g., waving goodbye, hitchhiking, etc.) or ML gestures once the demonstration made by the clinician is complete (i.e., delayed imitation; but see also Salter, Roy, Black, Joshi, & Almeida, 2004 for concurrent imitation). The interest of studying MF and ML gestures is based on several reports of patients showing selective impairments for imitating either MF or ML gestures. For instance, Goldenberg and Hagmann (1997) reported the case of two left brain-damaged (LBD) patients (LK and EN) who failed imitating ML gestures while MF gestures were preserved. However, in this study, the authors used MF transitive gestures (i.e., pantomime of tool use) rather than MF intransitive gestures for

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either available (i.e., hand posture displayed on a video; *true imitation*) or not (e.g., hand posture displayed on a picture; *emulation*). Hereafter, we will not distinguish *emulation* and *true imitation* and we refer to the term *imitation*.

imitation. A double dissociation between imitation of intransitive MF and ML gestures was reported by Bartolo et al. (2001): patient MF showed impaired imitation of MF gestures and preserved ML gestures, whereas patients BS and EE had the opposite pattern. This double dissociation has been also observed in a subsequent study by Tessari et al. (2007).

1.2.2. A PARTICULAR CASE OF MEANINGLESS GESTURES: THE HAND/FINGER POSTURES

Hand or finger postures are particular cases of ML gestures. Whereas imitation of finger postures requires that subjects reproduce a specific configuration of fingers, imitation of hand postures necessitates that subjects reproduce a hand position relative to a specific anchor point located on the face (i.e., nose, lib, neck, top head; Goldenberg, 1999). Goldenberg (1999) explored matching and imitation of ML postures in LBD and right brain-damaged (RBD) patients. In this study, RBD patients were found to make more errors with matching than with imitation. Regardless of whether imitation or matching was tested, RBD patients made more errors with finger than with hand postures. Another dissociation has been found between imitation of finger and hand postures within the left hemisphere (Goldenberg & Karnath, 2006). Disturbed imitation of finger postures was associated with left inferior frontal gyrus (IFG) lesions and underlying white matter, whereas disturbed imitation of hand postures was associated with lesions encompassing the left inferior parietal lobe (IPL) and the temporo-parieto-occipital junction. Taken together, these results suggest distinct involvement from intra- (anterior/posterior) and inter-hemispheric (left/right parietal) structures in hand/finger imitation.

1.3. Theoretical framework

These neuropsychological findings can be interpreted within the dual-pathway model of gesture imitation proposed by Rothi et al. (1991; see also Cubelli et al., 2000, for a similar model). According to this view, gesture imitation is subserved by both a 'sub-lexical' pathway, that enables the reproduction of perceived gestures irrespective of their content, and a 'lexical' pathway, through which gestures are produced by access to their meaning in the semantic memory. Whereas the lexical route is dedicated to MF gestures, the sub-lexical pathway prevalently processes ML gestures, but it could be used with MF gestures as well, when MF and ML gestures are presented intermingled within a block (Cubelli, Bartolo, Nichelli, & Della Sala, 2006; Tessari et al., 2007; Tessari & Rumiati, 2004). Although neuropsychological and neuroimaging studies have identified distinct neural correlates for the two routes (see Rumiati, Carmo, & Corradi-Dell'Acqua, 2009), evidence also indicates that neural representations of MF and ML gestures overlap in the parietal cortex (Goldenberg & Hagmann, 1997; Peigneux et al., 2004). Two theoretical frameworks focusing on the role of the left parietal lobe have attempted to explain the dissociation obtained in neurologically impaired patients between MF and ML gestures, namely "the categorical apprehension model" (Goldenberg & Hagmann, 1997) and "the representational and dynamic apraxia model" (Buxbaum, Kyle, & Menon, 2005). The predictions made by the two models are synthetized in **Table 2**.

< Insert **Table 2** about here >

1.3.1. THE CATEGORICAL APPREHENSION HYPOTHESIS (GOLDENBERG & HAGMANN, 1997)

In the categorical apprehension hypothesis, Goldenberg and Hagmann (1997) postulated that imitating gestures is based on the ability to configure a whole chain of mechanical relationships between multiple objects or multiple parts of objects, considering the human body as a multi-part mechanical object (Goldenberg, 2013). The categorical apprehension of spatial relationship may be supported by the left hemisphere and more precisely by the left IPL. According to the categorical apprehension of spatial relationships, the left parietal lobe may be fundamental for “body part coding” by decomposing the visual complexity of gestures into simple spatial relationships between a limited number of defined body parts (Goldenberg & Karnath, 2006; Goldenberg & Randerath, 2015).

Moreover, the authors suggested that, as the impact of inferior parietal lesions (i.e., angular gyrus; Goldenberg & Hagmann, 1997) is largely limited to ML gestures, categorical apprehension may be crucial specifically for the imitation of ML gestures (Goldenberg, 2009). Although no clear prediction was made concerning MF gestures, pre-existing representations in long term memory may support an alternative semantic route of imitation which can bypass categorical apprehension of spatial relationships (e.g., left inferior temporal gyrus; Rumiati et al., 2005).

Although the left parietal lobe presumably plays a major role in categorical apprehension, Goldenberg (2009) acknowledges the importance of the right parietal cortex in spatial and attentional processing (Husain & Rorden, 2003). Indeed, following RBD, imitation of finger postures was found to be particularly vulnerable compared to imitation of hand postures (Goldenberg, 1999) because perception of finger configurations may require the distribution of attention across five spatially distinct but otherwise fairly uniform elements (i.e., the fingers; Goldenberg, 2001). By contrast hand posture processing may be different as hand positions are determined by relationships between perceptually salient body parts (e.g., lips, ear, nose or the back and the palm of the hand). Thus, the ability to imitate hand configurations may rely upon general knowledge about the structure of the human body (i.e., conceptual mediation; Goldenberg, 1995; Goldenberg & Hagmann, 1997).

1.3.2. THE REPRESENTATIONAL AND DYNAMIC APRAXIA HYPOTHESIS (BUXBAUM ET AL., 2005)

In the representational and dynamic apraxia hypothesis, Buxbaum and colleagues (2005) distinguished two types of gesture representations: The “dynamic portion of gesture representation” and the “stored aspect of gesture representation”. The “dynamic portion of gesture representation” consists of representation of the body parts participating in a given action in a number of spatial reference frames. It is responsible for the imitation of ML actions using a direct mapping to transform an extrinsic code of the gesture (which reflects spatial relations between the body parts of the model) into an intrinsic code of the same relations in the imitator. The “stored aspect of gesture representation” stores gesture engrams (i.e., invariant and characteristic features of a given gesture). On the one hand, lesions to brain systems supporting the dynamic portion would be characterized by impairment in imitation of ML gestures with normal performance in MF gestures (e.g., visuoimitative apraxia; Goldenberg & Hagmann, 1997). Lesions in the left superior parietal lobe (SPL) are thought to be responsible for such apraxia (case B.G.; Buxbaum, Giovannetti, & Libon, 2000; but see Buxbaum, 2017, for bilateral SPL). However, in a recent work, Buxbaum and colleagues (2014) found that the left IPL - angular gyrus (AG) and supramarginal gyrus (SMG) - were critical to kinematics components of imitation of ML gestures. On the other hand, impairment of the stored gesture engrams would be characterized by a deficit in the production of MF gestures. Left inferior parietal lesions would be responsible for representational apraxia (i.e., impairment of the stored aspect of gesture representation). On this ground, there seems to be an overlap between the dynamic and the stored portion of gestures.

This theoretical account makes no clear predictions concerning the neuropsychological dissociations observed with hand and finger postures. According to Buxbaum (2005, 2017), ML gestures are processed within the dynamic portion of gesture representation which is dedicated to the transformation of an extrinsic code of the gesture into an intrinsic code of the same relations in the imitator. Thus, a deficit of imitation of hand/finger postures may be associated with lesions within left/bilateral SPL or/and left IPL.

1.4. Predictions

To sum up, the "categorical apprehension" and "the representational and dynamic apraxia" hypotheses offer two different alternative hypotheses to understand the relationships between parietal lesions and clinical deficits of brain-damaged patients in MF/ML and hand/finger imitation tasks. Predictions are synthetized in **Table 2**.

Imitation is a higher-order function that is predominantly disturbed following left parietal lesions (Buxbaum, 2001; Buxbaum et al., 2005; Goldenberg, 1999; Goldenberg & Hagmann, 1997), however other brain regions are involved during imitation. For instance, it is well-known that imitation engages fronto-parietal network (e.g., Mirror Neuron System; see for example Iacoboni et al., 1999). Thus, we also attempt to identify brain activations and/or lesions in brain areas that were not documented in the first section of this article. Brain structures reported in the results section will be discussed regarding the literature on imitation.

2. Method

2.1. Selection of studies

The aim of the present work is to better understand the cerebral correlates of intransitive gesture imitation. To do so, we searched for functional imaging studies (i.e., fMRI or PET) in healthy subjects and for structural studies (i.e., brain-damaged patients and virtual lesions using Transcranial Magnetic Stimulation studies), using the search engines "PubMed" and “PsycInfo”. We restricted our search to studies published between January 2000 and June 2017. Two authors (ML and ER) independently conducted the literature search, assessed the methodological quality of the included studies and screened the studies for the inclusion criteria.

2.1.1. NEUROIMAGING STUDIES

For the selection of functional imaging studies, we first used the terms ‘imitation’ AND ‘neuroimaging’ to identify studies of interest. This search returned 311 studies at the date of 01/06/2017. We initially identified 39 relevant studies and then restricted our selection to studies that met a series of selection criteria:

(1) Reviews were excluded.

(2) Papers had to use functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) as imaging modality.

(3) Only neurologically healthy adults were included.

(4) Relevance of the tasks used in relation to the scope of the present work. Only intransitive (i.e., non-use tasks) stimuli were included.

(5) Neuroimaging results had to be based on whole-brain scanning. Regions of interest analyses were therefore excluded from our selection.

(6) The complete list of activation peaks (i.e., foci) of main effects (i.e., conjunction analyses were not considered) with their coordinates had to be reported in a stereotactic space.

(7) We selected only reported results corrected for multiple comparisons with a statistical significance threshold of $p < .05$.

The final selection resulted in 17 studies (26 experiments) fulfilling our criteria, involving a total of 227 subjects and 312 peaks of activation. These studies are described in **Table 3.** We did not compute activation likelihood estimation (ALE) maps for meaning of gesture (i.e., MF/ML) nor for body parts (i.e., finger/hand), given the lack of data for some of the conditions (e.g., only 5 experiments included a MF condition). Consequently, although this design may give four experimental conditions (i.e., MF finger, MF hand, ML finger and ML hand postures), we did not consider these conditions together (e.g., only 2 experiments using MF finger postures were found).

< Insert **Table 3** about here >

2.1.2. STRUCTURAL STUDIES

For the selection of structural studies, we first used the terms 'imitation' AND 'brain lesions' to identify studies of interest. This search returned 80 studies at the date of 01/06/2017. We restricted our selection to 13 studies: 8 brain-damaged and 5 Transcranial Magnetic Stimulation (TMS) studies (see **Table 4** and **Table 5**, respectively).

We selected brain-damaged studies according to a series of criteria:

(1) Only patients presenting exclusively LBD or RBD were considered.

(2) Single case studies were not included.

(3) Studies using one of the following lesion mapping method were included: lesion-subtraction analysis (e.g., Goldenberg & Karnath, 2006) and voxel-based lesion symptom mapping (e.g., Kimberg, Coslett, & Schwartz, 2007).

(4) Reports had to provide lesion peaks data or at least overlay lesion plots associated with selective disturbances.

The final selection resulted in 8 studies including 494 LBD patients (no studies including RBD patients met our criteria). These studies are described in **Table 4**. We reported 72 maximum lesion overlap locations (see section *2.2.2. Analysis of structural data* for the method). According to the meaning of gesture, we found 56 maximum lesion overlap locations that caused defective imitation of ML gestures, 2 that caused defective imitation of MF gestures and 14 that were associated with both defective imitation of MF and ML gestures. According to the body parts, we reported 22 maximum lesion overlap locations that caused defective imitation of finger postures and 18 that caused defective imitation of hand postures (no precisions were given for the remaining 20).

< Insert **Table 4** about here >

We selected TMS studies according a series of selection criteria:

(1) Studies had to employ stimulation parameters known to interfere with brain activity, that is double pulse, low or high frequency, or continuous theta burst.

(2) Studies had to include only neurologically healthy subjects.

(3) Stimulations made on either left or right hemisphere were considered.

(4) Stimulation coordinates had to be reported in a stereotactic plane (i.e., MNI or Talairach).

The final selection resulted in 5 studies including 73 healthy controls. These studies are described in **Table 5**. We considered 31 brain stimulation sites (16 left and 15 right).

Finally, both TMS and brain-damaged patients studies had to consider only relevant tasks in relation to the scope of the present work (see also point 4 in section *2.1.1. Neuroimaging studies*), namely intransitive stimuli.

< Insert **Table 5** about here >

2.2. Data analysis

2.2.1. ANALYSIS OF FUNCTIONAL DATA

The meta-analysis of functional imaging studies was conducted using the revised version (Eickhoff et al., 2009; Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012) of the Activation Likelihood Estimation (ALE; Turkeltaub, Eden, Jones, & Zeffiro, 2002) method, as implemented by the GingerALE 2.3 software (http://www.brainmap.org/ale/). ALE is a coordinate-based method for pooling neuroimaging studies results. Its aim is to reveal brain regions that are reliably activated across studies. Based on the stereotactic coordinates of activation peaks collected in each study included in the meta-analysis, this method estimates at each voxel the probability that an activation focus truly exists within that given voxel, under Gaussian assumptions on spatial uncertainty. The voxel-wise union of probabilities over all activation foci permits to create an ALE map. Clusters of significantly high ALE are the significantly overlapping clusters of activation, revealing a convergence across included imaging studies.

To perform this meta-analysis, coordinates of every significant activation peak for each considered study were collected. The meta-analysis was performed in the Talairach reference space (Talairach & Tournoux, 1988). Coordinates that were reported in the Montreal Neurological Institute (MNI) space were first converted to Talairach space using the icbm2tal transformation (Lancaster et al., 2007) implemented in the GingerALE software. For each included study and at each voxel, ALE computes the probability that an activation focus lies at this voxel location. To account for spatial uncertainty, foci are considered to be the centers of three-dimensional Gaussian probability density functions. Full-widths-at-half maximum of the 3D Gaussian functions (FWHM) are dependent on the sample size, hence studies with a larger sample size have a stronger impact on the results.

The probability distributions of all foci in the considered experiment are combined in a Modelled Activation (MA) map. The union of all MA maps for all the experiments included in the meta-analysis allows computing an ALE score on a voxel-by-voxel basis. This score quantifies the likelihood of convergent activations at each voxel across all included studies. Significance tests are conducted by comparing the ALE scores with a null distribution obtained from the same number of randomly generated activation foci. All foci from a generic contrast are pooled together: The resulting non-parametric p-values are then thresholded at a false discovery rate (FDR) of $p < .05$, and clusters of a minimum volume of 120 mm^3 are reported.

Finally, the resulting thresholded ALE maps are visualized on fiducial and flat-map representations of a standardized brain atlas (PALS-B12: Population-Average, Surface- and Landmark-based human cortical atlas; Van Essen, 2005), using Caret, version 5.65 (http://brainmap.wustl.edu/caret.html; Van Essen et al., 2001).

2.2.2. ANALYSIS OF STRUCTURAL DATA

We processed the lesions based on the information available in the studies included in this work. Indeed, either coordinates of the lesion sites or overlay lesion plots were given.

When coordinates lesions were available, we depicted the location of the reported lesion sites on flat-map representations of a left or right hemisphere (PALS-B12: Population-Average, Surface- and Landmark-based human cortical atlas; Van Essen, 2005), using Caret, version 5.65 (http://brainmap.wustl.edu/caret.html; Van Essen et al., 2001). If stimulation or lesion coordinates were reported in MNI space, we first transformed them into Talairach-coordinates (Lacadie, Fulbright, Constable, & Papademetris, 2008). For one study (Heiser, Iacoboni, Maeda, Marcus, & Mazziotta, 2003), stimulations were made in BA 44 but no coordinates were provided. Thus, we obtained the approximate coordinates corresponding to BA 44 from the atlas of Talairach and Tournoux (1988).

If only overlay lesion plots were reported in the study, we made several transformations before depicting the lesions sites on the flat-map, by adopting a three-step method (**Fig.1**), very similar from the one used by Niessen et al. (2014).

< Insert **Figure 1** about here >

First, from the lesion sites depicted in the overlay plots, we identified the maximum lesion overlap locations for each slice reported (**Fig.1a**). Second, we projected the maximum lesion center onto the corresponding slice of the standard template brain (Colin27_T1_seg_MNI) provided by MRIcron to obtain the corresponding coordinates (**Fig.1b**) and we systematically used the Talairach Daemon (www.talairach.org/applet.html) to find the nearest grey matter for labelling each maximum lesion overlap coordinates (e.g., BA39, parietal lobe). Third, after transformation of MNI-coordinates into Talairach space, each coordinate was depicted on a flat-map representation of the corresponding hemisphere (**Fig.1c**). Finally, we used a specific shape (i.e., square: TMS stimulation; circle: brain-damage lesions), and a color depending on the deficit observed following this lesion (e.g., red: MF gestures or finger postures; green: ML gestures or hand postures, red and green: ML and MF gestures or hand and finger postures) and a number for each depicted lesion (e.g., 3: Goldenberg & Karnath, 2006). Note that conditions including either body parts or meaning of gestures are not mixed together, thus lesions associated with selective disturbance of hand or finger postures and lesions associated with MF or ML postures are represented in distinct figures.

3. Results

3.1. Functional data

We identified "the intransitive gesture imitation" network as defined by the regions of overlap between all the neuroimaging studies included. The results of the meta-analysis are given in **Fig.2**. A set of bilateral brain regions was consistently recruited (1) in the temporal cortex, namely, the right inferior temporal gyrus (ITG); (2) in the parietal cortex, namely, the SMG, the intraparietal sulcus (IPS) and the left post-central gyrus (PoG); and (3) in the frontal cortex, namely, the left superior frontal gyrus (SFG), the right middle frontal gyrus (MFG), the IFG (BA44), the left anterior cingulate cortex (ACC) and the pre-central gyrus (PrG). We also found strong activation in the right insula. This network is largely consistent with a previous meta-analysis that investigated the cerebral correlates of imitation (Caspers, Zilles, Laird, & Eickhoff, 2010) and is similar to the well-known core circuitry for imitation (e.g., Iacoboni, 2005).

< Insert **Figure 2** about here >

3.2. Structural data and meaning of gestures

A summary of the localization of brain lesions according to their impact on the meaning of gesture is displayed in **Table 6**.

< Insert **Table 6** about here >

MF and ML gestures. As can be seen in **Fig.3**, we reported 72 maximum lesion overlap locations (all located in the left hemisphere) and 31 stimulation sites (28 in the left and 3 in the right hemisphere). Concerning brain lesions, imitation of both MF and ML gestures was impaired predominantly after parietal lesions (40%, *n* = 29/72), and to a lesser extent following frontal (13%, *n* = 9/72), occipital (11%, *n* = 8/72), temporal (8%, *n* = 6/72) and insula (10%, *n* = 7/72) lesions. Interestingly, lesions in the white matter (10%, *n* = 7/72) and basal ganglia (8%, *n* = 6/72) were also associated with a deficit in imitation of both MF and ML gestures. Moreover, imitation of MF and ML gestures can be both impaired following same parietal lesions (Weiss et al., 2016). In line with this result, brain stimulations of IPL and SPL impaired both imitation of MF and ML gestures (Vanbellingen et al., 2014). Finally, stimulations applied over left BA44 produced a deficit for imitating both MF and ML gestures (Bohlhalter et al., 2011).

< Insert **Figure 3** about here >

MF gestures only. Lesions leading to a deficit in MF gesture imitation were located predominantly in the parietal lobe (50%, *n* = 8/16). More particularly, 19% (*n* = 3/16) of lesions were found in IPL (all in SMG) and 31% (*n* = 5/16) were observed in somatosensory cortices (BA1,2,3). Lesions were also found in the white matter (31%, *n* = 5/16), frontal lobe (13%, *n* = 2/16) and temporal lobe (6%, *n* = 1/16). The importance of white matter in MF gestures should be considered carefully as only one study reported all the maximum lesions overlap locations in the white matter (Binder et al., 2017). Brain stimulations confirmed the role of the parietal lobe for imitation of MF gesture imitation but they also stressed the role of frontal structures as brain stimulation made in the left IFG (BA44) produced an impairment for MF gesture production (Bohlhalter et al., 2011). Once again, this result should be considered carefully as Bohlhalter et al. (2011) mixed both transitive and intransitive gestures (i.e., TULIA; Vanbellingen et al., 2010).

ML gestures only. Lesions leading to a deficit in ML gesture imitation were also located predominantly in the left parietal lobe (40%, *n* = 23/58). More particularly, 33% (*n* = 19/58) of lesions were found in IPL (21% in AG and 12% in SMG), 5% (*n* = 3/58) of lesions were found in SPL (BA5,7) and 2% (*n* = 1/58) were reported in somatosensory cortices (BA1,2,3). To a lesser extent, lesions were found in occipital (14%, *n* = 8/58), frontal (12%, *n*

= 7/58), temporal (9%, *n* = 5/58) lobes and insula (12%, *n* = 7/58). Lesions in basal ganglia and white matter are also involved in ML gesture imitation deficits (10%, *n* = 6/58 and 3%, *n* = 2/58, respectively).

Right hemisphere. No studies including RBD patients were reported and only three brain stimulation studies were available (Heiser et al., 2003; Mengotti, Ticini, Waszak, Schütz-Bosbach, & Rumiati, 2013; Sowden & Catmur, 2015). These three studies showed that perturbing neural activity in the right IFG, in the right temporo-parietal junction (TPJ) or in the right parietal operculum (PO) may lead to a deficit in ML gesture imitation.

3.3. Structural data and body parts

A summary of the localization of brain lesions according to the body parts is displayed in **Table 6**.

Hand and finger postures. As it can be seen in **Fig.4**, we reported 40 maximum lesion overlap locations (all in the left hemisphere) and 5 stimulation sites (2 in the left and 3 in the right hemisphere). Concerning brain lesions, imitation of both hand and finger postures was impaired predominantly after parietal lesions (35%, *n* = 14/40), and to a lesser extent following basal ganglia (15%, *n* = 6/40) and occipital lobe (12.5%, *n* = 5/40) lesions. Lesions in the insula (12.5%, *n* = 5/40), the temporal lobe (10%, *n* = 4/40), the frontal lobe (10%, *n* = 4/40) and in white matter (5%, *n* = 2/40) were also associated with a deficit for imitating both hand and finger postures. Considering brain stimulations, all the stimulated sites were associated with defective imitation of both hand and finger postures.

< Insert **Figure 4** about here >

Hand postures only. Lesions leading to an impairment of imitation of hand postures were located predominantly in the parietal lobe (66.5%, *n* = 12/18). More particularly, 61% (*n* = 11/18) of lesions were found in IPL (44% in AG and 17% in SMG) and 5.5% (*n* = 1/18) in

SPL (BA5,7). Lesions associated with defective imitation of hand postures were also found in temporal lobe (17%, *n* = 3/18), occipital lobe (11%, *n* = 2/18) and insula (5.5%, *n* = 1/18).

Finger postures only. The distribution of the maximum lesion overlap location for finger posture imitation was less straightforward than for imitation of hand posture imitation. Indeed, lesions leading to a deficit in imitating finger postures were found mostly in basal ganglia (27%, *n* = 6/22) and to a lesser extent in the insula (18%, *n* = 4/22), the frontal lobe (18%, *n* = 4/22), the temporal lobe (9%, *n* = 2/22), the occipital lobe (14%, *n* = 3/22) and white matter (5%, *n* = 1/22). Finally, only two lesions were located in the left parietal cortex (9%, *n* = 2/22), one in IPL (AG) and the other in SPL (BA5,7).

Right hemisphere. No studies including RBD patients were reported. The 3 TMS studies already reported in section 3.2 showed that a virtual lesion in the right IFG, in the right TPJ or in the right PO may lead to an impairment of finger gesture imitation.

4. Discussion

The aim of this work was to provide an integrative review of functional and structural studies to better understand the cerebral correlates of intransitive gesture imitation. To do so, we chose to study specifically two dimensions, namely, the meaning of gestures (i.e., MF *vs* ML) and the body part specificity (i.e., hand *vs* finger), taken as a particular case of ML gestures. This endeavor has clinical importance since neuropsychological dissociations have been reported for meaning and body parts (Bartolo et al., 2001; Goldenberg, 1999; Tessari et al., 2007). We considered these neuropsychological dissociations through the prism of two neurocognitive hypotheses which both acknowledge the major role of the parietal lobes for imitation, namely the “categorical apprehension” (Goldenberg, 2013; Goldenberg & Hagmann, 1997) and the “dynamic and representational apraxia” (Buxbaum et al., 2005) hypotheses. A deficit in imitation often occurs following left parietal damage (e.g., Goldenberg, 2009) but other brain structures are involved in imitation (Mirror Neuron System; Iacoboni, 2005), which is why we also investigated the role of frontal structures.

4.1. It takes the whole brain to imitate intransitive gestures

Our comprehensive review of functional and structural data revealed that imitation of intransitive gestures is sustained by a large bilateral brain network (**Fig.5**). This network is coherent with the one identified by a recent meta-analysis of functional brain-imaging studies on imitation (Caspers et al., 2010). Our work goes further by combining these results with brain lesions and non-invasive stimulation studies, thereby revealing which subsets of regions are indeed crucial for intransitive gesture imitation. We now discuss the relevance of the main areas of this network.

< Insert **Figure 5** about here >

In the parietal lobe, functional data revealed consistent involvement of bilateral IPL and left SPL. Moreover, structural data showed that imitation of intransitive gestures was impaired mostly following left parietal lesions, thus confirming the major role played by this structure in imitation. Concerning the IPL, SMG (i.e., aSMG/PFt) and AG were both associated with defective imitation of intransitive gestures. The area aSMG/PFt has been described as an integrative hub for controlling transitive gestures (i.e., actual tool use; Reynaud et al., 2016) and our results suggest that aSMG/PFt may play the same role with intransitive gestures. We also found that lesions damaging the AG were reliably associated with defective imitation of ML gestures, which suggest that the AG may be essential for body part coding (Goldenberg, 2009). We found a strong involvement of the bilateral IPS (phAIP) which is often associated with hand-object interactions (e.g., Reynaud et al., 2016). However, it has been observed that the phAIP may be critically involved in the dynamic control of action at a goal level. Thus, its function might extend beyond low-level representation of grasp configuration (for a review see Tunik, Rice, Hamilton, & Grafton, 2007).

Concerning frontal regions, we found bilateral activations of the IFG (BA44) during imitation. Brain lesions occurring in left/right BA44 were also systematically associated with a deficit of ML gesture imitation. In line with this result, a recent meta-analysis reported reliable bilateral activations of IFG (BA44) during imitation (Caspers et al., 2010). Moreover IFG is involved in the processing of gestures communicative intentions during imitation (Mainieri, Heim, Straube, Binkofski, & Kircher, 2013). IFG also sustains gesture recognition (Villarreal et al., 2008; but see also Kalénine, Buxbaum, & Coslett, 2010 for a different observation): While the right IFG is engaged during recognition of gestures whatever the final goal, the left IFG is specifically involved during intransitive gesture recognition. Moreover, the left IFG is also involved in control of imitation (Cross, Torrisi, Reynolds Losin, & Iacoboni, 2013). Thus, our results may suggest that IFG (BA44) enables: (1) to detect meaning and communicative intentions; and (2) to control imitation, in cooperation with other frontal regions. Interestingly, we also found that 12% of lesions leading to defective imitation of ML gesture were located in the left insula, which is associated, as left BA44, with control of imitation (Cross et al., 2013). We also found activation in ACC, which supports many different mental functions (see for example Medford & Critchley, 2010). The ACC is a region where regulatory and executive processes interact (Paus, 2001) and it is particularly implicated in on-line behavioral adjustment (Magno, Foxe, Molholm, Robertson, & Garavan, 2006) and in the monitoring of action and the awareness of action-error (Klein et al., 2007). Finally, we observed activation in bilateral pre-motor areas (BA6) and in the left motor cortex (BA4) corresponding to upper limb representations in known somatotopic motor maps (Lotze et al., 2000).

We also found a strong activation in the right insula. Recently it has been proposed that insular cortex may play a critical role in the genesis of our self-awareness of limb movement and our sense of limb ownership (Karnath & Baier, 2010). The right insula seems to be involved in integrating input signals related to self-awareness about the functioning of body-parts, but it also plays a role in our awareness that our arms and legs belong to us and not to someone else. After RBD, patients may experience disturbed sense of agency (i.e., “anosognosia for hemiparesis/-plegia”) or disturbed sense of limb ownership (i.e., asomatognosia or somatoparaphrenia). Moreover, clinical observations of patients with brain lesions have indicated that disturbances of these senses occur more following RBD than LBD (Baier & Karnath, 2005). Thus, the right insula constitutes a central node of the network involved in human body schema representation. According to our data, one may assume that, to imitate someone else, we must integrate signals from different parts of our body and distinguish them from body parts of the model we are imitating. The right IPL is also involved in this function (Decety & Sommerville, 2003). Further studies are needed to investigate specifically the role of the right insula in imitation.

Our structural analyses also stress the potential involvement of subcortical structures, namely, the basal ganglia. For instance, we found that lesions in basal ganglia were associated with impairment of finger posture imitation. These subcortical structures play an important role in praxis, presumably via connections with frontal and parietal cortices (Leiguarda, 2001). Apraxia has been demonstrated in patients with subcortical vascular injury (Hanna-Pladdy, 2001) and also in patients with various movement disorders, including Parkinson’s disease, supranuclear palsy or cortico-basal degeneration (Soliveri, Piacentini, & Girotti, 2005), all of which compromise the basal ganglia. Nevertheless, it is not clear whether isolated basal ganglia dysfunction causes significant apraxia (Hermsdörfer et al., 2001).

Another possibility is that lesions in the basal ganglia involve surrounding white matter tracts, which may lead to deafferentation of frontal and parietal structures. In line with this notion, we found an important number of lesions in the frontal lobe (18%) associated with impairment of finger posture imitation, suggesting that frontal structures are of first importance for processing imitation of finger postures.

The present review puts forward fronto-parietal regions, but we found that lesions in other brain areas (e.g., temporal lobe: 8% and occipital lobe: 11%) were also associated with defective imitation, stressing their importance in imitation. Moreover, an important point of this study was the lack of data concerning brain lesions reported in the right hemisphere. Indeed, we did not find studies with RBD patients and there were only three studies that used TMS over the right hemisphere (Heiser et al., 2003; Mengotti, Ticini, et al., 2013; Sowden & Catmur, 2015). Interestingly all these studies reported impaired imitation following brain stimulations applied over either the right TPJ, the right BA44 or the right PO. Thus, the right hemisphere plays a role in imitation (e.g., De Renzi, 1980; Goldenberg, 1999; Husain & Rorden, 2003) and it is unfortunate that most studies on brain-damaged patients focus exclusively on the left hemisphere.

4.2. Neurocognitive hypotheses of intransitive gesture imitation

We looked at the predictions made by two neurocognitive hypotheses, namely the ‘categorical apprehension’ and the ‘dynamic and representational apraxia’ hypotheses. In this section, we compare these predictions with the results obtained in the present review.

4.2.1. The Meaning of gestures

According to the meaning of gestures, the ‘categorical apprehension’ hypothesis postulates that the left IPL – and more particularly AG – sustains imitation of ML gestures whereas the ‘dynamic and representational apraxia’ hypothesis assumes that the left IPL and left/bilateral SPL are involved in the ability to imitate ML gestures. Both hypotheses predict a major role of the left IPL but only the ‘categorical apprehension’ hypothesis stresses the critical involvement of AG in ML gesture imitation. Concerning imitation of MF gestures, the ‘categorical apprehension’ hypothesis does not make clear predictions on the brain structures whereas the ‘dynamic and representational apraxia’ hypothesis assumes that imitation of MF gestures relies upon the left IPL.

We found that 40% of lesions leading to a deficit of ML gestures and 50% of lesions leading to a deficit of MF gestures were located in the left parietal lobe, suggesting this lobe plays a key role irrespective of the meaning of gestures. In line with this observation, we found that brain stimulations of the left parietal lobe (IPL and SPL) produced a deficit in imitating both MF and ML gestures (Vanbellingen et al., 2014). This result is at odds with the ‘categorical apprehension’ hypothesis which suggests that ML gestures are more likely to be affected by left parietal lesions than MF gestures.

Concerning ML gestures, 33% of lesions were found in the left IPL (21% in AG and 12% in SMG), 5% in SPL and 2% in somatosensory cortices. Thus, within the left parietal cortex, the IPL is of particular importance when imitating ML gestures (Goldenberg, 2009). In line with the ‘categorical apprehension’ hypothesis, a lesion in AG is reliably associated with ML gesture impairment (Goldenberg & Hagmann, 1997). To a lesser extent, a lesion within SMG is also associated with the imitation of ML gestures (Buxbaum et al., 2014). Finally, in accordance to the ‘dynamic and representational’ hypothesis, lesions and activation data reported here both indicate a role of the SPL.

Amongst lesions affecting MF gestures, only 19% of lesions were found in left IPL (all in SMG) and 31% in somatosensory cortices. This result is in contradiction with the ‘dynamic and representational apraxia' hypothesis, which suggests that the left IPL is the locus of gesture engrams (Buxbaum, 2001; Haaland, Harrington, & Knight, 2000; Van Elk, 2014). If so, then we should have found a higher proportion of lesions within the left IPL concerning MF gestures, which was not the case. A possibility may be that MF gestures are processed according to a semantic route relying on temporal regions (i.e., inferior temporal gyrus; Rumiati et al., 2005), however, only 6% of lesions leading to MF gesture impairment were found in the temporal lobe but no lesions were found in the left inferior temporal gyrus. However, our results concerning MF gestures must be considered carefully, as only 16 lesions (3 studies) have been reported and 31% of them were found within the white matter. Thus, this distribution could be biased given the small number of lesions available for MF gestures.

4.2.2. THE BODY PARTS

Regarding body parts, the 'categorical apprehension' hypothesis posits that the left IPL sustains imitation of hand postures and the right IPL sustains imitation of finger postures whereas the 'dynamic and representational apraxia' hypothesis posits that left/bilateral SPL are involved in both hand/finger postures imitation.

Although 35% of lesions leading to a deficit of hand/finger posture imitation were situated in the left parietal cortex, we found a substantial difference between hand and finger postures. Indeed, whereas 66.5% of lesions in the left parietal cortex were associated with an impairment of imitation of hand postures, only 9% of lesions leading to an impairment of imitation of finger postures were in the left parietal cortex. This suggests that the left parietal cortex does not represent different types of ML gestures in the same way and its role in processing imitation of finger postures seems to be limited. This finding is clearly in line with the categorical apprehension hypothesis which assumes that imitation of hand postures depends more on the left parietal cortex than imitation of finger postures (Goldenberg, 2001; see also Della Sala, Faglioni, Motto, & Spinnler, 2006, for contradictory results).

Concerning hand postures, 61% of lesions were found in the left IPL (44% in AG and 17% in SMG) and 5.5% in SPL. For imitation of hand postures, the categorical apprehension of spatial relationships is fundamental for "body part coding" that decomposes the visual complexity of gestures into simple spatial relationships between a limited number of defined body parts (de Vignemont, 2010; Goldenberg & Karnath, 2006; Goldenberg & Randerath, 2015b). Thus, the left parietal cortex and more particularly the AG plays a key role in processing categorical apprehension of spatial relationships.

Concerning finger postures, 9% of lesions were found in the left parietal cortex: One lesion was found in IPL (AG) and the other in SPL (BA5,7). These data are at odds with the predictions made by the 'dynamic and representational apraxia' hypothesis in that few lesions were found in the left SPL associated with a deficit of hand (5.5%) and finger (4.5%, only 1 lesion) posture imitation.

4.2.3. 'CATEGORICAL APPREHENSION' AND 'DYNAMIC AND REPRESENTATIONAL APRAXIA' HYPOTHESES AND THE PARIETAL LOBE

To sum up, we found that lesions affecting the left IPL may lead to defective ML gesture imitation and hand posture imitation (33% and 61% of lesions, respectively) and, at a lower extent, to defective MF gesture imitation (19% of lesions). We also found that lesions affecting the left SPL have little impact on hand posture (5.5%) and finger posture imitation (only one lesion), but virtual transient lesions made in the left SPL, using non-invasive brain stimulation, can impact imitation of both MF and ML gestures (Vanbellingen et al., 2014). These results have two important implications.

First, the left IPL may not play a major role in the representation of gesture engrams. The idea that the left IPL is the locus of gesture engrams has already been challenged for transitive gestures (Lesourd, Osiurak, Navarro, & Reynaud, 2017; Osiurak, Jarry, & Le Gall, 2011) and it seems to be similar for intransitive MF gestures. Even though these data do not confirm the categorical apprehension hypothesis with regards to MF gestures (this hypothesis does not allow clear predictions on this point), they tend to rule out the 'dynamic and representational apraxia' hypothesis. Second, the left and right parietal cortices may assume distinct role in terms of body part specificity, which is more in line with the 'categorical apprehension' hypothesis. Structural data indicate that the left IPL, but not the right SPL, sustains body part coding and functional data revealed activation of right frontal and parietal structures that are involved in attentional functions. Indeed, IFG, IPL, IPS, MFG and insula were activated and brain stimulations of the right TPJ lead to a deficit when imitating intransitive gestures. Shifting attention is associated with superior parietal lobe activations whereas sustaining attention activates inferior parietal lobe (Vandenberghe, Gitelman, Parrish, & Mesulam, 2001) and middle frontal gyrus (Sturm et al., 1999). Visual salience was found to be associated with TPJ and inferior frontal regions (Downar, Crawley, Mikulis, & Davis, 2001). Finally visual selective attention was associated with IPS and insula (Sarter, Givens, & Bruno, 2001). Thus, imitating intransitive gestures may require attentional processes supported by the right hemisphere (Goldenberg, 1999, 2001), that is, sustained attention, processing of visual saliency and visual selective attention. However, no lesion data including the right parietal lobe were available, thus further studies are needed to assess specifically the link between imitation of hand/finger postures and the right hemisphere.

Considering parietal lobes, our results are more in line with the 'categorical apprehension' hypothesis than with the 'dynamic and representational apraxia' hypothesis.

However, our results showed that other brain structures and not only parietal lobes are involved when imitating intransitive gestures. Thus, a neurocognitive model of intransitive gesture imitation must consider the participation of other critical brain structures (e.g., left and right BA44/45).

4.3 Cerebral correlates of neuropsychological dissociations of imitation of intransitive gestures

At the beginning of the present paper, we presented two kinds of neuropsychological dissociations between imitation of MF and ML gestures and between imitation of hand and finger postures. These dissociations have been well documented in the literature on apraxia (Bartolo et al., 2001; Goldenberg, 1999). Nevertheless, based on the present findings, one may ask how these dissociations observed at the behavioral level are occurring at the cerebral level.

Concerning the meaning of gestures, the present study did not reveal a striking dissociation between the cerebral correlates sustaining MF and ML gestures: a lesion occurring in the left parietal lobe can disrupt both imitation of MF and ML gestures (Vanbellingen et al., 2014; Weiss et al., 2016). However, even if imitation of MF and ML gestures shares some neural resources, our analyses revealed that lesions leading to imitation of ML gesture impairment were more widespread than for MF gestures. Aside from parietal regions, lesions affecting more brain regions are likely to be associated with ML gestures deficit (occipital: 14%; frontal: 12%; temporal: 9%; insula: 12%; white matter/basal ganglia: 13%) than with MF gesture impairment (white matter: 31%; frontal: 13%; temporal: 6%). This suggests that processing novel gestures may rely upon a widespread brain network sustaining distinct functions whereas familiar symbolic gestures may rely upon a more restricted network. It is assumed that novel gestures can be imitated using a *sub-lexical route* whereas familiar gestures can be imitated using a *lexical route* (Bartolo et al., 2001; Rothi, Ochipa, & Heilman, 1991; Rumiati et al., 2009; Tessari et al., 2007; Tessari & Rumiati, 2004). The *sub-lexical route* is dedicated predominantly to the imitation of novel gestures and may rely upon bilateral dorso-dorsal pathways (i.e., the 2AS+ model; Buxbaum, 2017). This vision is not so far from the 'direct matching hypothesis' which postulates a common coding between perception and action (Iacoboni et al., 1999), and shared spatiomotor representations between observation and execution of actions. However, recent investigations in cognitive psychology and neuropsychology suggest that imitation of ML gestures relies on visuo-motor imagery (Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005; see also Lesourd, Navarro, et al., 2017) and depends also on body knowledge (i.e.; conceptual mediation; Goldenberg & Hagmann, 1997). Thus, the so-called direct route may not be as direct as it has been proposed (Goldenberg, 2013a; p.96) and our results confirm that imitation of ML gestures is sustained by a large network including brain areas undoubtedly involved in distinct cognitive processes.

Concerning imitation of hand and finger postures, we found a striking dissociation between brain-damaged structures associated with defective hand and finger imitation. Indeed, the proportion of lesions leading to defective imitation of hand and finger postures varied substantially in frontal (hand: 0% and finger: 18%) and parietal lobes (hand: 66.5% and finger: 9%). We reported here the anterior (finger)/posterior (hand) dissociation consistent with the results of a previous lesion subtraction analysis (Goldenberg & Karnath, 2006), and thus confirming the presence of both a behavioral and a neuroanatomical double dissociation between hand and finger imitation skills. However this result is challenged by a recent study, which used a multi-level Bayesian lesion-symptom mapping to investigate the body-part specificity in a large sample of 257 LBD patients (Achilles et al., 2017). The authors reported good evidence against a dissociation between hand and finger imitation skills at the voxel-level; instead, their analyses led them to conclude that hand and finger imitation share similar neural resources, in the occipital lobe and primary somatosensory/motor cortices. This result argues against the need to posit a ‘common code’ interposed between the perception and the reproduction of action. Moreover, only one study reported a neuroanatomical double dissociation between hand and finger imitation skills (Goldenberg & Karnath, 2006) and there was no evidence for this dissociation in more recent works which only reported a partial dissociation (Dovern et al., 2011; Hoeren et al., 2014). In line with the results from Achilles et al. (2017), we found that lesions occurring in the occipital lobe may lead to defective imitation of both hand and finger postures (11% and 14%, respectively) but no lesions in the somatosensory cortex were associated with any type of body part imitation impairment. We also found a strong involvement of the left parietal lobe (i.e., AG) for hand posture imitation which is at odds with the results from Achilles et al. (2017). Further studies are needed to resolve the discrepancies observed here.

To explain the neuroanatomical dissociation observed between hand and finger imitation, two hypotheses can be proposed. First, as multiple distinct representations of the human body have been proposed (i.e., body structural description, body image and body schema; Schwoebel & Coslett, 2005), it is possible that imitation of hand and finger postures relies on distinct representations of the human body and therefore on distinct cerebral regions. Body schema consists in on-line sensorimotor representations which code the relative positions of body parts with respect to one another (de Vignemont, 2010). Body structural description derives primarily from visual input and sustains the representation of the structure of the human body (Sirigu et al., 1995). Body image represents semantic and lexical information about the human body, such as body part names. Body structural description and body image are impaired by temporal lesions whereas impairments of the body schema are associated with lesions involving the dorsolateral frontal and/or parietal lobes (Schwoebel &

Coslett, 2005). Thus, imitation of hand configurations may be primarily sustained by body schema (parietal lobe) whereas imitation of finger configurations may depend on body image (dorsolateral frontal lobe) and then on body structural description and body image (temporal region). However, lesions reported in frontal lobe that were associated with defective imitation of finger postures were located only in primary motor cortex and IFG.

Second, the substantial different proportion of lesions affecting hand or finger postures, respectively, in frontal lobe (i.e., 0% *vs* 18%) may also be explained by the differential involvement of executive functions. Reproducing a visual model requires (1) to extract visual information about elements of the model and to maintain this information the time necessary to reproduce these elements (i.e., visual processing); and (2) to organize the production (i.e., executive control; Luria & Tsvetkova, 1964). In line with this, the involvement of executive control in imitation of hand postures might be minimal given the relative simplicity of the model (i.e., perceptually salient; Goldenberg, 2001). However, when postures involve finger configurations, the greater complexity of the model may require a significant involvement of executive processing.

4.4. Methodological considerations

The current review investigated the cerebral correlates of imitation of intransitive gestures by integrating structural lesion and functional imaging studies. It has been argued that the results from lesion studies are inconsistent with the findings obtained from imaging studies (Goldenberg, 2009). However, the structural and imaging studies reviewed here provide converging evidence for a major role of the parietal lobe (see also Niessen et al., 2014; for similar results with pantomime of tool use) and other brain structures (i.e., BA44) that subserve imitation of intransitive gestures. Here we chose to integrate the results from several neuroimaging studies by means of a quantitative meta-analysis (Turkeltaub et al.,

2002) rather than a qualitative review (Niessen et al., 2014). Quantitative meta-analyses are more powerful than any given neuroimaging experiment (Kober & Wager, 2010), however the potential presence of confounding factors must be acknowledged, that is, the issue of effectors and the age difference between subjects included in functional imaging studies and brain-damaged patients.

The issue of effectors and brain activations has already been addressed in a previous study (Caspers et al., 2010, p.1163). Our quantitative analysis argues in favor of a bilateral activation network for imitation of intransitive gestures. Since imitation implies a major motor component, it could have been assumed that bilateral activations would result in the use of either the right or the left limb. Imitation experiments, included in the neuroimaging meta-analysis, involved the imitation with either the right limb (67%, 10 out of 17), the left limb (6%, 1 out of 17) or both (27%, 4 out of 17). Moreover the only study where the left hand was used to imitate, reported strong bilateral activations (Buccino et al., 2004). Finally, our data are in line with other studies that showed bilateral brain activations during imitation (Caspers et al., 2010; Dapretto et al., 2006).

The mean age (± standard deviation) of the brain-damaged patients included in the above-mentioned studies was 60.0 ± 4.7 years. In contrast, healthy controls who participated in the neuroimaging studies had a mean age of 25.9 ± 7.6 years. Studies have reported a decrease in gesture performance of aged subjects, whether in pantomiming on verbal command or on imitation (Cavalcante & Caramelli, 2009; Ska & Nespoulous, 1987) or in more complex tool use tasks (Lesourd, Baumard, Jarry, Le Gall, & Osiurak, 2017). Thus, cerebral networks sustaining imitation abilities in healthy young and elderly may be different. However, in this review, we also reported non-invasive brain stimulation study in healthy young participants (Bohlhalter et al., 2011: 25-39 years old; Heiser et al., 2003: 19-34 years old; Mengotti et al., 2013: 26 years old; Sowden & Catmur, 2015: 26.2 years old; Vanbellingen et al., 2014: 23-63 years old) targeting brain areas which were: (1) activated in ALE analyses; and (2) impaired in aged patients. Thus, even if we cannot exclude that the aging brain either recruits alternative brain areas (Heuninckx, Wenderoth, & Swinnen, 2008) or has a modified functional organization (Cabeza, 2001) compared to young subjects, we can stand that the key structures involved in imitation of intransitive gestures are similar in healthy young and elderly subjects (e.g., left parietal lobe and left BA44). However, further studies, using functional imaging, are needed to investigate precisely the brain activation patterns involved during imitation of intransitive gestures in young and elderly healthy participants.

We found that 10% of lesions located in the white matter were associated with a deficit of imitation of intransitive gestures. One may assume that we overestimated the presence of lesions in white matter. Indeed, some maximum lesion overlap locations centers encompass sometimes both white matter and surrounding grey matter (see **Fig.1b**). As we systematically used the Talairach Daemon (www.talairach.org/applet.html) to find the nearest grey matter of maximum lesion overlap coordinates, it is therefore more likely that we underestimated the proportion of white matter extended from grey matter lesions, even if a possible damage to these projections contributed to an imitation deficit (Bonivento, Rothstein, Humphreys, & Chechlacz, 2014). Lesions in the white matter reported in this review are more likely to reflect interrupted intra- or inter-hemispheric association fibers which may also cause apraxia-like symptoms (Heilman & Watson, 2008).

5. Conclusions and clinical considerations

Due to its high sensitivity and specificity for detecting apraxic deficits, imitation of intransitive gestures task is of first clinical relevance. Moreover, several tests exist where a subset of items can easily be picked up (e.g., TULIA; Vanbellingen et al., 2010) to explore the integrity of imitation of intransitive gestures. In this work, we explored the link between focal brain lesions and a deficit for imitating MF/ML gestures and ML hand/finger postures. Presumably, brain diseases like neurodegenerative diseases (e.g., Alzheimer's disease; Lesourd et al., 2013a, 2013b) may impair imitation because of the disruption of a large brain network rather than focal brain lesions, preventing the clinician from inferring the specific brain structures involved.

We found that both MF and ML gestures were predominantly impacted following left parietal lesions. More particularly, lesions in AG were reliably associated with an impairment in the imitation of hand postures, suggesting that this parietal area may be a key node for body part coding (Goldenberg, 2013). We also found that the cerebral correlates of imitation of hand and finger postures were strikingly distinct. Imitation of hand postures is primarily sensitive to parietal lesions whereas imitation of finger postures impairment is associated with lesions in the basal ganglia and frontal lobe (IFG and motor cortex). Moreover, we found that imitating intransitive gestures rely upon several brain areas (i.e., BA44) and not only on parietal structures. This is of first importance particularly in the clinical assessment where the presence of apraxia may be explored not only following lesions within the parietal lobe.

Imitation is a complex function sustained by a network of bilateral brain areas (Caspers et al., 2010; Dapretto et al., 2006). Here we found that the left hemisphere, more particularly the parietal cortex, has a key role in imitation of intransitive gestures. However, the contribution of the right hemisphere is often neglected. This is unfortunate since RBD patients and right brain stimulations are often associated with defective imitation (De Renzi, 1980; Goldenberg, 1999; Stamenova et al., 2010). Further studies are now required to disentangle the role of right brain structures in imitation, in the parietal (SMG, AG and SPL) and in the frontal lobes (IFG and insula).

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Figures

Figure1. Explanation of the three-step method used to depict the anatomical location of lesion sites from overlay lesion plots. a) Original illustration from Goldenberg and Karnath (2006); red and yellow colors indicate the maximum lesion overlap. Three locations, surrounded by a red circle, were identified on three distinct slices (z = 8, z = 16 and z = 24). b) Each maximum lesion center was projected on a standard template (Colin27_T1_seg_MNI) brain provided by MRIcron and each coordinate was transformed from MNI to Talairach space (mni2tal; Lacadie et al., 2008). c) Then each coordinate was depicted on a flat-map representation of a left hemisphere using Caret, version 5.65 (Van Essen et al., 2001). The 3 maximum lesion overlap locations reported were associated with a selective disturbance of ML hand postures, thus, they were represented with a green (i.e., selective deficit of ML postures) circle (i.e., brain damage study).

Figure 2. The “intransitive gestures imitation” network. ALE map derived from all neuroimaging studies included, viewed on two PALS-B12 left and right hemispheres atlas surface configurations (Van Essen, 2005); Lateral fiducial surfaces (Top) and flat maps (Bottom). ACC: Anterior cingulate cortex; SFG: Superior frontal gyrus; PrG: Precentral gyrus; IFG: Inferior frontal gyrus; PoG: Postcentral gyrus; SMG: Supramarginal gyrus; IPL: Inferior parietal lobe; IPS: Intra-parietal sulcus; SPL: Superior parietal lobe; ITG: Inferior temporal gyrus; MFG: Middle frontal gyrus. Black outlines (Orban & Caruana, 2014; see also Peeters, Rizzolatti, & Orban, 2013) represent (1) IPL: aSMG, anterior portion of SMG, which largely overlaps with the cytoarchitectonic area PFt of SMG; (2) IPS: phAIP, putative human homologue of anterior intraparietal area; DIPSA, anterior dorsal intraparietal sulcus; (3) BA6, vPMC and dPMC (premotor cortex); (4) BA44, Broca area; (5) MT cluster as defined by Abdollahi et al. (2014).

Figure 3. Cerebral correlates of imitation of meaningful and meaningless gestures. ALE maps, maximum lesion overlap locations and stimulations are represented on two PALS-B12 left and right hemispheres (flat maps) atlas surface configurations (Van Essen, 2005). White circles represent lesions in the insula. Lesions in basal ganglia or in white matter are not projected on flat maps. Brain lesions: (1) Binder et al. (2017); (2) Buxbaum et al. (2014); (3) Goldenberg & Karnath (2006); (4) Goldenberg & Randerath (2015); (5) Hoeren et al. (2014); (6) Martin et al. (2016); (7) Mengotti et al. (2013); (8) Weiss et al. (2016). Brain stimulations : (1) Bohlhalter et al. (2011); (2) Heiser et al. (2003) ; (3) Mengotti et al. (2013); (4) Sowden & Catmur (2015); (5) Vanbellingen et al. (2014). Black outlines (Orban & Caruana, 2014; see also Peeters, Rizzolatti, & Orban, 2013) represent (1) IPL: aSMG, anterior portion of SMG, which largely overlaps with the cytoarchitectonic area PFt of SMG; (2) IPS: phAIP, putative human homologue of anterior intraparietal area ; and DIPSA, anterior dorsal intraparietal sulcus; (3) pMTG, posterior middle temporal gyrus; (4) BA6, vPMC and dPMC (premotor cortex); and (5) BA44, Broca area.

Figure 4. Cerebral correlates of imitation of finger and hand postures. ALE maps, maximum lesion overlap locations and stimulations are represented on two PALS-B12 left and right hemispheres (flat maps) atlas surface configurations (Van Essen, 2005). White circles represent lesions in the insula. Lesions in basal ganglia or in white matter are not projected in flat maps. Brain lesions: (3) Goldenberg & Karnath (2006); (4) Goldenberg & Randerath (2015); (5) Hoeren et al. (2014). Brain stimulations: (2) Heiser et al. (2003); (3) Mengotti et al. (2013); (4) Sowden & Catmur (2015). White outlines (Orban & Caruana, 2014; see also Peeters, Rizzolatti, & Orban, 2013) represent (1) IPL: aSMG, anterior portion of SMG, which largely overlaps with the cytoarchitectonic area PFt of SMG; (2) IPS: phAIP, putative human homologue of anterior intraparietal area; and DIPSA, anterior dorsal intraparietal sulcus; (3)

pMTG, posterior middle temporal gyrus; (4) BA6, vPMC and dPMC (premotor cortex); and (5) BA44, Broca area.

Figure 5. Schematic representation of the main cortical brain structures involved in imitation of intransitive gestures according to functional and structural data obtained in the present review. The potential role of these regions in imitation is provided in the text.

Fig.1

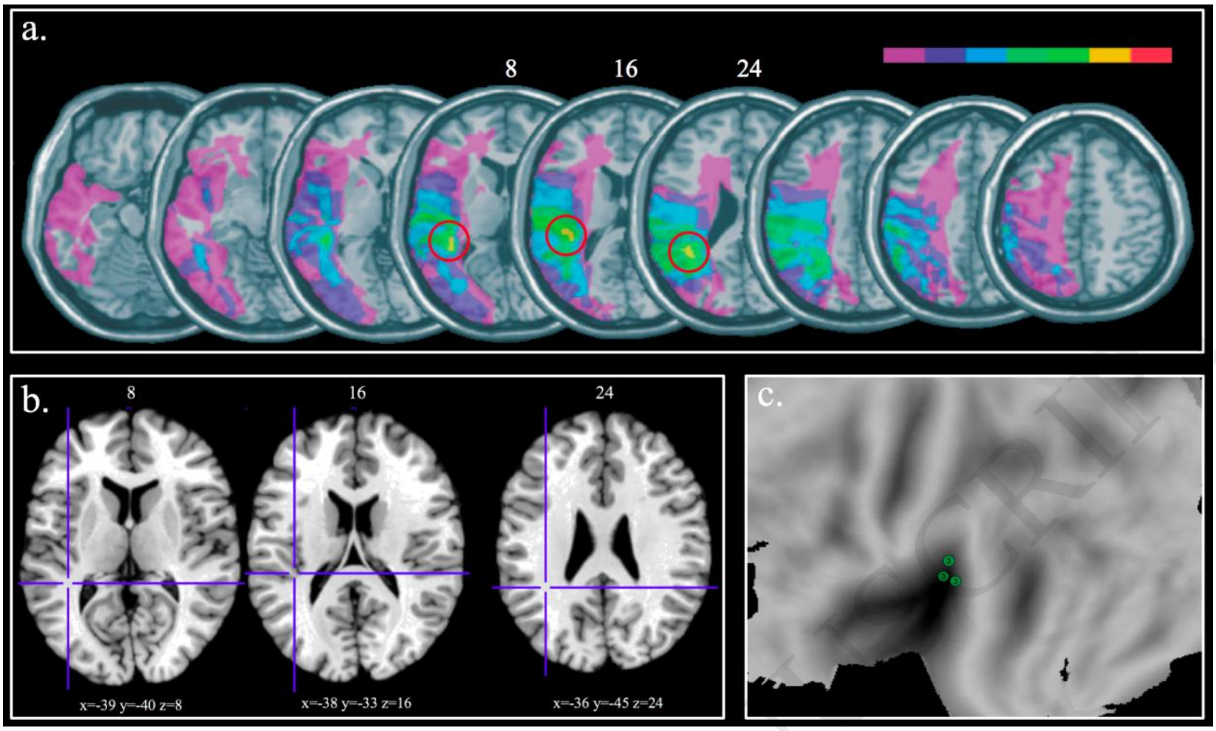

Fig.2

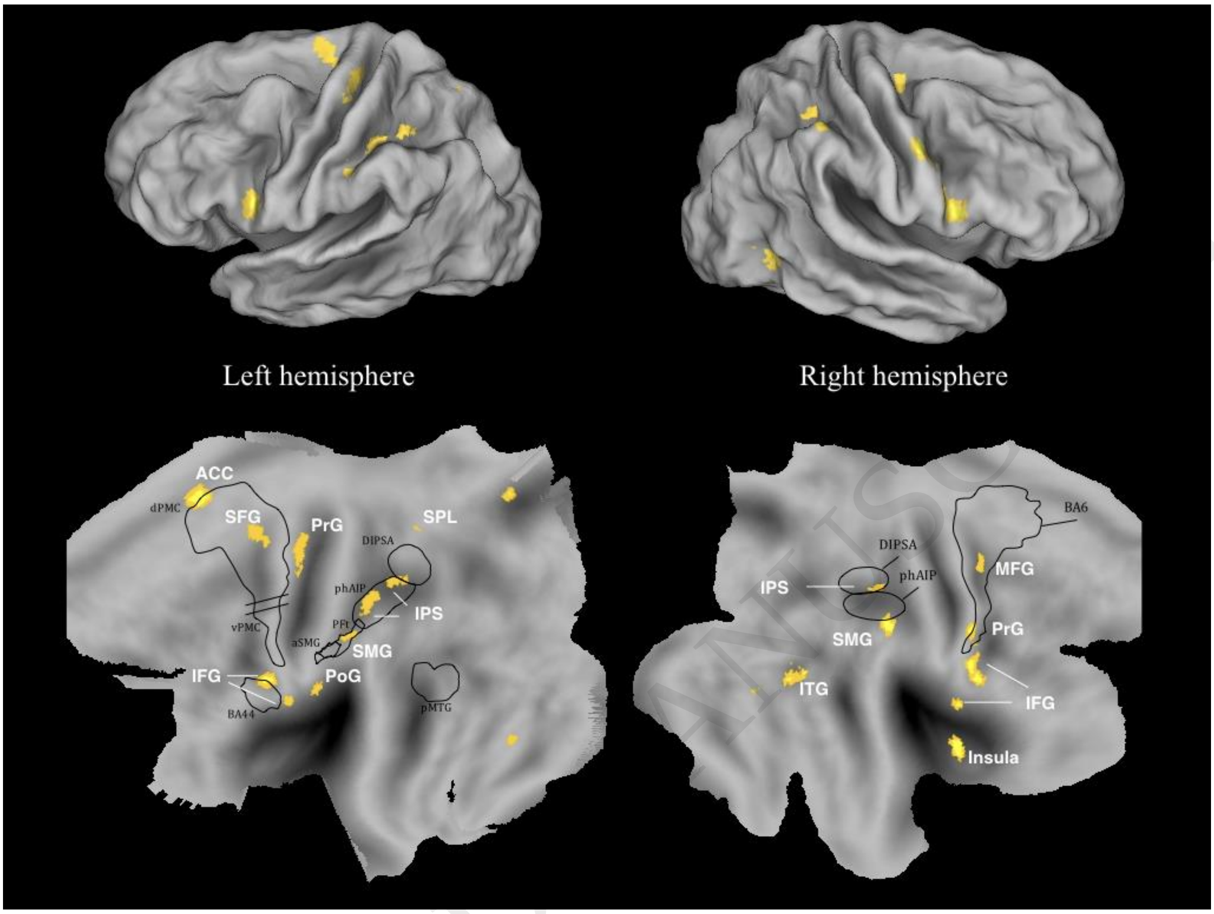
Left hemisphere
Right hemisphere
ACC
dPMC
SFG
PrG
SPL
DIPSA
phAIP
IPS
PFt
aSMG
SMG
vPMC
IFG
PoG
BA44
pMTG
BA6
DIPSA
phAIP
IPS
MFG
SMG
PrG
ITG
IFG
Insula

Fig.3

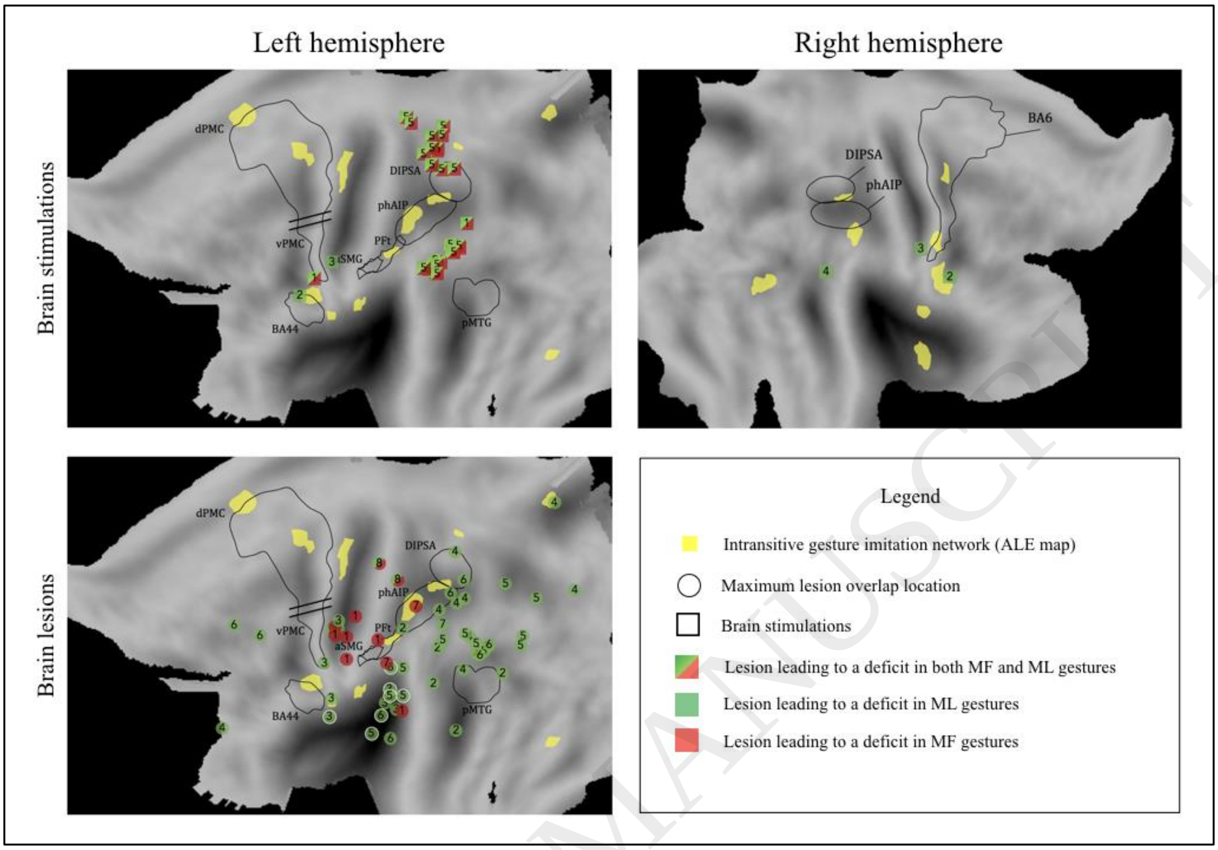
Left hemisphere
Right hemisphere
Brain stimulations
Brain lesions
dPMC
vPMC
BA44
DIPSA
phAIP
PFt
aSMG
pMTG
BA6
Legend
🟨 Intransitive gesture imitation network (ALE map)
○ Maximum lesion overlap location
☐ Brain stimulations
Lesion leading to a deficit in both MF and ML gestures
🟩 Lesion leading to a deficit in ML gestures
🟥 Lesion leading to a deficit in MF gestures

Fig.4

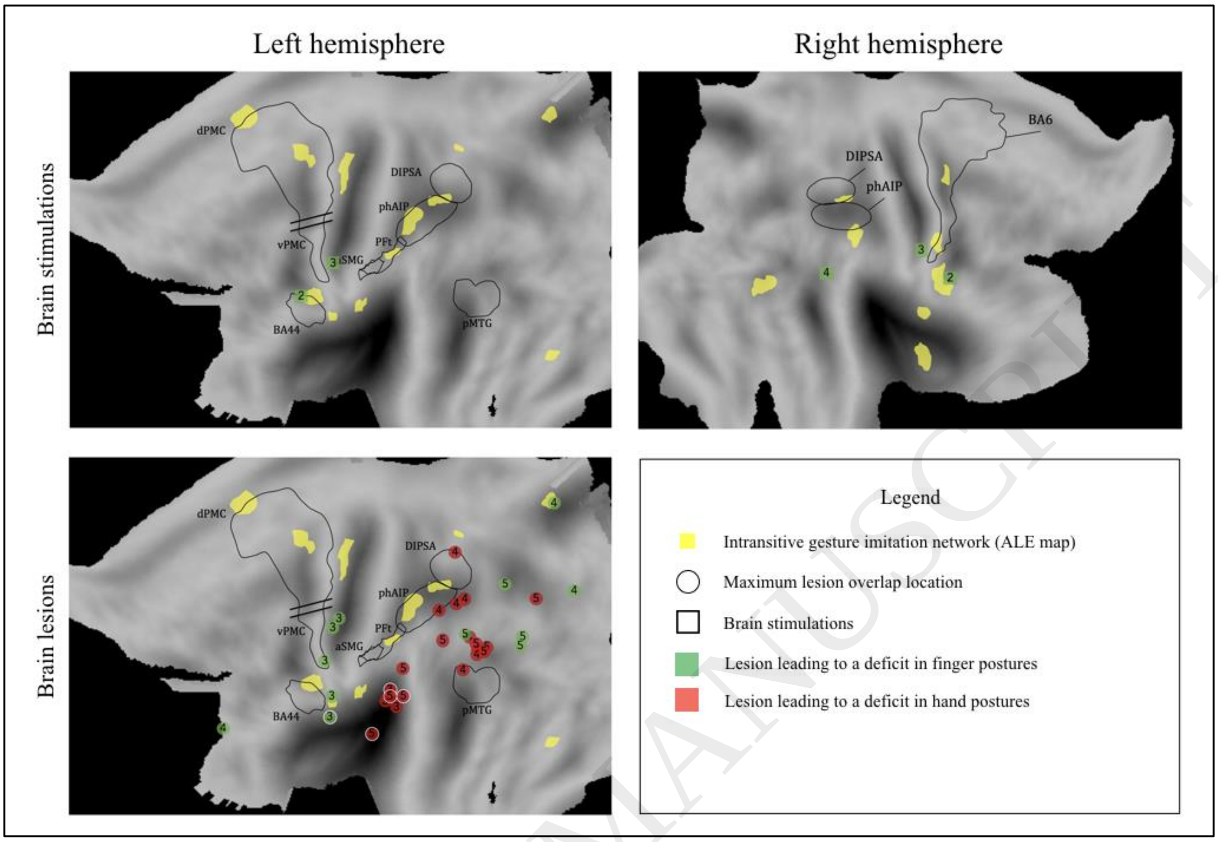
Left hemisphere
Right hemisphere
Brain stimulations
Brain lesions
dPMC
vPMC
DIPSA
phAIP
PFt
aSMG
BA44
pMTG
BA6
Legend
Intransitive gesture imitation network (ALE map)
Maximum lesion overlap location
Brain stimulations
Lesion leading to a deficit in finger postures
Lesion leading to a deficit in hand postures

Fig.5

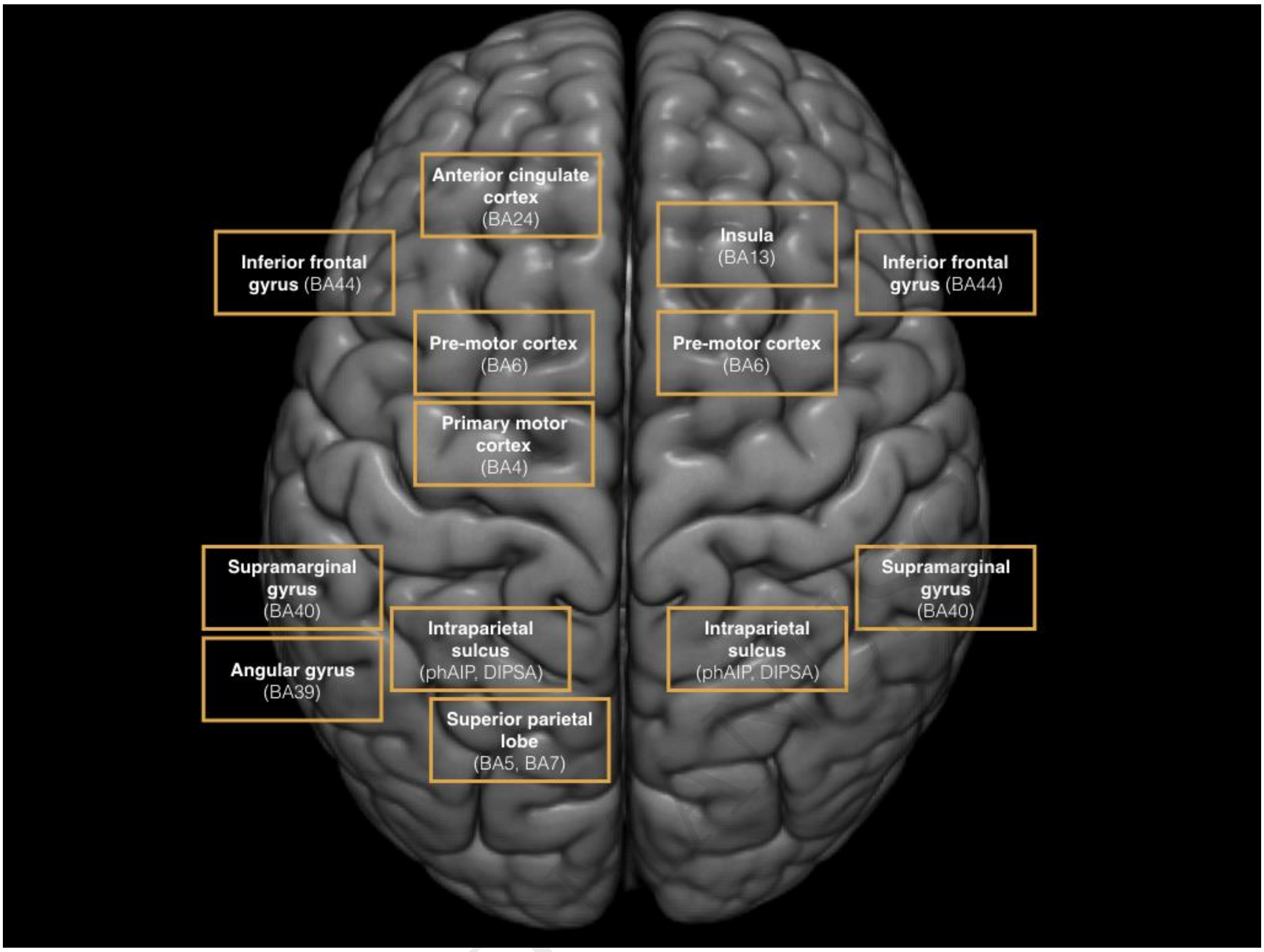
Anterior cingulate cortex (BA24)
Inferior frontal gyrus (BA44)
Insula (BA13)
Inferior frontal gyrus (BA44)
Pre-motor cortex (BA6)
Pre-motor cortex (BA6)
Primary motor cortex (BA4)
Supramarginal gyrus (BA40)
Supramarginal gyrus (BA40)
Intraparietal sulcus (phAIP, DIPSA)
Intraparietal sulcus (phAIP, DIPSA)
Angular gyrus (BA39)
Superior parietal lobe (BA5, BA7)

Table 1. Taxonomy of actions according to the domain (transitive vs. intransitive) and the meaning (meaningful vs meaningless)

Domain	*Meaning*	*Type of actions*
Transitive	Meaningful	Actual use of tool
		Pantomime of tool use
	Meaningless	Mechanical problem-solving
		Non conventional tool use
Intransitive	Meaningful	Imitation/Production of symbolic gestures
	Meaningless	Imitation of hand postures
		Imitation of finger postures

Table 2. "Categorical apprehension" and "dynamic and representational apraxia" predictions for the involvement of parietal lobes in meaning of gestures and body parts

		Categorical apprehension	Representational/dynamic apraxia
Meaning	Meaningful gestures	no prediction	left IPL
	Meaningless gestures	left IPL (AG)	left IPL (AG/SMG)
			left/bilateral SPL
Body parts	hand postures	left IPL	left/bilateral SPL
	finger postures	right IPL	left/bilateral SPL

IPL: Inferior Parietal Lobe; AG: Angular Gyrus; SMG: Supramarginal Gyrus; SPL: Superior Parietal Lobe

Table 3. Summary of the functional neuroimaging studies on the cerebral correlates of imitation

Author (year)	Subjects' age	Method	Task	Laterality and limb used to imitate	Stimulus	Control condition
Adamovich et al. (2009)	27.7	fMRI	Execute previously and concurrent observed finger sequence	Right hand	Moving hands in a virtual-reality environment	Observation of virtual static hands and non moving non-anthropomorphic objects
Buccino et al. (2004)	27	fMRI	Delayed imitation of finger configuration (guitar chord)	Left hand	Video clip of the hand of a guitar player	Watching a blank screen
Chaminade et al. (2005)	21.2	fMRI	Imitation of an action performed with either the same or a different limb	Left/right hand/foot	Video clips depicted single hand or foot action	Watching without acting action stimuli or a blue cross on a black screen
Jackson et al. (2006)	29	fMRI	Imitation of limb action in either 1st or 3rd perspective	Right hand/foot	Video-clips of left hand and foot	Watching a static cross on a blue background
Kubiak & Kròliczak (2016)	25.7	fMRI	Imitation of intransitive communicative gestures	Not provided	Video-clips of a right hand	Resting baseline (no more detailed)
Koski et al. (2003)	28.6	fMRI	Imitation of a lifting finger	Right hand	Picture of left and right hand	Lifting a finger as indicated by a black cross displayed on a static finger
Krüger et al. (2014)	24	fMRI	Imitation of bimanual meaningless gestures with a delay	Left and right hand	Video sequences displaying bimanual hand movements	Resting with closed eyes
Mainieri et al. (2013)	24.6	fMRI	Imitation of communicative and meaningless gestures	Right or both	Video clips of an actor producing hand gestures	Identifying the colour of a circle on the actor's pull-over

Mülhau et al. (2005)	50	fMRI	Imitation of meaningless hand or finger gestures	Left/right hand/fingers	Video clips of meningless	Imitating stereotyped gestures and watching
					gestures	passively neutral position
Montgomery et al. (2007)	22	fMRI	Imitation of communivative gestures	Right hand	Video clips of communicative	Watching passively a blank screen
					hand gestures	
Montgomery and Haxby (2008)	22-31	fMRI	Imitation of social hand gestures	Right hand	Picture of social hand gestures	Watching passively a neutral hand gesture
Rumiati et al. (2005)	26	PET	Imitation of meaningless hand gesture	Right hand	Video-clips of a person producing	Observing passively meaningful and
					gestures with his left hand	meaningless gestures
Suchan et al. (2008)	27	PET	Observation and imitation of meaningless finger gestures	Not provided	Video-clips of right hands	Observation of a right palm hand
Tanaka et al. (2001)	25.2	fMRI	Imitation of symbolic and meaningless finger configurations	Right hand	Picture of hand	Watching passively a fixation point
Tanaka and Inui (2002)	24.8	fMRI	Imitation of meaningless hand or finger gestures	Right hand/finger	Picture of hand/arm	Watching passively a hand posture
Vingerhoets and Clauwaert (2015)	21.8	fMRI	Imitation of meaningless hand gestures	Right hand	Picture of a right hand	Indicating if a green mark is located on the
						middle finger of the hand
Watanabe et al. (2011)	22.8	fMRI	Imitation of meaningless finger configurations relative to	Right hand	Sequential oppositional finger	Producing finger oppositional movements
			perspective (1st or 3rd) and specular-anatomical factors		movements produced by a model	

Table 4. Summary of the structural lesion studies on the cerebral correlates of imitation

Author (year)	Patients' age (range or sd)	Patient population	Task	Anatomical description of lesions
Binder et al. (2017)	60.8 (30-80)	44	Imitation of meaningful gestures	Left postcentral, middle and superior temporal gyri, left inferior parietal lobe, operculum, left insula
Buxbaum et al. (2014)	58 (35-80)	71	Imitation of novel gestures	Inferior temporal, middle temporal, fusiform, inferior occipital, fusiform, superior temporal, middle temporal, supramarginal, angular, inferior parietal, postcentral, precentral and middle occipital gyrii
Goldenberg and Karnath (2006)	51.2 (n.p.)	44	Imitation of meaningless hand/finger postures	Inferior frontal, inferior parietal lobule and temporo-parieto-occipital junction
Goldenberg and Randerath (2015)	56.9 (26-83)	96	Imitation of meaningless hand and finger gestures	Inferior parietal lobe
Hoeren et al. (2014)	63 (26-85)	96	Imitation of meaningless hand/finger postures	Lateral occipito-temporal cortex, posterior inferior parietal lobule, posterior intraparietal sulcus and superior parietal lobule
Martin et al. (2016)	60 (12)	36	Imitation of meaningless postures	Posterior superior temporal sulcus, superior temporal gyrus
Mengotti et al. (2013)	64.1 (n.p.)	57	Imitation of meaningful and meaningless gestures	Supramarginal and angular gyrus
Weiss et al. (2016)	65.9 (34-87)	50	Imitation of intransitive meaningful and meaningless gestures	Left inferior frontal, insular, inferior parietal and superior temporal lesions

Table 5. Summary of the virtual lesion studies on the cerebral correlates of imitation

Author (year)	Subjects' age	Method	Task	Results	Talairach Coordinates of the stimuation sites
Bohlhalter et al. (2011)	25-39	cTBS	Pantomime and imitation of transitive, intransitive	Effect on total TULIA scores more prominent follow-	Left IFG: x = -58, y = 10, z = 28
			and meaningless gestures (i.e., TULIA)	ing IFG stimulation	Left IPL: x = -44, y = -60, z = 46
Heiser et al. (2003)[a]	19-34	rTMS	Imitation of a sequence of finger keypress on a	Significant impairment in imitation during rTMS	Left pars opercularis (BA 44): x = -46 y = 11, z = 17
			computer keyboard	over left and right stimulations	Right pars opercularis (BA 44): x = 46 y = 11, z = 19
Mengotti et al. (2013)	26	double-pulse TMS	Anatomical imitation (moving the finger anatomically	Reduction of imitative compatibility following left	Left PO: x = -48, y = -12, z = 24
			compatible with the one moving on the screen)	and right PO stimulations	Right PO: x = 48, y = -11, z = 24
			Spatial imitation (moving the finger spatially		
			compatible with the one moving on the screen)		
Sowden and Catmur (2015)	26.2	rTMS	Imitation of a lifting finger (index or middle) of a left	Effect of imitative compatibility was significantly	rTPJ: x = 54, y = -45, z = 26
			hand or a right hand with the right hand	stronger during rTPJ stimulation	
Vanbellingen et al. (2014)[b]	23-63	cTBS	Imitation of meaningful and meaningless postures	Significant impairment of meaningful and meaningless	Left SPL Left IPL
				postures following left SPL and IPL stimulations	(1) x = -35, y = -51, z = 60 x = -57, y = -57, z = 32
					(2) x = -31, y = -52, z = 55 x = -56, y = -59, z = 32
					(3) x = -28, y = -52, z = 63 x = -50, y = -69, z = 35
					(4) x = -27, y = -44, z = 66 x = -54, y = -62, z = 39
					(5) x = -21 y = -58, z = 62 x = -57, y = -60, z = 29
					(6) x = -21 y = -45, z = 71 x = -55, y = -63, z = 32
					(7) x = -16 y = -60, z = 62 x = -57, y = -57, z = 27
					(8) x = -26 y = -55, z = 62 x = -58, y = -55, z = 28
					(9) x = -23 y = -53, z = 64 x = -58, y = -59, z = 24
					(10) x = -21 y = -47, z = 68 x = -50, y = -63, z = 31
					(11) x = -31 y = -47, z = 61 x = -50, y = -64, z = 34
					(12) x = -25 y = -52, z = 63 x = -58, y = -52, z

					= 33

cTBS: continuous theta-burst stimulation; rTMS: repetitive transcranial magnetic stimulation; TULIA: Test of upper limb apraxia; IFG: Inferior Frontal Gyrus; PO: Parietal Opercularis: rTPJ: Right Temporo-Parietal junction; SPL: Superior Parietal Lobe; IPL: Inferior Parietal Lobe

[a] Heiser et al. (2003) stimulated left and right BA 44 but did not provide any coordinates. The approximate coordinates reported here were obtained from the atlas of Talairach and Tournoux (1988) for left and right BA 44

[b] Stimulation coordinates were provided for each subject in Vanbellingen et al. (2013)

Table 6. Summary of lesions leading to defective imitation of intransitive gestures according to the meaning and the body parts

		Parietal Lobe				Frontal Lobe	Temporal Lobe	Occipital Lobe	Insula	Basal Ganglia	White Matter
Dimension	Types of action	AG	SMG	SPL	Somato.						
Meaning	MF gestures	50%				13%	6%	-	-	-	31%
		-	19%	-	31%						
	ML gestures	40%				12%	9%	14%	12%	10%	3%
		21%	12%	5%	2%						
Body parts	Hand postures	66.5%				-	17%	11%	5.5%	-	-
		44%	17%	5.5%	-						
	Finger postures	9%				18%	9%	14%	18%	27%	5%

				4.5%		-		4.5%		-												

MF: Meaningful; ML: Meaningless; AG: Angular Gyrus; SMG: Supramarginal Gyrus; SPL: Superior Parietal Lobe; Somato.: Somatosensory cortices