NeuroImage: Clinical 6 (2014) 488–497

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Neural correlates of transitive and intransitive action imitation: An investigation using voxel-based morphometry

Abbreviated title: Neuroanatomy of action imitation

Carolina Bonivento[a,b,*], Pia Rothstein[b], Glyn Humphreys[b,c], Magdalena Chechlacz[b,c]

[a] IRCCS Eugenio Medea polo di, San Vito al Tagliamento, PN, Italy
[b] School of Psychology, University of Birmingham, Birmingham, UK
[c] Department of Experimental Psychology, University of Oxford, Oxford, UK

ARTICLE INFO

Article history:
Received 8 October 2013
Received in revised form 12 September 2014
Accepted 13 September 2014
Available online 19 September 2014

Keywords:
Voxel-based morphometry
Ideomotor apraxia
Action imitation
Transitive gestures
Intransitive gestures

ABSTRACT

The ability to reproduce visually presented actions has been studied through neuropsychological observations of patients with ideomotor apraxia. These studies include attempts to understand the neural basis of action reproduction based on lesion–symptom mapping in different patient groups. While there is a convergence of evidence that areas in the parietal and frontal lobes within the left hemisphere are involved in the imitation of a variety of actions, questions remain about whether the results generalize beyond the imitation of tool use and whether the presence of a strong grasp component of the action is critical. Here we used voxel-based lesion–symptom mapping to assess the neural substrates of imitating meaningful (familiar, MF) and meaningless (unfamiliar, ML) tool-related (transitive) and non-tool related (intransitive) actions. The analysis showed that the left parietal cortex was involved in the imitation of transitive gestures, regardless of whether they were meaningful or not. In addition there was poor reproduction of meaningless actions (both transitive and intransitive) following damage of the right frontal cortex. These findings suggest a role of right frontal regions in processing of unfamiliar actions.

1. Introduction

Imitation is an innate tendency in humans (Meltzoff and Moore, 1977; Meltzoff and Moore, 1983; Meltzoff and Moore, 1989) as well as in newborn chimpanzees (Bard and Russell, 1999; Myowa, 1996; Myowa-Yamakoshi et al., 2005) and macaques (Ferrari et al., 2006). The ability to reproduce gestures may provide one of the foundations of social communication and it may have an important role in learning effective tool use (e.g. how to use a hammer).

Following a brain lesion people with apraxia can suffer from a deficit in reproducing and generating gestures (Mehler, 1987). In right handed people this syndrome has classically been described in relation to lesions of the left posterior parietal cortex (Liepmann, 1900; Liepmann, 1905; Rothi et al., 1991) though other studies point to the role of right brain areas as well as sub-cortical structures (Leiguarda et al., 1997; Leiguarda, 2001; De Renzi et al., 1980; Tessari et al., 2007; Bonivento et al., 2013), especially when finger configurations (Della Sala et al., 2006; Goldenberg and Strauss, 2002) or movement sequences (Canavan et al., 1989) have to be copied.

Prior neuropsychological evidence indicates that apraxia is not a unitary phenomenon, and frequently symptom dissociations have been reported in neuropsychological patients (Rumiati et al., 2009). For example, neuropsychological observations suggest a double dissociation between the production of meaningful and meaningless gestures, with some studies reporting patients who are more impaired when imitating meaningless (ML) compared to meaningful (MF) gestures (Tessari et al., 2007; Bartolo et al., 2001; Goldenberg and Hagmann, 1997; Peigneux et al., 2000) and others showing the opposite pattern (Tessari et al., 2007; Bartolo et al., 2001). Double dissociations have also been observed between finger and hand gestures, with patients able to imitate hand postures but not finger configurations and other patients with the opposite pattern of deficits (Goldenberg and Karnath, 2006).

A cognitive neuropsychological model of praxis was first proposed by Rothi et al. (1991) and then modified by other authors (Goldenberg and Hagmann, 1997; Buxbaum, 2001; Cubelli et al., 2000; Rumiati and Tessari, 2002). This model postulates (i) a *semantic route to action*, relying on long-term memory representations, which allow the reproduction of the MF (known) gestures, and (ii) a *direct route*, depending on a short-term memory representation of the action (i.e. the *innervatory pattern* in the original model from Rothi et al., 1991), which supports the reproduction of ML (new) gestures. For gesture reproduction the starting point of both routes is a *visual analysis* component, through

---

* Corresponding author at: IRCCS“E. Medea”, c/o Clinica Psichiatrica, Azienda Ospedaliera Universitaria, Piazzale Santa Maria della Misericordia, 15, 33100 Udine, Italy.
E-mail address: boniventocarolina@gmail.com (C. Bonivento).

http://dx.doi.org/10.1016/j.nicl.2014.09.010

which the visual properties of actions are processed. Also both the semantic and the direct processes end at the level of the *motor system*, which determines the actual implementation of the action.

Neuropsychological observations of unilateral brain damaged patients (Goldenberg and Hagmann, 1997; Peigneux et al., 2000; Buxbaum, 2001; Cubelli et al., 2000), as well as behavioural and imaging studies with healthy participants (Rumiati et al., 2009; Tessari and Rumiati, 2004; Peigneux et al., 2004), support the idea of these two separate neural systems for imitating MF and ML gestures but the results are inconsistent with respect to the neuro-anatomical structures involved (particularly concerning their hemispheric location). Lesions involving the parietal cortex, especially the angular gyrus, have been reported to cause a deficit in the imitation of meaningful (MF) as compared to meaningless (ML) actions in left-brain damaged patients (LBD; Tessari et al., 2007). On the other hand, Peigneux et al. (2000) reported a patient, with a lesion in the left occipito-parietal cortex, who imitated MF gestures better than ML gestures. Furthermore, Tessari et al. (2007) reported two right brain damaged patients (RBD), with lesions including the caudal portion of the pallidum, the putamen and the posterior limb of the internal capsule, who were more impaired in imitating ML than MF gestures. In the same study Tessari et al. (2007) presented data from LBD patients whose performance was worse with ML gestures, and this was associated with lesions to the superior temporal gyrus.

In studies using positron emission tomography (PET), the imitation of MF actions has been linked to activation in the left angular gyrus, the left middle frontal gyrus, the right supramarginal gyrus, and the right inferior parietal lobule (Peigneux et al., 2004), as well as the inferior temporal, angular and parahippocampal gyri in the left hemisphere (Rumiati et al., 2005). The parieto-occipital and occipito-temporal junctions on the right, the superior temporal gyrus on the left, and the superior parietal cortex bilaterally have also been shown to have increased activation linked to the imitation of ML actions (Rumiati et al., 2005).

Goldenberg et al. (2007) used lesion subtraction analysis to determine the locations specifically associated with defective pantomime of tool use in patients with left-brain damage and aphasia. Their results showed that the left inferior frontal cortex was associated with a deficit in pantomime — though the area of lesion overlap further extended into the underlying white matter so it is possible that damage to the white matter projections contributed to the observed deficit (Liepmann, 1905; Catani and Ffytche, 2005; Geschwind, 1975). The left inferior frontal and inferior parietal cortices were also found to be damaged in a group of stroke patients having a deficit in at least one of two tests assessing ideomotor apraxia (De Renzi et al., 1980) and ideational apraxia (De Renzi and Lucchelli, 1988) respectively, with the inferior frontal lesions being more frequent in those patients who were additionally impaired in recognizing transitive and intransitive actions (Pazzaglia et al., 2008).

Finally, a recent DTI study (Ramayya et al., 2010) with healthy right handed male volunteers investigated the connections between four regions that previous fMRI studies indicated to be involved in processing and performing complex tool use gestures: i) the posterior middle temporal cortex (linked to semantic representations of tools); ii) the posterior inferior parietal cortex (coding spatial invariant components of learned gestures to tools, such as the swing of the elbow to use a hammer); iii) the anterior inferior parietal cortex (proposed to integrate non-spatial semantic representations of tools with the spatial information relevant for effective tool use); and iv) the posterior inferior frontal and ventral premotor cortices that convert the planned gesture into the proper activation pattern for the movement implementation. The results highlighted the role of white matter pathways connecting the posterior middle temporal cortex and the anterior inferior parietal cortex, as well as the anterior inferior parietal cortex and the posterior inferior frontal and ventral premotor cortices. In both cases there was an asymmetry with significantly more subjects showing those connections in the left than the right hemisphere. Also the inferior posterior parietal cortex showed connections with the posterior middle temporal cortex, lateralized on the left, and with the inferior frontal and premotor cortices, lateralized in the right hemisphere. However in both cases the fibre terminations did not fall in the same location as the posterior parietal activations identified by previous functional neuroimaging studies and hence the role in tool use may be questioned (Ramayya et al., 2010).

The neuropsychological studies described above have typically relied on categorical subdivisions of patients based on a given cut-off as well as on observer-dependent lesion demarcations. The use of a cut-off, especially in tasks where each answer is scored either 1 or 0, introduces the risk that patients having scores differing only for one point are treated differently (scores that equal the cut-off will be considered as defective, while scores one point higher than the cut-off may be treated as not defective). Also manual demarcations of lesion sites can lead to under- or over- estimation of tissue differences according to the strictness of the observer's criteria. The present study aimed to investigate the neural substrates of action imitation using a procedure based on continuous rather than categorical scoring that is not biased by either its sampling of patients or lesion demarcation. To achieve this we employed whole-brain voxel-based morphometry (VBM) (Ashburner and Friston, 2000) based on the segmentation of grey matter (GM) and white matter (WM) tissue. VBM uses the general linear model to statistically assess the relations between brain tissue integrity and behavioural performance. Here, continuous MF and ML imitation scores were used as predictors of change in signal intensity within each voxel across the whole brain in a group of consecutively sampled patients, not pre-selected on the basis of having apraxia. This approach also allowed us to enter into the model covariates of no interest such as age, gender, handedness and lesion volume (i.e. the extent of the patients' lesions), which might otherwise confound the results.

For the first time in a single study we examined the neural substrates of MF and ML intransitive actions, relative to MF and matched ML transitive actions. We used the scores for patients obtained when imitating MF transitive and intransitive pantomimes, along with matched ML transitive and intransitive actions, as predictors of voxel signal intensity. The results are discussed in terms of previous findings, the mechanisms of apraxia and the neuronal underpinnings of action imitation.

2. Methods

2.1. Participants

2.1.1. Patients

Twenty-one consecutively-sampled patients (20 males and 1 female, 18 right-handed, 3 left-handed; mean age: 68.18; SD: 11.13. Age range: 36–82) were recruited from the panel of neuropsychological volunteers at the Behavioural Brain Science Centre, School of Psychology of the University of Birmingham. All patients had acquired brain lesions due to a stroke, were in the chronic stage (>9 months after the occurrence of the lesion) and had no contraindications to magnetic resonance imaging (MRI) scans. No other exclusion criteria were used. Seven patients had a lesion involving the left side of the brain (left brain damaged, LBD), eleven had a lesion on the right (right brain damaged, RBD) and three had bilateral brain lesions (BBL). According to the Edinburgh Handedness Inventory (Oldfield, 1971), 18 patients were right handed before the stroke and three were left-handed. Patients' demographic data and their Edinburgh Handedness Inventory scores are summarized in Supplementary Table 1.

2.1.2. Healthy controls

Eighteen English-speaking healthy participants (mean age = 65.56, SD = 10.18, age range = 37–78) with no reported history of neurological and/or psychiatric disease served as controls. Fifteen controls self-reported as right-handed while three reported as left-handed. All had normal or corrected-to-normal vision. Data from controls were used only to perform a preliminary categorization of each patient's imitation