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Using multi-level Bayesian lesion-symptom mapping to probe the body-part-specificity of gesture imitation skills

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ABSTRACT

Past attempts to identify the neural substrates of hand and finger imitation skills in the left hemisphere of the brain have yielded inconsistent results. Here, we analyse those associations in a large sample of 257 left hemisphere stroke patients. By introducing novel Bayesian methods, we characterise lesion symptom associations at three levels: the voxel-level, the single-region level (using anatomically defined regions), and the region-pair level. The results are inconsistent across those three levels and we argue that each level of analysis makes assumptions which constrain the results it can produce. Regardless of the inconsistencies across levels, and contrary to past studies which implicated differential neural substrates for hand and finger imitation, we find no consistent voxels or regions, where damage affects one imitation skill and not the other, at any of the three analysis levels. Our novel Bayesian approach indicates that any apparent differences appear to be driven by an increased sensitivity of hand imitation skills to lesions that also impair finger imitation. In our analyses, the results of the highest level of analysis (region-pairs) emphasise a role of the primary somatosensory and motor cortices, and the occipital lobe in imitation. We argue that this emphasis supports an account of both imitation tasks based on direct sensor-motor connections, which throws doubt on past accounts which imply the need for an intermediate (e.g. body-part-coding) system of representation.

1. Introduction

Even within the first few weeks after birth, infants appear to be able to imitate certain facial and manual gestures (Meltzoff and Moore, 1977). These apparently hard-wired skills (Meltzoff and Moore, 1977, 1997) may provide the foundation for much of our subsequent learning, including language acquisition, socialisation and enculturation (Brass and Heyes, 2005). Clues to the neural substrates of imitation skills can be garnered by localizing the brain damage which disrupts them. Deficits of imitation skills are a common symptom of apraxia, a disorder of motor cognition which most often occurs after left hemisphere (LH) stroke (Donkervoort et al., 2000), and which cannot be explained by primary deficits of the sensor-motor system or disturbed communication (Dovern et al., 2012). Past studies of apraxic patients suggest that there is a body-part-specific distribution of imitation skills across the two hemispheres of the brain. Hemispheric asymmetries in damage-deficit associations have been reported for postures of the upper versus lower face or of the fingers and feet versus hand (Bizzozero et al., 2000; Goldenberg and Strauss, 2002). LH damage can impair all of these skills, whereas right hemisphere (RH) damage appears only to impair a subset (upper face, feet and fingers: (Goldenberg and Karnath, 2006)).

While these hemispheric asymmetries in imitation skills are well confirmed, analogous distinctions within the LH are still debated. Some of the earliest evidence in favour of body-part-specific mechanisms within the left hemisphere causing a dissociation between hand and finger imitation skills was reported by Haaland and colleagues (Haaland et al., 2000), who tested 41 stroke patients' abilities to imitate gestures combining finger and hand postures, but distinguished between "target errors" of hand position and "internal hand position" errors of finger postures. Hand position errors were found in most (4/5) patients whose lesions were exclusively posterior to the central sulcus, and in none whose lesions were exclusively anterior to the same sulcus (n = 4), whereas finger position errors were found in all of those same patients with exclusively anterior lesions (n = 4), and in 3/5 with posterior

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lesions. Though somewhat equivocal, this anterior (finger)/posterior (hand) dissociation is consistent with the results of a later lesion subtraction analysis (with 44 patients), which associated disturbed imitation of finger postures with lesions anterior to the central sulcus including the opercular portion of the inferior frontal gyrus (IFG), and disturbed imitation of hand postures with lesions posterior to the central sulcus affecting the left inferior parietal lobe (IPL) and the temporo-parieto-occipital junction (Goldenberg and Karnath, 2006). This latter study also goes further than that by Haaland and colleagues, reporting both a behavioural and a neuroanatomical double dissociation between hand and finger imitation skills.

Evidence for an apparently similar posterior (hand)/anterior (finger) dissociation was also reported in a more recent study employing voxel-based lesion symptom mapping (VLSM) in 43 LH stroke patients, associating deficits of hand imitation with lesions of the inferior and superior parietal cortex, and deficits of finger imitation with smaller frontal regions (Dovern et al., 2011). However, these authors also associated finger imitation deficits with inferior parietal lesions, posterior to the central sulcus. Moreover, there was no evidence at all for a posterior/anterior distinction in a recent VLSM study with a larger sample of 96 acute LH stroke patients by Hoeren and colleagues, which associated both types of deficit with lesions of the posterior inferior parietal lobe (Hoeren et al., 2014). Unlike the other studies mentioned so far, this latter work also went beyond a descriptive comparison of the lesions associated with one or the other deficit (Gelman and Stern, 2006), and probed for deficit-by-lesion-location interactions (henceforth 'interactions') more formally. Their results suggest that damage to the left lateral occipito-temporal cortex was associated with relatively greater impairments of hand than finger imitation, but no reverse interaction was found (i.e. no locations where damage was associated with greater deficits in finger than hand imitation). However, these authors found no significant voxels at all when lesion volume was controlled, which raises the concern that there is a confound at play here, with the apparent interaction potentially driven by lesion volume differences, perhaps only accidentally correlated with damage to the lateral occipito-temporal cortex (Karnath and Smith, 2014).

It seems fair to say that these prior studies tell a complex and inconsistent story about the body-part-specificity of gesture imitation. Most studies report only a partial dissociation between hand and finger imitation skills: i.e. damage which impairs finger imitation but not hand imitation (Haaland et al., 2000), or vice versa (Hoeren et al., 2014). The only study, at least that we could find, which reports a full double dissociation between these tasks (Goldenberg and Karnath, 2006), emphasises qualitative methods and has not been replicated in larger samples. One interpretation of these results is that the studies to date have been underpowered. In what follows, we search for task by lesion interactions in a much larger sample of LH stroke patients (n = 257), both to test this notion, and to characterise the effect on the results after controlling for lesion volume (along with two other nuisance covariates: age at onset and time post-stroke). Another interpretation of the result is that there really are no significant associations (or interactions) to be found – either because the neural substrates of the two skills are actually similar, or because voxel-based methods are simply inappropriate to find them. To test this interpretation, we (a) introduce a lesion analysis method based on Bayesian statistics to quantify the evidence both for and against voxel-wise lesion-symptom associations (and interactions), drawing on the logic proposed in (Wetzels and Wagenmakers, 2012); and (b) explore how the evidence for those associations and interactions changes as we ascend hierarchical levels of analysis, from voxels, through anatomically defined brain regions, to pairs of those regions.

2. Material and methods

2.1. Patient sample

We retrospectively analysed hand and finger imitation scores and lesions of 257 patients who had suffered a single (first ever) unilateral left-hemispheric ischaemic stroke: 82 women; age = 56 ± 14 years; time since stroke at assessment = 33 ± 82 weeks; 75% (194) of the patients were assessed < 6 months post-stroke, and 58% (148) were assessed within a month post-stroke. The data were drawn from a database providing lesion and behavioural information of stroke patients enrolled in previous studies of motor cognition of the University Hospital of Cologne and the Research Centre Jülich. Recruitment sites included the University Hospital of Cologne and the surrounding neurological rehabilitation centres. Other aetiologies than ischaemic strokes such as haemorrhage or tumors were excluded. All patients were right-handed prior to stroke. Furthermore, patients suffering from any other neurological or psychiatric diseases (e.g. depression) were excluded. Subjects were also included if they were between 18 and 80 years old when assessed.

We had only sparse quantitative data concerning the patients' language skills, but they were excluded if they presented with aphasia thought to be severe enough to compromise either their consent to participate, or their understanding of the imitation tasks. Our exclusion only of those patients whose aphasia was so severe that it compromised their grasp of the tasks is consistent with the approach used in (Hoeren et al., 2014), and all of the patients in (Goldenberg and Karnath, 2006) were aphasic. Patients had given written informed consent for participating in the original studies on motor cognition from which these data are drawn from (each of these studies was performed in accordance with the Declaration of Helsinki and was approved by the local ethics committee). Retrospective analyses using these data were approved by the institutional review board.

2.2. Testing procedures

All patients were assessed with the test of imitating finger and hand gestures by Goldenberg (1996). Here, the examiner sits opposite to the patient and demonstrates ten hand and ten finger gestures in a mirror like fashion. The examiner uses the hand opposite to the patient's non-paretic ipsilesional hand, which the patient is supposed to use for imitation. After the first demonstration of each gesture, the examiner forms a fist (neutral gesture) and the patient is asked to imitate the previously shown gesture. Two points are allocated for correct imitation, based solely on the final position of the gesture (self-corrections or hesitations do not influence the score). If imitation is incorrect, the examiner repeats the demonstration of the gesture and then returns to the neutral gesture (fist). The patient is asked to imitate the gesture once more. One point is allocated for correct imitation in this second trial, and no points are awarded if the patient fails at the second attempt. A patient is considered to suffer from a hand imitation deficit if the total imitation score for the ten hand gestures is 17 or less of the 20 possible points (two available points for each of the ten gestures) (Goldenberg, 1996). A patient is considered to suffer from a finger imitation deficit if the total imitation score for the ten finger gestures is 16 or less of the 20 possible points (Goldenberg, 1996; Hoeren et al., 2014).

The gestures employed in Goldenberg's test were originally meant to be 'meaningless', in the sense that they conveyed no direct semantic content. However, this characterization has been challenged with a recent analysis suggesting that most of the finger gestures can be interpreted as meaningful (Achilles et al., 2016). The difference is important because meaningful and meaningless gestures might be processed differently in the brain (Rumiati et al., 2009), which raises the possibility that any apparently body-part-specific differences that we find might in fact be driven by semantics. We did not attempt to exclude this possibility in the analyses that follow, simply to maximize their comparability with analogous past work. But we note that in both the analyses that follow, and the prior work that inspired them, this 'semantic confound' might drive false positive results (i.e. regions where damage appears to impair imitation skills in an effector-specific manner) simply because our measurement tool is confounded by semantics.