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Lénia Alexandra Leal Amaral

UNCOVERING THE INTERACTION BETWEEN HANDS AND TOOLS

ARE THESE CATEGORIES DISSOCIABLE?

Tese no âmbito do Doutoramento em Psicologia, especialidade em Neuropsicologia orientada pelo Professor Doutor Jorge Manuel Castelo Branco de Albuquerque Almeida e pelo Doutor Fredrik Bergström e apresentada à Faculdade de Psicologia e de Ciências da Educação da Universidade de Coimbra.

Dezembro de 2021

Faculdade de Psicologia e de Ciências da Educação
da Universidade de Coimbra

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Title	Uncovering the interaction between hands and tools – are these categories dissociable?
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Para o meu avô Fausto.

Para o meu avô Manel.

Para a minha avó Angelina.

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Resumo

Introdução: Os neurocientistas cognitivos há muito que tentam perceber como é que nós reconhecemos os objetos. Uma das principais questões de investigação nesta área tem sido tentar entender como é que o conhecimento sobre objetos está organizado no cérebro. Os dados reportados mostram a existência de regiões cerebrais específicas altamente especializadas no processamento de várias categorias, tais como mãos, ferramentas, faces e animais. As teorias clássicas focam-se nas propriedades visuais e em domínios dos objetos para explicar a especialização destas regiões cerebrais. Ainda assim, estas diferentes teorias partilham um princípio importante: que as representações conceptuais dependem principalmente de computações locais. No entanto, descobertas recentes sugerem que outros fatores (por exemplo, constrangimentos impostos pela conectividade) podem desempenhar um papel importante na organização funcional destas regiões e que as computações distais desempenham um papel na representação conceptual local. A maior parte da investigação neste campo tem-se centrado em regiões cerebrais que respondem a uma única categoria, mas uma região de sobreposição (ou seja, uma região que responde a mais de uma categoria) poderá oferecer a possibilidade de procurar dissociações nos constrangimentos impostos pela conectividade. O trabalho desta tese focou-se em duas categorias que estão funcionalmente ligadas – mãos e objetos manipuláveis (i.e., ferramentas) – e que mostram uma sobreposição anatómica em duas regiões do cérebro, no lóbulo parietal inferior (IPL, do inglês *inferior parietal lobule*) esquerdo e no córtex occipito-temporal lateral (LOTC, do inglês *lateral occipitotemporal cortex*) esquerdo.

Metodologia: Nesta tese apliquei uma abordagem multi-método, utilizando diferentes técnicas como a ressonância magnética funcional (RMf), a estimulação transcraniana por corrente contínua (ETCC) e a eletroencefalografia (EEG). Tanto a análise univariada como a análise multivariada foram utilizadas para examinar os dados, proporcionando resultados mais sensíveis e precisos. O meu principal objetivo foi explorar os princípios organizacionais subjacentes às representações das mãos e ferramentas dentro do IPL esquerdo e do LOTC esquerdo, assim como das restantes regiões pertencentes às redes neuronais de cada categoria.

Resultados principais: De acordo com o primeiro estudo de RMf, tanto o IPL como o LOTC revelam diferentes identidades de conectividade que são específicas para cada categoria – ou seja, o processamento em cada uma das duas regiões depende dos constrangimentos impostos pela conectividade (específicos para cada categoria) provenientes de regiões distais que fazem parte de uma rede funcional. O segundo estudo (utilizando a RMf e a ETCC) mostra como podemos estimular o processamento em direção a uma das categorias numa região de sobreposição e, assim, expor ainda mais as identidades de conectividades específicas para cada categoria. Finalmente, no terceiro estudo (um estudo de EEG), eu avaliei a dinâmica temporal do processamento de mãos e ferramentas e encontrei diferenças e semelhanças nas suas séries temporais. Apesar de as mãos e as ferramentas serem processadas de diferentes formas em diferentes momentos, acabam por chegar a um ponto no tempo em que a representação neural específica das ferramentas é informativa da representação neural das mãos.

Conclusões: Globalmente, estes resultados mostram que, apesar da sobreposição anatómica partilhada por mãos e ferramentas, as identidades de conectividade dessas regiões dependem da categoria que está a ser processada, revelando o papel crucial da conectividade distal na representação conceptual local e na representação de objetos no geral. Os resultados desta tese demonstram também quando é que o processamento de mãos e de ferramentas diverge e quando é que os dois convergem.

Palavras-chave: mãos, ferramentas, conectividade, série temporal, sobreposição, RMf, ETCC, EEG

Abstract

Introduction: Cognitive neuroscientists have long been trying to understand how we recognize objects. One of the main avenues of research in this area has been on trying to understand how object knowledge is organized in the brain. Evidence has been reported for the existence of particular brain regions that are highly specialized for the processing of various categories such as hands, tools, faces, and animals. The classical theories focus on the visual properties and object domains to explain the specialization of these brain regions. Nevertheless, these different theories share a major tenet: that conceptual representations are mainly dependent on local computations. However, recent findings suggest that other factors (e.g., connectivity constrains) may play an important role in the functional organization of these regions and that distal computations play a role in local conceptual representation. Most of research in this field has been focusing on brain regions that respond to a single category, but an overlap region (i.e., a region that responds to more than one category) could offer the possibility of looking for dissociating connectivity constrains. Here I focused on two categories that are functionally connected – hands and manipulable objects (i.e., tools) - and that show an anatomical overlap in two regions of the brain, left inferior parietal lobule (IPL) and left lateral occipitotemporal cortex (LOTC).

Methodology: In this thesis I applied a multi-method approach, using different techniques such as functional magnetic resonance imaging (fMRI), transcranial direct current stimulation (tDCS), and electroencephalography (EEG). Both univariate and multivariate analyses were used to examine the data, providing for more precise and sensitive results. My main goal was to explore the organizational principles underlying hand and tool representations within the left IPL and left LOTC, and remaining nodes of the category-specific networks.

Main results: According to the first fMRI study, both IPL and LOTC have different category-specific connectivity fingerprints – processing within each region is dependent on category-specific connectivity constraints from distal regions that are part of a functional network. The second study (using fMRI and tDCS) shows how we can boost the processing towards one of the categories in an overlap region and thus further expose category-specific connectivity fingerprints. Finally, in the third study (an EEG study), I assessed the temporal dynamics of hand and tool processing and found both differences and similarities in their time-courses. Despite the fact that hands and tools are processed in different ways at different times, they eventually reach a time point where category-specific neural representations of tools are informative of the neural representations of hands.

Conclusions: Overall, these results show that, despite the spatial overlap shared by hands and tools, the connectivity fingerprints from those regions depend on the category being processed, revealing the crucial role of distal connectivity in local conceptual representation and overall object representation. The findings here also demonstrate when hand and tool processing diverge and when they converge.

Keywords: hands, tools, connectivity, time-course, overlap, fMRI, tDCS, EEG

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Chapter I.

GENERAL INTRODUCTION

1. Introduction

Take a moment to look around and observe everything that is around you. Try to name all the things that you can see – easy, right? The way we recognize the world that surrounds us is so fast and effortless that we might think this is a simple process. When we see an object, we are immediately able to recognize and name it even if the object is not presented in its normal position/orientation or if it is partially hidden. Simple? Not at all. The human visual system is highly efficient and organized, but also very complex – going from a visual input to a cognitive interpretation requires a full journey. It all starts with the light concentrated in the cornea and lens. As the light is reflected onto the retina, the light-sensitive photoreceptive cells in the retina generate electric signals that travel via the optical nerve to the lateral geniculate nucleus (LGN) and other subcortical structures. Visual information is then handled in visual cortex. But does it stop there? How do we achieve *object recognition*?

Object recognition requires high-level visual processing whereby (low-level) visual features from an object are aggregated. For instance, cells located within LGN are responsible for providing different types of visual information – such as movement (magnocellular cells), color and form/detail information (parvocellular cells). This information is further processed into a conceptual representation, allowing us to identify animals, tools or plants, among other things. This research aims to add a new layer of insight to the subject of object recognition by focusing on how we interpret two distinct categories: hands and tools (i.e., handheld manipulable objects).

1.1. Perception and action – two distinct pathways

One of the most accepted theories on the visual system was proposed in 1992 by Goodale and Milner (Goodale & Milner, 1992). According to these authors, the visual system can be divided into two major pathways: the dorsal stream, which is responsible for volumetric and spatial analysis of the visual stimulus, and the ventral stream, which allows for form-based object identification (Goodale & Milner, 1992). Research dedicated to the study of brain lesions supports this division of labor within the visual system. On the one hand, patients with lesions to ventral stream regions have impaired visual object recognition and difficulties with perceptual decisions, but show spared object-related reaching and grasping (i.e., visual agnosia; e.g., Carey et al., 1996; Milner et al., 1991). A well-known illustration of this impairment is the case of patient D.F. (Goodale et al., 1991). The authors described this patient as someone with a strong impairment in recognizing the physical features of visually presented objects, but also with strikingly accurate visual guidance of movements directed at the exact same objects. For instance, patient D.F.'s performance was severely affected when she was asked to make perceptual judgments about an object’s orientation and size. However, her performance was flawless when she was instructed to reach and pre-shape her hand according to the orientation and size of the same object (Goodale et al., 1991). On the other hand, lesions to dorsal stream structures lead to difficulties with reaching and/or grasping visually presented objects, but normal performance in recognizing and perceptually judging those same objects (i.e., optic ataxia; e.g., Jakobson et al., 1991; Jeannerod et al., 1994; Milner et al., 2003; for a review see also Pisella et al., 2009). For instance, patient R.V. (who suffered from optic ataxia) had no trouble in visually distinguishing one irregularly shaped object from another, but was unable to position her fingers accurately around those objects when asked to pick them up (Goodale et al., 1994).

The idea that the visual system was not unitary but segregated was not novel. The first theory about an anatomical brain separation between identification and localization was proposed by Schneider (Schneider, 1969). Schneider observed that golden hamsters whose superior colliculus was resected could identify an object (i.e., they performed normally on pattern discrimination tasks), but could not orient themselves towards that same object. The opposite effect was observed in hamsters that had their visual cortical areas ablated. Later, in 1982, Mishkin and Ungerleider (Mishkin & Ungerleider, 1982; see also Mishkin et al., 1983) identified two cortical visual systems in the macaque monkey brain: the “what” pathway (ventral stream), going from primary visual area (V1) to ventral occipital-temporal cortex, that was responsible for object vision; and the “where” pathway (dorsal stream) that goes from V1 to dorsal-occipital and posterior parietal cortex, and was responsible for spatial vision. The proposal made by Goodale and Milner (Goodale & Milner, 1992; see also Milner & Goodale, 2006) was a re-interpretation of this separation between the streams. These authors suggest deemphasizing the differences in the input that these streams receive, and rather highlighting the computational goals and outputs achieved by each stream. In the end, both streams receive information (mainly) from retinogeniculate inputs, but the main difference between the streams lies on how that information is used: the ventral stream is responsible for the perceptual representations of the objects that surround us, while the dorsal stream focuses on our actions toward those objects.

With the discovery of the functional magnetic resonance imaging (fMRI) in the nineties, it was possible to further our understanding of the organization of visual information in the brain beyond V1. The division of labor between the two streams was observed in numerous studies (human and non-human primates) showing that object identity is processed in the ventral stream, that projects from V1 to occipito-temporal and ventral-temporal regions; and that object-directed action is processed in the dorsal stream, that projects to posterior parietal and occipito-parietal regions from V1 and subcortical structures such as the superior colliculus and lateral geniculate nucleus (e.g., Culham et al., 2003; James et al., 2002; Malach et al., 1995; Schmid et al., 2009, 2010; Shmuelof & Zohary, 2005). A good demonstration of this division of labor can be seen in how ventral temporal cortical regions are engaged by different object categories (e.g., Bar & Aminoff, 2003; Chao et al., 1999; Chao & Martin, 2000; Downing et al., 2001; Epstein & Kanwisher, 1998; Kanwisher et al., 1997; Mahon et al., 2007; Peelen & Downing, 2007; Perani et al., 1995); whereas (dorsal stream) parietal regions seem to be engaged during object grasping and manipulation (e.g., Binkofski et al., 1998, 1999; Boronat et al., 2005; Ishibashi et al., 2011; Kellenbach et al., 2003; Monaco et al., 2011). Note, however, that recent evidence has been accrued that suggest that the dorsal stream can have a role in object recognition (for a review see Freud et al., 2016). For example, Freud and colleagues have suggested that the dorsal stream computes object-specific 3D perceptual aspects that are important for object recognition (Freud, Culham, et al., 2017; Freud, Ganel, et al., 2017; see also Almeida et al., 2008, 2010, 2014).

As can be seen from the above, the division of labor between the two streams and the way in which they process the visual input separately is very well established. Nevertheless, object recognition is dependent on information that is processed by both pathways and researchers have been focusing on how the interaction between the two streams and the integration of information into a global conceptual representation takes place (e.g., Brandi et al., 2014; Gallivan et al., 2014; Konen & Kastner, 2008; Mahon et al., 2007; for a review see Milner, 2017). For instance, Almeida and colleagues (Almeida et al., 2013; Kristensen et al., 2016; Mahon et al., 2013) have used different psychophysical techniques to explore the interaction between the two visual streams during object recognition. In one set of experiments, they explored how different subcortical visual pathways enervate dorsal and ventral visual stream to understand how these streams interact. They focused on two subcortical pathways – the magnocellular and parvocellular pathways – that separate already in the retina and project differently to the LGN. Importantly, the ventral stream is primarily served by the parvocellular pathway, whilst both dorsal and ventral streams are served by the magnocellular network (Merigan & Maunsell, 1993). In their work, Almeida and colleagues showed that parvocellular input (that projects mainly to ventral stream) impacts processing within the inferior parietal lobule (IPL), demonstrating that information processing within ventral temporal cortex interacts with dorsal stream processes. Other studies also showed the interaction between the two streams when responding to action (Xu et al., 2021), converting object-related information into goal-directed movements (Gallivan et al., 2016) or even when processing categories that activate regions within the two pathways (Almeida et al., 2018).

It is also worth noting that, in addition to the interaction between the two streams, there is growing evidence that another anatomical and functional subdivision exists within the dorsal stream. In fact, Rizzolatti and Matelli (2003) suggested two subdivisions of the dorsal stream: the dorso-dorsal stream, that includes area V6 and the superior parietal lobule (SPL) and is responsible for the control of actions; and the ventro-dorsal stream, that projects to area MT/V5 and IPL and seems to integrate perception and action (Rizzolatti & Matelli, 2003). Several studies with patients support this view, suggesting that these two subsystems refer to grasp and use knowledge, separately. On the one hand, optic ataxia – a deficit in reaching objects – is a consequence of lesions to the dorso-dorsal stream. On the other hand, deficits in skilled object-use (e.g., limb apraxia) are caused by lesions to the ventro-dorsal stream (for a review see Binkofski & Buxbaum, 2013). This macroscopic division of labor in visual cortex plays a central role in computing object representations. But how are these representations organized in the brain?

1.2. The organization of object knowledge in the brain

One of the most intriguing challenges in cognitive neuroscience is understanding how conceptual knowledge is organized in the brain. Neuropsychological studies with brain-damaged patients that showed category-specific semantic deficits were amongst the first to focus on the question of the organization of conceptual knowledge in the brain and brought important evidence to this field (e.g., Caramazza & Shelton, 1998; De Renzi & Lucchelli, 1994; Farah et al., 1991; Hillis & Caramazza, 1991; Tyler & Moss, 1997; Warrington & Mccarthy, 1983; Warrington & Shallice, 1984). Different claims have been put forth about the representation of conceptual knowledge, highlighting the role of sensorimotor systems, object features and/or object domain as major principles of organization of information.

One of the major theoretical proposals was the Sensory/Functional theory (SFT), put forth by Warrington and Shallice (e.g., Warrington & Shallice, 1984). In this seminal study, the authors performed a series of experiments with patients that presented a selective recognition impairment for certain categories (e.g., living things and foods), and argued that these categories are mainly distinguished by their visual features. So, if a lesion occurs in a region that handles information about visual properties, a category-specific disorder for living things will occur. Advocates of STF assume that: 1) the organization of conceptual knowledge in the brain is based on modalities (e.g., visual, olfactory, auditory, motor/functional, etc.); and 2) visual properties are crucial when recognizing living things and functional properties are more important for nonliving categories. Tyler and Moss (1997) expanded the second assumption arguing that different types of functional information exist, and that biological information is particularly important when recognizing living categories. For instance, they observed a patient that could not process functional information (e.g., where an animal lives or what it eats), but his knowledge of biological information (e.g., that an animal breathes, eats, etc.) was relatively intact (Tyler & Moss, 1997). Later, Tyler and Moss (and other authors) have challenged the SFT and proposed that categories and domains emerge from structure and content of semantic representations, rather than from sensory and functional separated stores (for a review see Tyler & Moss, 2001). Tyler and colleagues suggested that category-specific impairments arise because of changes in the content and structure of concepts across categories (Tyler et al., 2000). These authors proposed two main assumptions for their Conceptual-Structure model: 1) living things share several features and non-living things have more distinctive features; and 2) the internal structure of concepts depends on the proportion of the different features (e.g., perceptual, visual) and it also depends on the correlation among features – highly correlated features are more resistant to damage than uncorrelated features (Tyler et al., 2000).

But can conceptual knowledge be reduced to the sensory and motor systems? This is one of the oldest debates in cognition and various studies corroborate this so-called embodied view. One of the most cited works in support of this view is the mirror neuron theory, which claims that motor simulation (activation of the motor system) is necessary to understand someone else's actions (Rizzolatti et al., 1996; for a review see also Rizzolatti & Sinigaglia, 2010; for another embodied view of conceptual representation see Barsalou, 1999; Barsalou & Wiemer-Hastings, 2005). Thus, in extreme embodied views, conceptual knowledge relies on motor-related information. Neuroimaging studies showing activation of sensory and motor systems during object-category recognition (Hauk et al., 2004; Simmons et al., 2007) are putatively in line with this idea that conceptual knowledge relies on the simulation of sensorimotor representations. However, other authors have been arguing that these results are not necessary evidence for an embodied view of cognition, but are just consistent with it, and suggest that there is an exchange among sensorimotor and non-sensorimotor representations during conceptual processing (Caramazza et al., 2014; Mahon, 2015).

Another major theoretical approach to the organization of conceptual knowledge is the domain-specific theory (Caramazza & Mahon, 2003; Caramazza & Shelton, 1998). This theory proposes that knowledge is organized by domain, and that these domains are those that were crucial in our evolutionary past – that is, those domains of objects whose rapid and efficient recognition conferred a survival advantage (i.e., the domains of conspecifics, animals, fruits and vegetables, and manipulable objects). Our brain evolved in such a way that we have neural circuits dedicated to specific domains in order to facilitate rapid and efficient recognition (Caramazza & Mahon, 2003). A latter version of this theory enhances the contribution of distributed representations (sensorimotor or others), proposing that while object domain may be the primary principle of organization of conceptual knowledge in the brain, a distributed network of modality-specific representations may also guide organization of conceptual knowledge (the distributed domain-specific hypothesis; Mahon & Caramazza, 2009).

The importance of local computations, as well as feedforward (e.g., Van Essen & Gallant, 1994) and feedback connections (e.g., Bar et al., 2006), on object processing and conceptual representation has been clearly demonstrated. Recognizing an object depends not only on ventral stream processing, but also on the connections between that stream and other regions in the brain (Mahon & Caramazza, 2011). Early neuroimaging studies show that ventral stream regions reveal specific categorical responses. For example, seeing object categories such as faces (e.g., Epstein & Kanwisher, 1998; Fox et al., 2009), places/scenes (e.g., Bar & Aminoff, 2003; Epstein & Kanwisher, 1998), animals (e.g., Chao et al., 1999; Martin et al., 1996; Perani et al., 1995), tools (e.g., Almeida et al., 2013; Mahon et al., 2007), bodies (e.g., Downing et al., 2001; Peelen & Downing, 2007), and hands (e.g., Bracci et al., 2012) engage different regions within ventral temporal cortex (VTC) – a group of cortical regions that evidently display a variety of responses that are categorical in nature. However, other studies do not support these sharp categorical boundaries, arguing instead for a distributed pattern of activity (Haxby et al., 2001; Rogers et al., 2005).

Lately, however, a role for distal processing on local computations and representations has been suggested. Specifically, an association between categorical processing occurring within a particular category-preferring region and the connectivity from that region to distant areas that are at the same representational level and share category-preferences has been shown (Almeida et al., 2013; Chen et al., 2017; Garcea et al., 2019; Garcea & Mahon, 2014; Hutchison et al., 2014; Hutchison & Gallivan, 2018; Lee et al., 2019; Mahon et al., 2009; Mahon & Caramazza, 2011; Saygin et al., 2016; Walbrin & Almeida, 2021). This is particularly true for the VTC, within which it has been shown that categoric representations depend on remote processing (Chen et al., 2017; Garcea et al., 2019; Lee et al., 2019; Ruttorf et al., 2019).

These sorts of connectivity constraints on processing have been shown in a variety of investigations employing different approaches. In an fMRI study where participants viewed images of tools and animals, Garcea and Mahon showed that different clusters of the left parietal cortex (a tool region) displayed different patterns of category-specific connectivity to other tool regions in the brain (Garcea & Mahon, 2014; see also Garcea et al., 2019). In another interesting fMRI study, the importance of connectivity was demonstrated by Walbrin and Almeida (2021), showing not only that distal connectivity is related with representations within the occipitotemporal cortex, but also that strongly connected voxels are associated to higher discriminability than voxels with local activation (Walbrin & Almeida, 2021). Using resting-state fMRI, Hutchison and colleagues (2014) found specific connectivity patterns between regions that share identical categorical preferences (Hutchison et al., 2014). Structural connectivity also shows the same pattern for the visual word form area (VWFA; Saygin et. al, 2016). In this study, Saygin and colleagues demonstrated that the location of VWFA in children at age 8 (when they learn to read) can be predicted by the connectivity present of that region at age 5 – before learning how to read (Saygin et al., 2016). Finally, in a neuromodulation study, Lee and colleagues (2019) applied transcranial direct current stimulation (tDCS) to the tool-preferring IPL, and found that representations in a tool-preferring region within VTC (the left medial fusiform gyrus – mFUG), but not in other regions of VTC, changed in category-specific manner (Lee et al., 2019; see also Ruttorf et al., 2019).

1.3. The case of hands and tools

Most of the work that pinpoint connectivity constrains as principles that rule conceptual knowledge focus on responses to specific categories. However, what happens when more than one category engages the same cortical region? Does this indicate an overlap in terms of processing? Are the distal connectivity patterns, those that implement the kinds of connectivity constraints described above, distinct, or similar for both of those categories? To illustrate this case, I will further discuss the case of hands and tools.

When we see a tool, several types of information – such as the size of the object, its function, its location or how to grasp it – become available. Importantly, some of this information pertains to aspects that relate the target manipulable object with the effector (i.e., the hands) that typically manipulate it. One such important type of information is related to object affordances. The idea of object affordances emerged in 1979, when Gibson put forth an ecological perspective, whereby possible actions to be performed on an object are readily available from the inspection of the objects, presumably without cognitive mediation (Gibson, 2014). These action possibilities – the so-called affordances – show us how important the relation between a hand and a tool can be. For instance, several studies have shown that human subjects are faster to conduct hand movements that are compatible with the affordances of a (task-irrelevant) graspable object (Bub & Masson, 2010; Craighero et al., 1997; Ellis & Tucker, 2000; Makris et al., 2011; Phillips & Ward, 2002; Riddoch et al., 1998, 2003; Tipper et al., 2006; Tucker & Ellis, 1998; Vainio et al., 2007; Vingerhoets et al., 2009). Furthermore, (task-irrelevant) images of hands, particularly presented in grasping postures, have been shown to influence (manipulable) objects categorization. This implies that simply looking at a hand in a particular grasp posture activates motor information that can influence the processing of graspable objects (e.g., Almeida et al., 2018; Borghi et al., 2007; Bub et al., 2013; Vainio et al., 2008). Neuroimaging and electrophysiological studies also show that seeing images of hands and tools activate motor and parietal areas in response to affordances (Grèzes, Armony, et al., 2003; Grèzes, Tucker, et al., 2003; Grèzes & Decety, 2002; Johnson-Frey et al., 2005; Valyear et al., 2006).

Thus, although hands and tools are two categories that can be dissociated at the perceptual level, it is clear that they are functionally related. In a priming study, Almeida and colleagues (2018) showed that unconscious processing of pictures of hands affects the recognition of visible tool pictures, and the unconscious processing of pictures of tools affects the recognition of visible pictures of hands – this illustrates the functional link between the two categories (Almeida et al., 2018). Interestingly, hands and tools present remarkably similar neuronal responses. For instance, IPL is involved in tool processing, but is also engaged during hand-related grasping and manipulation (Grafton, 2010; Jacobs et al., 2010; Johnson-Frey et al., 2005). Additionally, in a series of groundbreaking papers, Bracci and colleagues (Bracci et al., 2012, 2016) demonstrated that the processing of these categories shares several neural loci. For instance, in an fMRI study they found that left lateral occipitotemporal cortex (LOTC) prefers both hands and tools to other categories of objects (Bracci et al., 2012). This response overlap was confirmed by a set of different results. Specifically, the authors showed 1) an overlap in neural response to hands and tools (but not to other object categories or other body parts) in left LOTC; 2) greater similarity in multivoxel response patterns between hands (but not other body parts) and tools; and 3) selective functional connections between the specific overlap region in left LOTC (for hands and tools) and regions that are related to the processing of these categories, when compared to neighboring body-, motion- and object-selective regions (Bracci et al., 2012). In another study, Bracci et al. (2016) showed that this overlap extends to other regions in the brain. Specifically, the authors observed that hands and tools activate not only a specific portion of left LOTC, but also the left intraparietal sulcus (IPS) and the ventral occipitotemporal cortex (VOTC). However, the authors also showed that the patterns of response for each category (hands and tools) are different in each one of those regions:

although left LOTC seems to integrate both action and object/perceptual information, VOTC is mainly interested in the object domain and left IPS is focused on tool action-related processing (Bracci et al., 2016). The overlap response to hands and tools is probably based on the action-related properties that the two categories share: understanding how to use a tool requires computing information about hand posture and grip configuration in relation to that specific tool.

At this point, the close functional relation between hands and tools is clear, and its implementation within regions whose neural responses for hands and tools overlaps may indicate that hands and tools are (neuronally) handled in a very similar way. But what are the similarities and differences in processing between these two categories?

Chapter II.

AIMS AND HYPOTHESES

2. Aims and hypotheses

In this dissertation I included three different approaches to explore the differences and similarities between neural processing of hands and tools by: 1) using fMRI and looking at the functional connectivity patterns of the regions that share (hand and tool) categorical preferences in search for differences between hand and tool networks; 2) applying non-invasive neuromodulation (e.g., transcranial direct current stimulation – tDCS) to an overlap area to see if we can affect hand and tool processing separately; and 3) assessing temporal differences and/or similarities during the processing of hands and tools using electroencephalography (EEG).

2.1. Study 1

In the first functional magnetic resonance imaging (fMRI) study I measure the connectivity fingerprints revealed by two regions that respond both to hands and tools (i.e., left inferior parietal lobule/intraparietal sulcus – IPL/IPS and left posterior middle temporal gyrus/lateral occipitotemporal cortex – pMTG/LOTC). My goal is to investigate if the connectivity patterns are category-dependent: if so, they will be distinct between hand and tool processing. For that purpose, I employ a multivariate method in which functional connectivity with distal areas is related to local voxel-wise category preferences. I am particularly interested in how connectivity from the two overlap areas correlates with voxel-wise category preferences in ventral temporal regions dedicated to hand and tool processing independently (the fusiform body area, FBA; and the medial fusiform gyrus, mFUG respectively), as well as across the brain. I expect that functional connectivity from the overlap regions will correlate with categorical preferences for each category independently. That is, I anticipate that hand-preferences (but not tool-preferences) in FBA will be correlated with functional connectivity between each of the overlap areas and the FBA; and tool-preferences (but not hand-preferences) will correlate with functional connectivity between the overlap regions and the mFUG. Finally, I predict different distal interactions emerging from the two overlap areas for hand and tool-preferences, when applying a whole-brain searchlight analysis. This study is presented in Chapter III of this thesis.

2.2. Study 2

In the second study, I want to test if we can disentangle the processing of hands and tools in the overlap area of left pMTG/LOTC through the use of neuromodulation coupled with a category-specific task that could bias the processing towards one of these categories (hands or tools). To examine this, I applied tDCS to left pMTG/LOTC or medial prefrontal cortex (mPFC – control area not related to hand or tool processing), while participants completed either a hand or a tool-related training task. After the tDCS/training session, participants went through an fMRI experiment and visualized images of hands, tools, and animals. Using a multivoxel pattern analysis, I compare the classification accuracies when discriminating hands vs. animals (or tools vs. animals) for the following conditions: 1) tDCS on pMTG/LOTC plus hand training task; 2) tDCS on pMTG/LOTC plus tool training task; 3) tDCS on mPFC plus hand training task; and 4) tDCS on mPFC plus tools training task. In the first condition I predict an improvement in classification accuracy for hands vs. animals, and in the second condition I expect an improvement in classification accuracy for tools vs. animals. This study is presented in Chapter IV of this thesis.

2.3. Study 3

I also aim to characterize the temporal unfolding of hands and tools. In the previous studies, I focused on the spatial organization of object knowledge, and here I want to understand the importance of temporal dynamics during object recognition. I am particularly interested in how the spatial overlap is transposed to the temporal domain in the case of hands and tools. Does this overlap relate to similar time-courses for both categories? Or is it possible to disentangle the temporal dynamics of hands and tools? In this study, I used EEG to measure the electrical activity in response to images of hands, tools, animals, and feet. Then I compare classification accuracy for images of hands (vs. animals) and tools (vs. animals) using multivariate pattern analysis on different time points of an experimental visualization task. I hypothesize that classification accuracy will differ (in specific time intervals) when comparing hands and tools. Using a cross-decoding approach, I also want to test if the discrimination between tools and animals can lead to a generalized learning allowing for the classifier to classify hands as tools (and vice-versa). Although hand and tool processing may have different time-courses, I predict they will share some key temporal patterns, enabling for cross-decoding between the two categories. The results of this last investigation are presented in Chapter V.

Chapter III.

OVERLAPPING BUT DISTINCT: DISTAL CONNECTIVITY DISSOCIATES HAND AND TOOL PROCESSING NETWORKS – STUDY 1

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3.1. Abstract

The processes and organizational principles of information involved in object recognition have been a subject of intense debate. These research efforts led to the understanding that local computations and feedforward/feedback connections are essential to our representations and their organization. Recent data, however, has demonstrated that distal computations also play a role in how information is locally processed. Here we focus on how long-range connectivity and local functional organization of information are related, by exploring regions that show overlapping category-preferences for two categories and testing whether their connections are related with distal representations in a category-specific way. We used an approach that relates functional connectivity with distal areas to local voxel-wise category-preferences. Specifically, we focused on two areas that show an overlap in category-preferences for tools and hands – the inferior parietal lobule/anterior intraparietal sulcus (IPL/aIPS) and the posterior middle temporal gyrus/lateral occipital temporal cortex (pMTG/LOTC) – and how connectivity from these two areas relate to voxel-wise category-preferences in two ventral temporal regions dedicated to the processing of tools and hands separately – the left medial fusiform gyrus and the fusiform body area respectively – as well as across the brain. We show that the functional connections of the two overlap areas correlate with categorical preferences for each category independently. These results show that regions that process both tools and hands maintain object topography in a category-specific way. This potentially allows for a category-specific flow of information that is pertinent to computing object representations.

Keywords: tools, hands, distal connectivity, representation, functional organization, fMRI

3.2. Introduction

The human brain has the ability to immediately recognize familiar objects on sight, and it does so while managing many different kinds of information (e.g., shape, texture, function). However, the cortical organization of this information, and the neural computations supporting these processes are still under debate (Grill-Spector & Malach, 2004). Here we will take on a recent proposal on how object information is represented in the brain, which proposes that local processing is influenced, in part, by processing happening distally within the neural network dedicated to the processing of the target category. We will focus on the processing of tool and hand stimuli to further explore how representations are modulated distally.

Early neuroimaging studies showed that different object categories engage different sets of cortical areas (e.g., faces, Kanwisher et al., 1997; places/scenes, Epstein & Kanwisher, 1998; tools, Almeida et al., 2013; Chao & Martin, 2000; Mahon et al., 2007; bodies, Downing et al., 2001; and hands, Bracci et al., 2012, 2016). However, current theories differ in their understanding of what drives this object topography – whether it is the distributed representation of object features (Haxby et al., 2001; Konkle & Caramazza, 2013), the typical visual field location of different categories (Levy et al., 2001); or domain-specific constraints (e.g., Caramazza & Shelton, 1998; Kriegeskorte et al., 2008; Mahon & Caramazza, 2011, for a review see Grill-Spector & Malach, 2004). Importantly, most share the view that neural specificity and conceptual representations arise from local computations, feedforward connectivity from early visual regions, and attentional and/or perceptual feedback connections (e.g., Bar et al., 2006; Buffalo et al., 2010; Kreiman et al., 2010).

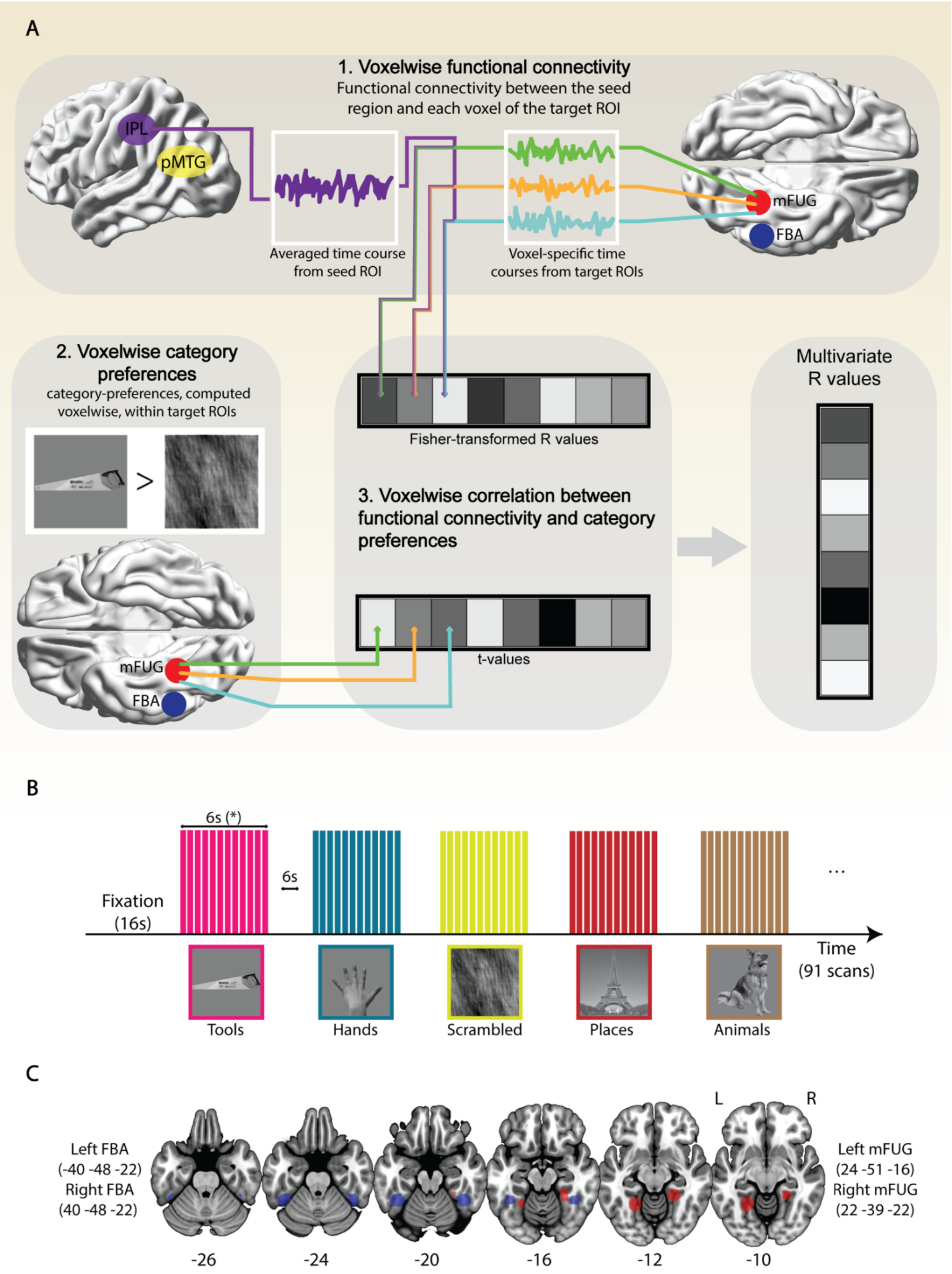
A conceptually different approach for thinking about object topography is that local representations also depend on connections from distal regions that share categorical preference. In this view, local representations do depend on local computations, feedforward and feedback connections, as described before, but also, and importantly, on connections from distal regions that share categorical preference (and that pertain to the same level of representation). That is, local representations are constrained by connectivity with other brain areas at the same level in the visual processing hierarchy (Almeida et al., 2013; Chen et al., 2017; Garcea et al., 2019; Hutchison et al., 2014; Hutchison & Gallivan, 2018; Lee et al., 2019; Mahon & Caramazza, 2009, 2011; Walbrin & Almeida, 2021). In support of this view, representations in a tool-preferring region (the left medial fusiform gyrus; mFUG) within the ventral temporal cortex (VTC) are causally dependent on computations in remote but functionally connected tool-preferring regions within parietal cortex (the Inferior Parietal Lobule, IPL, Lee et al., 2019; see also Ruttorf et al., 2019; Garcea et al., 2019). Moreover, functional and structural connectivity from distant regions correlate with categorical preferences in VTC in a category-specific way (e.g., functional connectivity between tool-preferring IPL and VTC correlated with tool preferences but not place, animal, or face preferences in the VTC, Chen et al., 2017; see also Pessoa et al., 2006; Saygin et al., 2016; Zhang et al., 2009).

Most of the work that tried to dissect the relationship between local computations and distal connectivity has been done over distal regions that respond preferentially to one specific object category (out of those being tested, e.g., tools in an experimental design that includes stimuli from the category of animals, faces or places; Chen et al., 2017). A stronger case of this hypothesis could be made by testing distal regions that respond preferentially to more than one category of those tested. For instance, if a region responds equally to two categories as revealed by BOLD signal, do its connections relate to object topography elsewhere in a category-specific way – i.e., do its connections disentangling the processing of the two categories? According to the hypothesis proposed above, the functional connections of these regions should nevertheless correlate with response preferences in regions that are distally located in a category-specific manner, and should do so independently for each one of the categories, thus maintaining object topography irrespectively of the overlap in BOLD signal responses for the two categories.

Here we will focus on the categories of tools and hands because tools and hands are functionally related (Almeida et al., 2018), and because some of the regions that these stimuli preferentially engage are shared (e.g., Almeida et al., 2013; Bracci et al., 2012, 2016; Bracci & Peelen, 2013; Chao & Martin, 2000; Mahon et al., 2007; Peeters et al., 2013). On the one side, tool stimuli (when compared to items from other categories such as animals or faces) lead to heightened activation bilaterally in superior parietal cortex, dorsal occipital cortex, and the mFUG, and within left inferior parietal regions, the anterior intraparietal sulcus (aIPS), ventral premotor cortex, and posterior middle temporal areas (e.g., Almeida et al., 2013, 2017; Binkofski et al., 1999; Binkofski et al., 1998; Chao et al., 1999; Chao & Martin, 2000; Chen et al., 2017; Freud et al., 2017; Kristensen et al., 2016; Mahon et al., 2013, 2007; Noppeney et al., 2006; Peeters et al., 2013). On the other side, hand stimuli (when compared to other categories of interest such as animals) lead to stronger responses within lateral fusiform gyrus bilaterally, lateral occipital temporal cortex (stronger on the left), in inferior and superior parietal regions, and in premotor, somatosensory, and motor regions (e.g., Bracci et al., 2010, 2012, 2016; Bracci & Peelen, 2013; Grosbras & Paus, 2006; Meier et al., 2008; Peeters et al., 2013).

Importantly, in a series of studies Bracci and colleagues have demonstrated that tool and hand stimuli concurrently engage two regions – the left IPL and left posterior middle temporal gyrus/lateral occipital temporal cortex (pMTG/LOTC) (Bracci et al., 2012, 2016; Bracci & Peelen, 2013; Peeters et al., 2013). Given this response overlap between tool and hand stimuli within the left IPL and the left pMTG/LOTC, we predict that functional connectivity from each of these overlap regions (i.e., left IPL or left pMTG/LOTC) to distal regions (e.g., regions within the VTC) should be correlated with voxel-wise response preferences within those distal regions. This should be so in a category-specific way and thus should be able to disentangle the tool and hand networks despite the BOLD response overlap for tools and hands within left IPL and left pMTG/LOTC.

We answer this question by focusing on the two overlap sites (IPL and pMTG/LOTC) and examine how multivoxel categorical preferences for tools and hands in particular areas of the tool and hand networks, and across the brain, correlate with functional connectivity emerging from these overlapping areas (see Figure 3.1A). We predict that voxel-wise tool-preferences but not hand-preferences in the medial aspects of the fusiform gyrus (the mFUG; an area that is part of the tool network; Chao & Martin, 2000; Mahon et al., 2007) will correlate strongly with functional connectivity computed from each overlap region (i.e., IPL or pMTG/LOTC) to the voxels within the medial fusiform, whereas the inverse will be true in more lateral aspects of the fusiform (i.e., the Fusiform Body Area - FBA; an area that shows preferences for body parts and hands; Downing et al., 2001). We will then inspect the whole brain for similar category-specific distal modulations by using a searchlight approach and expect to observe different distal relationships for tools and hands emerging from the two overlap areas.



(*) 12 images * 500ms = 6s

Figure 3.1 - Experimental procedures and analysis pipeline.

Figure 3.1. (**A**) Schematic workflow of analysis. (1) an average seed time-series (e.g., IPL/aIPS) is correlated with the time-series of each voxel in a target ROI (e.g., mFUG) to produce a vector of Fischer transformed r-values. (2) a univariate contrast (e.g., tools > all scrambled) in the same target ROI is used to produce a vector of category-preference (t-values). (3) the Fischer transformed r-values are correlated with the t-values within the target ROI to produce multivariate r-values. (**B**) Blocked fMRI design with 12 images (each 500 ms) per block (each 6 s) of tools, hands, animals, places, and phase-scrambled images, with 16 s fixation between blocks (**C**) The VTC regions of interest used during the analysis (FBA in blue and mFUG in red). The regions were defined around peak coordinates obtained in the literature.

3.3. Methods

Participants

We recruited sixteen participants (M = 21 years, SD = 4.7, 12 females) from the subject pool of the Faculty of Psychology and Educational Sciences of the University of Coimbra following previous studies (e.g., Mahon et al, 2013). All participants had normal or corrected to normal vision, were right-handed, gave written informed consent, and received course credits for their participation. The study adhered to the Declaration of Helsinki and was approved by the Ethical Committee of the Faculty of Psychology and Educational Sciences at the University of Coimbra. Due to excessive head motion, we excluded data from all runs for one participant. Thus, 15 participants were used for statistical analyses.

Stimuli and procedure

The study consisted of a category-preference experiment (6 runs with a total of 546 volumes per participant) and a tool/hand experiment (5 runs; participants also went through another session of this experiment, but that data was not used herein) where task-related BOLD signal was regressed out in order to calculate functional connectivity measures unrelated to the task. Stimulus delivery and response collection was controlled using “A Simple Framework” (Schwarzbach, 2011) based on the Psychophysics Toolbox on Matlab R2014a (The MathWorks Inc., Natick, MA, USA). Stimuli (Figure 3.1B) were presented on an Avotec projector with a refresh rate of 60 Hz, and viewed by the participants through a mirror attached to the head coil inside the bore of the MR scanner.

In the category-preference experiment participants passively viewed grey-scaled images (400 x 400 pixel-size) of tools, hands, animals, famous places, and phase-scrambled versions of each category (adapted from Fintzi & Mahon, 2014; see also Almeida et al., 2017; Lee et al., 2019). Each category was pseudo-randomly presented block-wise (with 12 consecutive images presented for 500 ms each per block) twice per run. Each phase-scrambled object category was presented once per run, each block was separated by 6s fixation periods, and each run began and ended with a 16 s fixation period.

In the tool/hand experiment we used a mixed design with six 54s blocks, 8s inter-block-intervals, and each block contained 18 randomly mixed trials with 1.5s stimulus and 1.5s fixation. There were two blocks of grey-scaled (8 power and 8 precision) tool images, two blocks of grey-scaled (8 power and 8 precision) grasp videos filmed from a first-person viewpoint, and two blocks of grasp videos filmed from a third-person viewpoint. Additionally, each block contained two “catch” trials, which were either tool chimeras (i.e., a combination of two tools) in the tool-image block, or a non-grasping movement (e.g., rotating the hand while maintaining an open palm) in the grasp-video blocks. Participants were instructed to pay attention to the presented stimuli and press a button whenever they detected a catch trial. Critically, however, the experimental design of this tool/hand task was regressed out (see below) and the residuals were used to compute functional connectivity (e.g., Almeida et al., 2013).

For all experiments, we used an eye tracker to (subjectively) monitor the individual's attention (and wakefulness) during the task.

MRI acquisition

We collected MRI data with a 3T MAGNETOM Trio whole body MR scanner (Siemens Healthineers, Erlangen, Germany) with a 32-channel receive-only head coil across two sessions (one structural run, six runs for the category-preference experiment and five runs for the tool/hand experiment). We acquired structural MRI data using a T1-weighted magnetization prepared rapid gradient echo (MPRAGE) sequence (repetition time (TR) = 1900ms, echo time (TE) = 2.32ms, slice thickness = 0.9 mm, flip angle = 9 degrees, field of view (FoV) = 256 x 256, matrix size = 256 x 256, bandwidth (BW) = 200 Hz/px, GRAPPA acceleration factor 2). Functional MRI (fMRI) data were acquired using a T2*-weighted gradient echo planar imaging (EPI) sequence (TR = 2000ms, TE = 22ms, slice thickness = 2.3, FoV = 256 x 256, matrix size = 96 x 96, flip angle = 90 degrees, BW = 1578 Hz/px, GRAPPA acceleration factor 3). Each image volume consisted of 40 contiguous transverse slices recorded in interleaved slice order oriented parallel to the line connecting the anterior commissure to the posterior commissure covering the whole brain.

fMRI data Preprocessing

We used SPM12 (Welcome Trust Centre for Neuroimaging, London, UK), run in Matlab R2018b (Mathworks, Inc., Sherborn, MA, USA), for processing and analysis of structural and functional data. The structural and functional images were reoriented to approximate MNI space with SPM12 after slice-time correction. During preprocessing, the functional data were slice-time corrected to the first slice using a Fourier phase-shift interpolation method, corrected for head motion to the first volume of the first session using 7th degree b-spline interpolation. Structural images were co-registered to the first functional images. Functional data were normalized to MNI anatomical space using a 12-parameter affine transformation model in DARTEL (Ashburner, 2007) and down-sampled to 3mm^3 voxel size prior to applying an 8mm (for ROIs definition) and 6mm (for category-preferences and functional connectivity analyses) FWHM Gaussian filter.

Statistical analysis of fMRI data

In order to preserve independence between voxel selection and testing (Kriegeskorte et al., 2009), each participant's data were split into three datasets: i) the first two runs from the category-preference experiment were used to define ROIs, ii) the remaining four runs were used to measure category-preferences, and iii) the five runs from the tool/hand experiment were used to compute functional connectivity.

Moreover, we followed two main analytical pipelines. In the first (Figure 3.1A) we used specific target ROIs within VTC that are preferentially engaged by either tools (the mFUG) or hands (the FBA) from which we extracted categorical preferences (t-values) for each voxel in the ROI and correlated these preferences with functional connectivity data from our seed ROIs. In the second analysis, we computed categorical preferences across the brain (for each voxel within the sphere visited) using a searchlight analysis and correlated these with functional connectivity from our seed ROIs.

Univariate analysis. For each participant and for each experiment (category-preference and tool/hand experiment), a fixed effects analysis was performed independently by setting up a General Linear Model (GLM) including the following regressors of interest for the category-preference experiment: animals, hands, places, tools, and phase-scrambled pictures. For the tool/hand experiment, the following nuisance regressors were used: grasp (first person perspective), grasp (third person perspective), tools, grasp catch trials, and tool catch trials. We used these regressors to remove task-based signal. All regressors of interest were convolved with a canonical hemodynamic response function (first order expansion) to create the design matrix. The motion correction parameters were used as a nuisance regressor to covary out signal correlated with head motion. Model estimations for each participant were used in a second-level random-effects analysis to account for inter-individual variability.

Seed definition. A conjunction contrast (tools > animals ∩ hands > places) was used to define left IPL (average peak MNI coordinates: -34 ± 4.8, -47 ± 5.04, 49 ± 3.96; see Supplementary Figure 3.1 and Supplementary Table 3.1) and left pMTG/LOTC (average peak MNI coordinates: -44 ± 4.83, -69 ± 2.97, -1 ± 3.96) as seed regions for the functional connectivity. Because the left IPL seed also encompassed regions within the aIPS (see Supplementary Figure 3.1 and Supplementary Table 3.1), we will refer to it as the IPL/aIPS seed. We created a 10mm sphere around each participant's peak voxel, within which the 100 voxels with highest t-value were selected. One participant only performed 4 runs from the category-preference experiment, so we did not use any data from this participant to define the ROIs. For this particular participant, we created the spheres around the group peak voxels.

Target ROI definition. Two target ROIs per hemisphere were selected: the tool- and body-preferring areas within the fusiform gyrus (Figure 3.1C). We used both hemispheres as the category preferences for tools and hands in these VTC regions are bilateral. We defined spheres with 9mm radius centered on peak-voxel coordinates reported in previous studies (tool-preferring mFUG – left MNI coordinates: [-24 -53 -9], right: [24 -42 -16] – Mahon et al., 2007; body-preferring FBA – left MNI coordinates:

[-40 -48 -22], right: [40 -48 -22] – Vocks et al., 2010). Voxels located in the cerebellum were removed from the spherical ROIs.

Measuring category-preferences. Category-preferences for each voxel within the target ROIs or the searchlight kernel were computed by contrasting each target category (tools or hands) against all scrambled categories (e.g., tools > all scrambled). Contrast weighted t-values of each contrast were thus obtained for each voxel of the target ROI or the searchlight sphere.

Functional connectivity analysis. All functional connectivity was computed from the data collected from the tool/hand experiment using the CONN Toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012). Time courses were extracted from the 5 runs and potential confounding effects were estimated and removed separately for each voxel and for each participant and run. Potential confounding effects used in CONN Toolbox that we included in our analysis were: noise components from white matter and cerebrospinal fluid, subject-motion parameters and main task effects. All these confounding effects were regressed out, and functional connectivity was computed over the residual time series, after covarying out the experimental design. Design-regressed task data has been extensively used in the past to calculate functional connectivity (e.g., Almeida et al., 2013; Norman-Haignere et al., 2012; Tran et al., 2018), and it has been shown that it effectively leads to similar functional connectivity estimates as when using resting scans (Fair et al., 2007). Functional connectivity was then computed between a seed ROI (averaging all time courses from each voxel) and each voxel in a target ROI. The resulting r-values were then Fisher transformed. Thus, each voxel in the target ROIs had two r-value scores – one for each seed ROI, corresponding to the functional connectivity of each voxel with each of the overall seed ROI – along with two t-values from the hand and tool category-preferences (as described above).

Analysis of the correlations between functional connectivity from the seed ROIs and category preferences distally

ROI Analysis. We computed the multivoxel linear correlation between the distribution of functional connectivity (with each seed region) and the category-preferences for each voxel in the target ROIs (for a similar approach see Chen et al., 2017). Specifically, and for each combination of target ROI, seed ROI, and categorical preference (tool-preferences or hand-preferences) separately, we correlated the category-preferences for the specific category in each voxel of the target ROI with the functional connectivity of those voxels with the selected seed region. That is, at each voxel in the target ROI we would have a contrast weighted t-value for the particular category preference being tested, and a fisher-transformed r-value from the functional connectivity analysis to the specific seed ROI being tested. These multivoxel values (t-values and r-values) were then linearly correlated as a proxy of modulation between the functional connections of a region and category-preferences in a distal region. Before computing this correlation, we also checked for heteroscedasticity of the variables (Table 3.1) using the Breusch-Pagan test (Kamarov, 2020). We rejected the null hypothesis that the residuals are homoscedastic for tests showing a $p < .05$. For these cases (4 out 16), we calculated the Spearman's correlation instead of Pearson's. Consequently, we had a 2 (seed ROI: left IPL/aIPS, left pMTG/LOTC) * 2 (target ROI: mFUG, FBA) * 2 (category-preferences: tools, hands) * 2 (hemisphere of the target ROIs: left and right) factor design. The multivariate correlations between functional connectivity and category-preferences were therefore analyzed with a repeated measure ANOVA with these four factors. Specifically, we were interested in whether there was an interaction between the target ROIs and the category-preferences. Moreover, and as a control, we were interested in the interaction of these two main factors with the factors seed ROI and hemisphere.

Table 3.1 – Breusch-Pagan tests.

	Preferences (t-values)	
Functional connectivity (r-values)	**Hands**	**Tools**
IPL/aIPS - left FBA	.0125*	.4299
IPL/aIPS - right FBA	.6343	.8796
IPL/aIPS - left mFUG	.0015**	.9776
IPL/aIPS - right mFUG	.7067	.4378
pMTG/LOTC- left FBA	.0296*	.1752
pMTG/LOTC- right FBA	.8502	.5883
pMTG/LOTC- left mFUG	.0907	.3503
pMTG/LOTC - right mFUG	.5475	.0255*

*LOTC – lateral occipital temporal cortex; pMTG – posterior middle temporal gyrus; IPL – inferior parietal lobule; aIPS – anterior intraparietal sulcus; mFUG – medial fusiform Gyrus; FBA – fusiform body area; *p < .05; ** p < .01*

Searchlight analysis. We conducted a whole-brain searchlight analysis (e.g., Chen et al., 2017; Kriegeskorte et al., 2006) in order to relate functional connectivity to category-preferences. For each participant, we had two different whole-brain functional connectivity maps for each seed region (IPL/aIPS and pMTG/LOTC), and two whole-brain category-preference t-maps for tools and hands. For every sphere (number of surrounding voxels = 50) in the searchlight, we extracted: (i) contrast-weighted t-values for a given object-preference, and (ii) Fisher transformed correlation coefficients (functional connectivity) from each seed region. These values were then correlated. The resulting Fisher transformed correlation coefficient was saved in each sphere's center voxel, which resulted in a whole-brain Fisher transformed r-value map. The searchlight procedure was performed 4 times for each participant (2 connectivity maps [IPL/aIPS and pMTG/LOTC seeds] * 2 category-preferences maps [tools and hands]). Finally, we created statistical group maps for all four conditions by performing two-tailed one-sample t-tests on the Fisher transformed correlation coefficients across participants. The resulting z-maps were corrected for multiple comparisons using threshold-free cluster-enhanced (TFCE; Smith & Nichols, 2009) Monte Carlo simulations with 10,000 iterations as implemented in CoSMoMVPA Toolbox (Oosterhof et al., 2016). Furthermore, to analyze differences between maps generated by hand- and tool-preferences, we only used voxels with r > .45 (corresponding to *p* = .001), and performed a one-tailed two-sample t-test to compare tools vs. hands for each seed region (IPL/aIPS and pMTG/LOTC). The resulting z-maps were corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016).

3.4. Results

Relating functional connectivity from distal (IPL/aIPS and pMTG/LOTC) regions and local category-preferences in tool- or hand-preferring VTC regions

We used a 2 (seed ROI: left IPL/aIPS or left pMTG/LOTC) * 2 (target ROI: mFUG or FBA) * 2 (category-preference: tools or hands) * 2 (hemisphere of the target ROIs: left or right) factor repeated-measures ANOVA to analyze the Fisher transformed r-values from correlating category-preference contrast-weighted t-values and Fisher transformed functional connectivity r-values.

As predicted, there was a significant target ROI and category-preference interaction (*F* (1,14) = 24.691, *p* < .0001) such that the correlation between category-preferences and connectivity measures differs between the two target regions (mFUG and FBA) within the VTC (Figure 3.2). Post-hoc tests (Holm-Bonferroni corrected; Holm, 1978) revealed that the correlation between tool-preferences and functional connectivity (irrespective of the seed region) was higher than the correlation between hand-preferences and functional connectivity in mFUG (*t* (14) = 4.73, adjusted *p* = .0006). The reverse was true for FBA – the correlation between hand-preferences and functional connectivity was higher than the correlation between tool-preferences and functional connectivity (*t* (14) = 2.26, adjusted *p* = .040). There was no target ROI * category-preference * hemisphere interaction (*F* (1,14) = 1.187, *p* = .294), seed ROI * target ROI * category-preference interaction (*F* (1,14) = .085, *p* = .775), nor target ROI * category-preference * seed ROI * hemisphere interaction (*F* (1,14) = 1.546, *p* = .234). This shows that seed ROI and the hemisphere of the target region are not leading to differential results in the correlation of functional connectivity and category-preferences in the target ROIs.

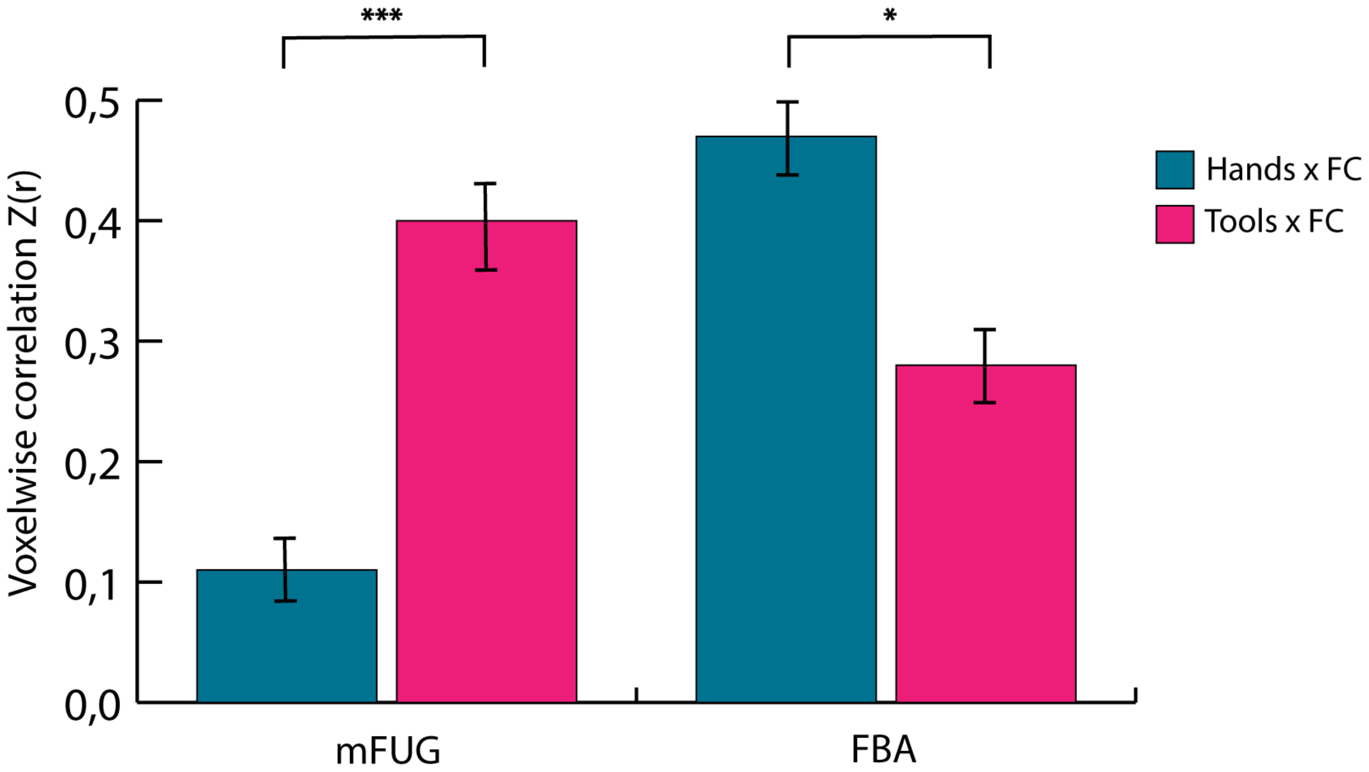


Figure 3.2 – ROI results.

Figure 3.2. Voxel-wise correlation between category-preferences (t-values) and functional connectivity (Fischer transformed r-values) within target regions of interest, demonstrating an interaction. All error bars reflect one standard error of the mean across participants. P-values are Holm-Bonferroni corrected for 2 tests (* = adjusted *p* value < .05; *** = adjusted *p* value < .001). (mFUG – medial Fusiform Gyrus; FBA – Fusiform Body Area; FC – Functional Connectivity).

In addition to the tests of interest, we obtained other significant effects. There was a main effect of category-preference (*F* (1,14) = 7.085, *p* = .019) such that correlations involving tool-preferences were greater than those involving hand-preferences. There was also a seed * target ROI interaction (*F* (1,14) = 5.046, *p* = .041). However, post-hoc tests only indicated a trend in the correlations between category-preferences and functional connectivity over mFUG and FBA from the two seed ROIs. Correlations between category-preferences and functional connectivity over the mFUG were nominally higher from IPL/aIPS than pMTG/LOTC (*t* (14) = 1.84, *p* = 0.087), whereas correlations between category-preferences and functional connectivity over FBA were nominally higher from pMTG/LOTC than IPL/aIPS (*t* (14) = 1.82, *p* = 0.091). Finally, there was a target ROI * hemisphere interaction (*F* (1,14) = 4.668, *p* = .049), but post-hoc comparisons were not significantly different from 0. Accordingly, correlations between category-preferences and functional connectivity over mFUG were not different between hemispheres (*t* (14) = 1.32, *p* = 0.207), whereas correlations between category-preferences and functional connectivity over FBA were nominally higher in the left hemisphere (*t* (14) = 1.95, *p* = 0.071). No other main effects or interactions were significant (all *p* > .1).

Connectivity from IPL/aIPS and from pMTG/LOTC correlated with tool and hand preferences differ for different parts of the brain, constraining object topography across the brain

The searchlight analysis showed that connectivity from IPL/aIPS and pMTG/LOTC correlated with tool and hand preferences differentially across the brain (Table 3.2, Figure 3.3 and Figure 3.4; see also Supplementary Figure 3.2). On the one hand, functional connectivity from IPL/aIPS correlated with tool-preferences in the left mFUG, and functional connectivity from the left pMTG/LOTC correlated with tool-preferences in the mFUG (bilaterally), and in the left dorsal occipital cortex (including cuneus, precuneus, and partly superior parietal lobule). On the other hand, functional connectivity from the left IPL/aIPS correlated with hand-preferences in the left postcentral gyrus/somatosensory cortex, specifically in the hand area (Roux et al., 2018), and the left superior temporal sulcus (STS), and functional connectivity from the left pMTG/LOTC correlated with hand-preferences in right the STS extending inferiorly and posteriorly, but not overlapping with the functionally defined right pMTG/LOTC (see Supplementary Figure 3.3).

Table 3.2 – MNI coordinates from the brain regions extracted during the searchlight analyses.

Seed ROI	**Category-preference**	**Brain regions**	**MNI coordinates**			**Cluster size**	**Peak z-value**
			x	**y**	**z**		
pMTG/LOTC	Tools	Left dorsal occipital cortex	-18	-81	21	287	2.42
pMTG/LOTC	Tools	Left mFUG	-30	-63	-21	234	3.19
pMTG/LOTC	Tools	Right mFUG	30	69	21	41	1.95
pMTG/LOTC	Hands	Right STS	57	-48	9	182	2.82
IPL/aIPS	Tools	Left mFUG	-24	-51	-24	65	2.77
IPL/aIPS	Hands	Left postcentral gyrus	-36	-36	66	77	2.25
IPL/aIPS	Hands	Left STS	-39	-54	12	52	1.94

LOTC – lateral occipital temporal cortex; pMTG – posterior middle temporal gyrus; IPL – inferior parietal lobule; aIPS – anterior intraparietal sulcus; mFUG – medial fusiform Gyrus; STS – superior temporal sulcus.

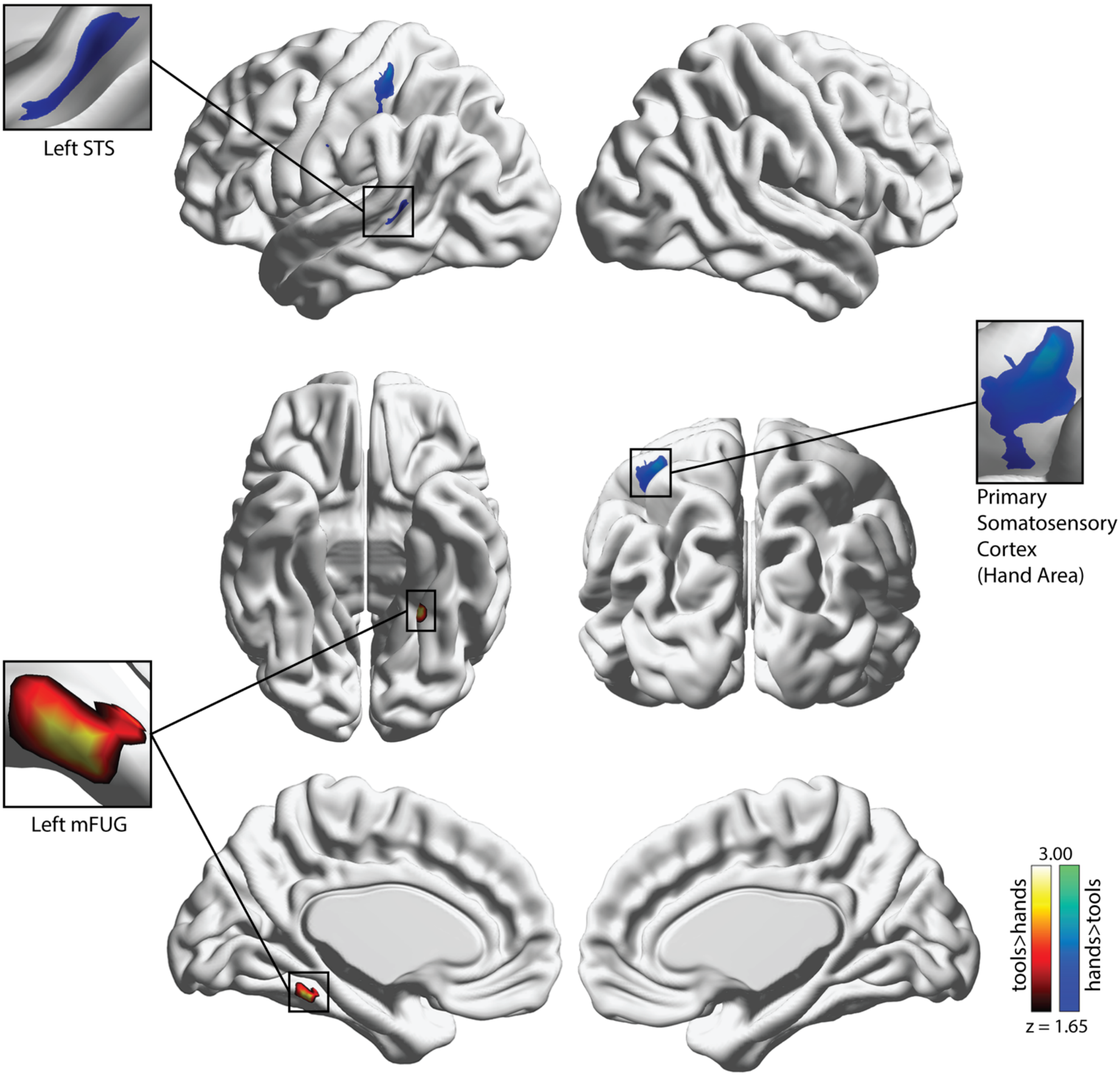


Figure 3.3 – Whole-brain searchlight correlation between category-preferences and functional connectivity to IPL/aIPS (surface maps).

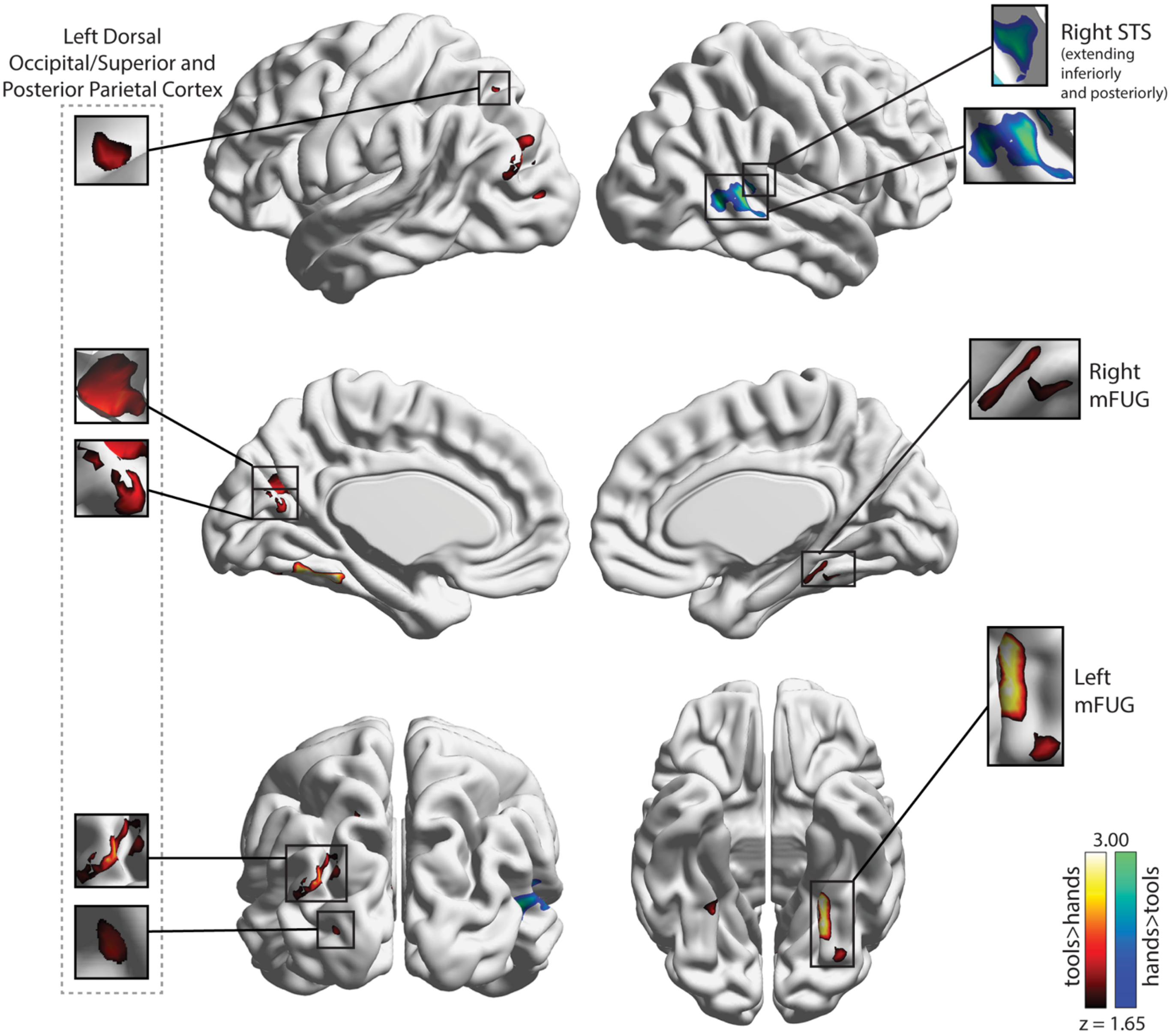


Figure 3.4 – Whole-brain searchlight correlation between category-preferences and functional connectivity to pMTG/LOTC (surface maps).

Figure 3.3. Warm colors indicate higher voxel-wise correlations between tool-preferences and functional connectivity to IPL/aIPS (compared to hand-preferences). Cold colors indicate higher voxel-wise correlations between hand-preferences and functional connectivity to IPL/aIPS (compared to tool-preferences). All z-maps were corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016).

Figure 3.4. Warm colors indicate higher voxel-wise correlations between tool-preferences and functional connectivity to pMTG/LOTC (compared to hand-preferences). Cold colors indicate higher voxel-wise correlations between hand-preferences and functional connectivity to pMTG/LOTC (compared to tool-preferences). All z-maps were corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016).

3.5. Discussion

Here we set out to test the hypothesis that local representations relate to distal representations in a category specific way – suggesting that local computations are modulated by local constraints, bottom-up and top-down connections, as well as representations that are distally processed within a category-specific network (Chen et al., 2017; Lee et al., 2019; Mahon & Caramazza, 2011). We did so by looking at regions that are engaged by two different categories – hands and tools – and tested whether functional connectivity from these overlap areas (the tool- and hand-preferring left IPL and left pMTG/LOTC) relate to category-preferences in other distal regions (in this case category-preferring regions in the VTC) in a category-specific way (i.e., differently for hands and tools). That is, we looked at whether functional connections of regions that belong to more than one functionally specified network (in our case the networks that prefer tools and that prefer hands) related to the local processing within distal areas in a category-specific way, disentangling these networks.

Firstly, we focused on VTC and showed that functional connectivity from IPL/aIPS and pMTG/LOTC to tool-preferring mFUG correlated more with tool-preferences than hand-preferences, while functional connectivity from IPL/aIPS and pMTG/LOTC to body-preferring FBA correlated more with hand-preferences than tool-preferences. This suggests that despite the processing overlap for tools and hands in IPL/aIPS and pMTG/LOTC, the functional connections of these regions maintain object topography by allowing for a category-specific flow of information that is pertinent to computing category-specific representations. This is especially important because VTC has been widely implicated in object recognition, and consistently shows a mosaic of regions engaged by different object categories (e.g., Moshe Bar & Aminoff, 2003; Bracci et al., 2012, 2016; Chao et al., 1999; Chao & Martin, 2000; Downing et al., 2001; Epstein & Kanwisher, 1998; Fox et al., 2009; Kanwisher et al., 1997; Kristensen et al., 2016; Lee et al., 2019; Mahon et al., 2007; Martin et al., 1996; Peelen & Downing, 2007; Perani et al., 1995). This mosaic is related with (and may potentially be dependent on) the information flow from distal regions that belong to the network that is dedicated to the processing of the target network.

Secondly, we explored whether and how this relationship between functional connectivity from our two seed "distal" regions and local category preferences across the whole-brain was present – that is, whether and how the overlap regions allowed for disentangling parts of the tool and hand network across the brain. In our searchlight analysis, we showed that left IPL/aIPS and left pMTG/LOTC correlated with local category preferences in different regions across the brain for the two categories. Specifically, connectivity from pMTG/LOTC was correlated with tool-preferences in a large part of left dorsal occipital cortex, including the superior parietal lobule, and in the mFUG bilaterally, whereas connectivity from IPL/aIPS was correlated with tool-preferences in left mFUG. In what concerns hand representations, connectivity from pMTG/LOTC was correlated with hand-preferences in the right STS, whereas connectivity from IPL/aIPS was correlated with hand-preferences in the left postcentral gyrus and the left STS.

Our data therefore shows that these long-range distal connections function in a category-dependent fashion irrespective of whether the remote region is engaged by different (but specific) categories. On the one hand, we show that (local) tool representations are associated with computations happening distally within the tool network – the "local" regions that emerged from both of our analyses are clearly part of the tool network (e.g., Almeida et al., 2010; Garcea & Mahon, 2014; Mahon et al., 2007). In fact, using neurostimulation we have shown before that interfering with processing within one node of the tool network will cascade down to the full network (Ruttorf et al., 2019). On the other hand, we show that regions emerging from our analyses for hand representations are part of the hand network and are related to multisensory and movement-sensitive processing (e.g., STS and postcentral gyrus/somatosensory hand area; Beauchamp et al., 2008; Macaluso, 2006).

Furthermore, our data points to representational differences in the kinds of distal relationships observed for these two overlap regions. For tool processing, the results obtained for pMTG/LOTC may suggest that this region connects posterior parietal and dorsal occipital regions working on aspects of volumetric analysis of graspable objects such as elongation and grasping status (i.e., is this object graspable; Almeida et al., 2008, 2010, 2014; Fabbri et al., 2016; Fang & He, 2005), with aspects of tool representations in mFUG, potentially related with shape, material, and surface properties (Cant et al., 2009; Cant & Goodale, 2007). On the other hand, IPL and aIPS seem focused exclusively on the left mFUG, a result that seems in line with previous literature showing a preferred relationship between IPL and left mFUG for tool processing (Almeida et al., 2013; Garcea & Mahon, 2014; Kristensen et al., 2016; Lee et al., 2019; Mahon et al., 2013), and potentially related to the passage of information pertinent to object manipulation and functional grasps (e.g., Almeida et al., 2013; Kristensen et al., 2016; Mahon et al., 2013; Valyear and Culham, 2010).

Interestingly, IPL has been heavily associated with acessing function-specific object manipulations (Boronat et al., 2005; Ishibashi et al., 2011; Kellenbach et al., 2003; Mahon et al., 2007) and patients with lesions to IPL present with ideomotor apraxia (i.e., an inability to manipulate everyday objects, Almeida et al., 2018; Buxbaum, Giovannetti, et al., 2000; Buxbaum, Veramonti, et al., 2000; Garcea et al., 2013; Mahon et al., 2007; Ochipa et al., 1994), whereas aIPS is known to be strongly involved in the computation of hand-shapes for object grasping (Binkofski et al., 1999; Binkofski et al., 1998; Culham et al., 2003; Monaco et al., 2011), and in particular in shaping the hand for functional grasps (i.e., grasps that are specific for the manipulation programs necessary to use an object, e.g., Buchwald et al., 2018). This passage of information to IPL and aIPS from ventral temporal cortex may reflect the necessary passage of semantic and functional information that allows for accessing praxis and selecting associated functional grasps (Almeida et al., 2013; Chen et al., 2017; Garcea et al., 2016, 2019; Kristensen et al., 2016).

For hand processing, the difference in the pattern of distal relationships relayed by IPL/aIPS and pMTG/LOTC may be related to either more motor or more social aspects pertinent to the computations being performed locally. On the one hand, IPL/aIPS is distally related with regions that are purportedly implicated in motor planning and execution such as the left STS (Liebenthal et al., 2014; Rizzolatti et al., 1996) and postcentral gyrus – an area well known for being the location of the primary somatosensory cortex (Penfield & Boldrey, 1937), but also involved in grasp action (Castiello, 2005; Iwamura & Tanaka, 1996). More specifically, connectivity with postcentral gyrus/somatosensory cortex was restricted to a location involved in somatosensory processing for hands (Horovitz et al., 2013; Lavrysen et al., 2012). On the other hand, distal relationships associated with pMTG/LOTC were found within the right STS – a region that has been implicated in aspects of social cognition and face and body expression (Bonda et al., 1996; Narumoto et al., 2001; Puce et al., 1998; for a review see Puce & Perrett, 2003) and also implicated in the imitation of observed actions (Iacoboni et al., 2001).

Note that there are some differences in results between our a priori category-specific ROIs and our whole-brain searchlight analysis, specifically in what concerns the lack of an effect in FBA under the searchlight approach. This could be due to differences in the two analytical pipelines – namely that in the ROI analysis we use a more focused theoretically based approach, whereas in the searchlight we are less theory-driven and have to account for a much larger number of comparisons by using stringent corrections. It may also mean, however, that while for tool items, the medial aspects of the fusiform gyrus are truly central for the passage of information within the network, the same may not be true for hand stimuli in terms of the FBA – perhaps motor and social information, aspects that seem to be central in governing hand processing, are not central drivers of the computations happening within FBA. Nevertheless, and albeit not so prominently, the information within FBA may still flow within the hand network.

Our study has some caveats that could not be fully taken care of. Although functional connectivity and stimulus preferences were computed over entirely independent datasets, so there was no circularity when selecting datasets (Kriegeskorte et al., 2009), we cannot infer causality concerning how these connectivity constraints are imposed. Nevertheless, and because our results are robust, we believe that we should obtain similar results if a causal approach was to be followed as we have done before (Lee et al., 2019; Ruttorf et al., 2019) – i.e., if we were to use non-invasive neurostimulation within these areas of overlap, we should see category-specific effects in the parts of the brain implicated in the current study (e.g., the dorsal occipital cortex for tool-preferences and their correlation with functional connectivity from IPL/aIPS).

In conclusion, our results show how areas that purportedly respond equally to two different categories (that of tools and hands) present different patterns of connections for their preferred categories. This suggests that the same neurons (or at least neurons within the same voxels) in such areas process and send category pertinent information to particular category-specific networks in a way that is dependent on the stimuli being processed. That is, distal connections from an overlap area are dependent on the category being processed at a particular time point, perhaps changing representations and computations, while attributing connectivity a crucial role in determining object representation.

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Chapter IV.

DISENTANGLING HAND AND TOOL PROCESSING: DISTAL EFFECTS OF NEUROMODULATION – STUDY 2

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4.1. Abstract

The neural processing within a brain region that responds to more than one object category can be separated by looking at the horizontal modulations established by that region, which suggests that local representations can be affected by connections to distal areas, in a category-specific way. Here we first wanted to test whether by applying transcranial direct current stimulation (tDCS) to a region that responds both to hands and tools (posterior middle temporal gyrus; pMTG), while participants performed either a hand- or tool-related training task, we would be able to specifically target the trained category, and thereby dissociate the overlapping neural processing. Second, we wanted to see if these effects were limited to the target area or extended to distal but functionally connected brain areas. After each combined tDCS and training session, participants therefore viewed images of tools, hands, and animals, in an fMRI scanner. Using multivoxel pattern analysis, we found that tDCS stimulation to pMTG indeed improved the classification accuracy between tools vs. animals, but only when combined with a tool training task (not a hand training task). However, surprisingly, tDCS stimulation to pMTG also improved the classification accuracy between hands vs. animals when combined with a tool training task (not a hand training task). Our findings suggest that overlapping but functionally-specific networks can be separated by using a category-specific training task together with tDCS – a strategy that can be applied more broadly to other cognitive domains using tDCS – and demonstrates the importance of horizontal modulations in object-category representations.

Keywords: tools; hands; distal connectivity; tDCS; fMRI

4.2. Introduction

Object recognition is a complex process that engages different sets of cortical regions. In fact, the way conceptual information is organized in the human brain is still under debate (e.g., Grill-Spector & Malach, 2004; Op de Beeck et al., 2019). Recently, we (and others) have shown that neural processing and the organization of information in one area is dependent not only on local aspects, but also on processes happening within distal but functionally connected regions (Amaral et al., 2021; Lee et al., 2019; Walbrin & Almeida, 2021; see also Almeida et al., 2013; Garcea et al., 2016; Kristensen et al., 2016; Ruttorf et al., 2019). These modulations between areas that belong to a particular domain-specific network – horizontal modulations within a domain – allow for the exchange and integration of different kinds of conceptual information. According to this hypothesis, object topography – that is, the organization of object-related information in the brain – is not only dependent on local computations, but also on connections from distal regions that share a propensity for processing a specific category of objects (Chen et al., 2017; Garcea et al., 2019; see also, Mahon & Caramazza, 2011; Sporns, 2014). Here we will explore these horizontal modulations and focus on the processing of two related categories – hands and tools – as a way of further understanding the organization of object knowledge in the brain.

Early neuroimaging studies suggest that object recognition depends on local neural processes (mainly) within the ventral temporal cortex (VTC) (Grill-Spector & Weiner, 2014; Peelen & Downing, 2017). In fact, several studies have shown that different regions inside VTC present higher BOLD signal change for specific object categories like faces (fusiform face area – FFA, Kanwisher et al., 1997), places (parahippocampal place area – PPA, Epstein & Kanwisher, 1998), bodies (fusiform body area – FBA, Peelen et al., 2005; Schwarzlose et al., 2005), hands (Bracci et al., 2012, 2016) or tools (medial fusiform gyrus – mFUG, Almeida et al., 2013; Chao & Martin, 2000; Garcea & Mahon, 2014) when compared to other high-level categories.

However, recent studies show that these local representations within VTC are (at least partly) shaped by information shared via structural and functional connectivity from distal regions (Hutchison et al., 2014; Saygin et al., 2011, 2016). According to this hypothesis, category-specific representations rely not only on local computations, but also on information processed within distal regions outside VTC that is transferred via long-distance horizontal modulations. As an illustration of this claim, Lee, Mahon and Almeida (2019) used transcranial Direct Current Stimulation (tDCS) over tool-preferring left inferior parietal areas (e.g., inferior parietal lobule – IPL), and showed that BOLD signal patterns were modulated by tDCS polarity and, most importantly, that representations in tool-preferring regions within the VTC (specifically, the left mFUG), but not in other regions of VTC, changed in a category-specific way (i.e., tDCS changed multivoxel patterns that were elicited by tool stimuli, but not those elicited by face or place stimuli; Lee et al., 2019; see also, Amaral et al., 2021; Chen et al., 2017; Garcea et al., 2019; Walbrin & Almeida, 2021). That is, it is possible to modulate the representational patterns within a specific target region by stimulating a distal area that is functionally connected to, and that shares categorical preferences with that target region. We, therefore, argue that local representations of a specific category can be modulated by information from distal regions that are functionally connected.

One important test to the relevance of distal connectivity and horizontal modulations in conceptual representation and the organization of information in the brain is the situation where a particular region figures critically in the processing of more than one higher-level category (i.e., shows preferential responses to two categories) – can within-domain horizontal modulations disentangle the functionally distinct category-specific networks? Recently, we have demonstrated this to be the case. Specifically, in an fMRI study, we found that functional connectivity from two regions that show an overlap in their preference for tools and hands (left IPL and left posterior middle temporal gyrus – pMTG) with other distal areas (e.g., tool or hand preferring regions of the VTC) is differently correlated with categorical preferences: in tool-preferring VTC areas, functional connectivity from left IPL and left pMTG (i.e., the tool/ hand-preferring overlap areas) correlates with local response preferences for tools but not hands, whereas in hand-preferring VTC areas, it correlates with local response preferences for hands but not tools (Amaral et al., 2021). That is, horizontal modulations connecting regions of a domain-specific network (for hands or tools) allow for the separation of the two different networks, despite the overlap response that occurs for both categories in left IPL and left pMTG.

If an overlap response can be separated by focusing on the different domain-specific horizontal modulations, then questions arise as to whether we can enhance this separation effect by biasing the processing towards one of those categories? That is, if we have two categories that both drive responses in a particular overlap region, will enhancing the processing of one of those categories lead to an increase of the category-specific responses elsewhere via horizontal modulations? Here, we address this question by combining tDCS with (cognitive) training tasks to enhance processing for a particular category.

We focused on two functionally related categories – hands and tools (Almeida et al., 2018; Amaral et al., 2021; Bergström et al., 2021; Bracci et al., 2012). First, we wanted to investigate if tDCS applied to one of the areas where preferences for tool and hand stimuli overlap (i.e., pMTG) would provoke distal effects in other regions of the brain (see Lee et al., 2019; Ruttorf et al., 2019). Second, we wanted to test if we could disentangle the functionally-specific networks for hands and for tools, as these have some overlapping nodes. We did this by applying tDCS to pMTG (or to a control area – medial Prefrontal Cortex; mPFC) in combination with a category-specific training task, prior to an fMRI session.

tDCS is a neuromodulation procedure that adapts neuronal excitability through the depolarization or hyperpolarization of resting membrane potential (Nitsche et al., 2008; Nitsche & Paulus, 2011). Unlike other brain stimulation techniques (e.g., Transcranial Magnetic Stimulation, TMS), tDCS does not produce action potentials in the neuronal cell membranes. For this reason, several authors believe that tDCS action relies on the activity already present in the tDCS areas (i.e., before and/or during stimulation) (Stagg & Nitsche, 2011). If tDCS is activity-dependent, we could potentially enhance its effects by triggering a specific cognitive processing prior to (and during) stimulation. That is, we may enhance tDCS effects by cognitively manipulating the network-specific engagement of the system in preparation for tDCS stimulation. As such, in tandem with the tDCS stimulation, we asked the participants to perform an online (pre-MRI) task that focused on one of the categories (hands or tools). By hypothesis, the task will produce task-related neural spiking and tDCS stimulation will be added on top of augmented neural responses.

After the simultaneous high-definition tDCS (to improve focality) and task training session, participants went through an event-related fMRI experiment where we presented images of tools, hands, and animals. The tDCS montages and category tasks were manipulated within participants (such that each participant went through 4 sessions). Using Multivoxel Pattern Analysis (MVPA) over the BOLD patterns for tools or hands from the fMRI session, we showed that stimulating pMTG (combined with the training tasks) leads to different patterns of classification between hands and tools (vs. animals).

4.3. Methods

Participants

Twenty-five subjects participated in this experiment (M = 22 years, SD = 3.5, 8 males). All participants had normal or corrected to normal vision, were right-handed, had no history of neuropsychiatric disorders (e.g., stroke, epilepsy, dementia, depression) or head injury, had no metallic implants, did not intake concurrent medication likely to affect cognition and had no history of alcohol and drug abuse or dependence. Written informed consent was obtained from all participants prior to the beginning of the study. Participants were each paid €40 upon completion of the study. Students from the Faculty of Psychology and Educational Sciences of the University of Coimbra also received course credits for their participation. The study was approved by the Ethical Committee of the Faculty of Psychology and Educational Sciences of the University of Coimbra. Due to signal problems, we excluded data from all runs for one participant. Four participants did not complete all sessions, so we also excluded the data from those participants: two did not finish the experiment, one showed neurological abnormalities, and, for the last subject, the monitor inside the scanner was not working. Consequently, 20 participants (M = 23 years, SD = 3.5, 6 males) were used for the analyses of this study.

Experimental procedure

All participants included in the analyses completed four sessions with a minimum interval of one week: two sessions using pMTG as the stimulated area and two sessions with mPFC. For each pair of sessions, the training task could be either hand or tool-related ($\text{pMTG}_{\text{hands}}$, $\text{pMTG}_{\text{tools}}$, $\text{mPFC}_{\text{hands}}$, $\text{mPFC}_{\text{tools}}$). The order of the sessions was randomized and counterbalanced across subjects. Each session always started with the HD-tDCS application and a training task, followed by the fMRI experiment in which participants viewed images of tools, hands, and animals.

HD-tDCS

We used a battery-driven HD-tDCS system composed of a direct current generator, connected to a HD-tDCS adaptor (Soterix Medical, NY, USA). The electrode montage was planned with the aid of a current flow modeling software which employs finite element method to calculate the resulting electric field in brain regions during the stimulation (HD-Explore – Soterix Medical, NY, USA). The resulting simulation is based on the electrodes' positions. Electrodes' deployment was planned in order to optimize focality over the stimulation target area (pMTG), while avoiding the current flow into parietal regions (e.g., IPL). Since IPL is also known as an overlap area when processing hands and tools, in order to ensure that stimulation targeted the temporal lobe, we only used 3 electrodes (1 anodal centered at TP7, according to the 10-10 EEG system, and two cathodal located 5cm distant from the anodal, see Figure 4.1). Regarding the mPFC stimulation, we kept the same setup using only 3 electrodes with the anodal located at the Fpz position. The HD-electrodes were placed inside a holder filled with Signa Gel (Parker Laboratories, NJ, USA). Impedance values were examined for each electrode and the intensity of the current was set to 2 mA, delivered for 20 minutes (ramp duration of 1 minute). The tDCS room was immediately adjacent to the MRI scanner, allowing for a fast transfer to the MRI environment right after stimulation. For simplicity, we henceforth refer to it as tDCS.

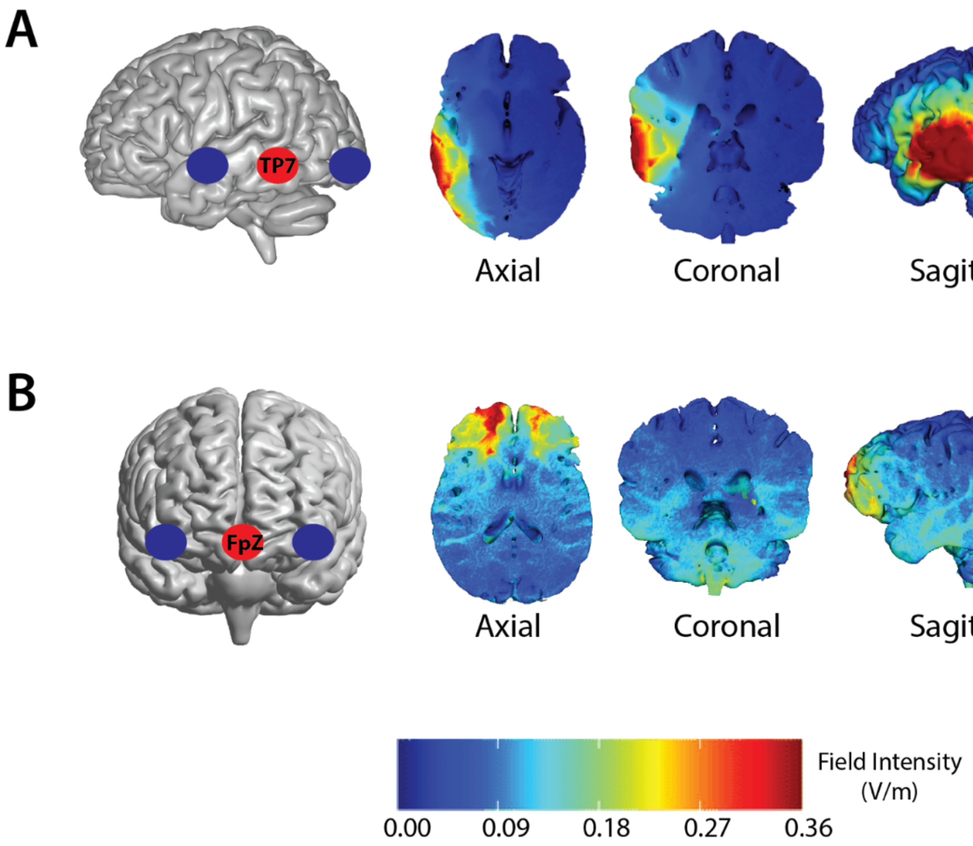

Figure 4.1 – Electrode montage and modeling of the brain current flow.

Figure 4.1. (A) Electrode montage targeting posterior middle temporal gyrus (pMTG) and the respective brain current flow based on HD-explore software (Soterix Medical, NY, USA). **(B)** Electrode montage targeting medial prefrontal cortex (mPFC) and the respective brain current flow showing that this montage did not affect the brain regions included in the pMTG montage.

Training task

Participants performed two equivalent one-back tasks, one with tool images and another with hand images. All images were black and white, and appeared on the screen for 400ms with a refresh rate of 60 Hz. During the tool training, participants pressed a button when the current and the previous image belonged to a different object (e.g., a glass and a bowl), but not when they belonged to the same (basic level) object, despite potential changes in perspective or exemplars (e.g., different angles or types of a glass).

During the hand training, participants pressed a button when the current and previous hand image referred to a different hand side – i.e., right or left hand. Participants saw different perspectives and hand postures.

The responses were collected with a button box (Cedrus Corp.), with their dominant hand (right). We used Matlab and “A Simple Framework” (ASF; Schwarzbach, 2011) to present stimuli. We measured accuracy and reaction times, and the experiment lasted for 30 minutes (tDCS started at minute 10). Due to a technical problem, the files corresponding to the session $\text{pMTG}_{\text{hands}}$ in one subject were not saved. Thus, we excluded this participant from our behavioral analysis.

fMRI task

We used an event-related design with four runs for the fMRI experiment. Participants were presented with centrally fixated gray-scaled images (400*400 pixels) of tools, hands, animals, and places. Each image was presented for 2s, followed by a 4s fixation period. Participants were asked to detect catch trials (i.e., trials consisting of place images) and press a button every time they saw a place image. The purpose of this task was to keep participants alert while attending to all stimuli. Nonetheless, for all sessions, we used an eye tracker to (subjectively) monitor the individual’s attention (and wakefulness) during the entire task. Stimulus delivery and response collection were controlled using Psychtoolbox (Brainard, 1997) in Matlab (The MathWorks Inc., Natick, MA, USA). Stimuli were presented on an Avotec projector with a refresh rate of 60 Hz and viewed by the participants through a mirror attached to the head coil inside the bore of the MR scanner. Each run began with an 8s fixation period and ended with a 16s fixation period. Eight different exemplars of tools, hands and animals were used, and each run contained 3 repetitions per stimulus. Six different exemplars of places were used as catch trials and each run contained 1 repetition per each of this stimulus.

Due to a technical problem, we were not able to collect the button responses in the first two sessions of subject 1 and 2.

Data acquisition

MRI data were acquired using a 3T MAGNETOM Trio whole body MR scanner (Siemens Healthineers, Erlangen, Germany) with a 64-channel head coil. There were four sessions, and each one included four functional runs and one structural scan. Structural MRI data was collected using T1-weighted rapid gradient echo (MPRAGE) sequence (repetition time (TR) = 2530ms, echo time (TE) = 3.5ms, slice thickness = 1 mm, flip angle = 7 deg, field of view (FoV) = 256 * 256, matrix size = 256 * 256, bandwidth (BW) = 190 Hz/px, GRAPPA acceleration factor 2). Functional MRI (fMRI) data were acquired using a T2*-weighted gradient echo planar imaging (EPI) sequence (TR = 2000ms, TE = 30ms, slice thickness = 3mm, FoV = 210 * 192, matrix size = 70 * 64, flip angle =75 deg, BW = 2164 Hz/px, GRAPPA acceleration factor 2). Each image volume consisted of 37 contiguous transverse slices recorded in interleaved slice order oriented parallel to the line connecting the anterior commissure to the posterior commissure covering the whole brain.

Image preprocessing

We used SPM12 (Welcome Trust Centre for Neuroimaging, London, UK), run in Matlab R2018b (The MathWorks Inc., Natick, MA, USA), for processing and analysis of structural and functional data. All images were reoriented to approximate MNI space with SPM12 after slice-time correction. The functional data were slice-time corrected to the first slice using a Fourier phase-shift interpolation method, corrected for head motion to the first volume of the first session using 7th degree b-spline interpolation. Structural images were co-registered to the first functional images. Functional data were then normalized to MNI anatomical space using a 12-parameter affine transformation model in DARTEL (Ashburner, 2007) and smoothed with an 8mm (for ROI localization) and 3mm (for MVPA) FWHM Gaussian filter.

Univariate analysis

For each participant, a fixed-effects analysis was performed by setting up a General Linear Model (GLM) with animals, hands, and tools as regressors of interest; and places (catch trials) as well as motion correction parameters (to covary out signal correlated with head motion) as nuisance regressors. All regressors of interest were convolved with a canonical hemodynamic response function to create the design matrix. Model estimations for each participant were used in a second-level random-effects analysis to account for inter-individual variability.

Regions of interest (ROIs)

Two univariate contrasts (tools > animals and hands > animals) were used to select group and individual peak-coordinates for regions engaged by tools and hands. ROIs were defined in two steps, as proposed by Oosterhof and colleagues (Oosterhof et al., 2012). First, we created group-level spheres with 15mm radius using MarsBaR (Brett et al., 2002) centered on the group's univariate peak-voxel coordinates. Second, we created individual-level spheres with 15mm radius centered on each individual's univariate peak-voxel coordinates but within the group-level spheres.

Multivariate pattern analysis

We used a leave-one-run-out cross-validation procedure to train a Support Vector Machine (SVM) classifier to discriminate between z-score normalized beta patterns of two experimental conditions (hands vs. animals OR tools vs. animals). The leave-one-run-out cross-validation procedure ensured that training and testing data was kept completely independent. The multivariate classification analysis was performed with The Decoding Toolbox (Hebart et al., 2015). The group's average classification accuracies were computed for each condition (i.e., $pMTG_{hands}$, $pMTG_{tools}$, $mPFC_{hands}$, and $mPFC_{tools}$) and for each ROI (i.e., the six hand- and eight tool-related ROIs, separately). ROIs defined by the hands > animals contrast were used to classify hands vs. animals, and ROIs defined by the tools > animals contrast were used to classify tools vs. animals. Thus, we had two different designs depending on the ROIs that were analyzed: (i) 2 (tDCS area: pMTG or mPFC) * 2 (training task: hands or tools) * 6 (hand-ROIs: described in detail in the results section), and (ii) 2 (tDCS area: pMTG or mPFC) * 2 (training task: hands or tools) * 8 (tool-ROIs). The accuracy results were therefore analyzed with a repeated measure ANOVA with these three factors. Specifically, we were interested in whether there was an interaction between the tDCS area and the training task. In addition, we analyzed (for each ROI) the difference in classification accuracy between the pMTG and mPFC conditions. To do this, we compared the classification accuracy between pMTG and mPFC in a paired t-test for each ROI. For the statistical analyses (e.g., ANOVA) we used IBM SPSS Version 22 (IBM Corp., Armonk, NY).

4.4. Results

Training task

We used a 2 (training task: hands or tools) * 2 (tDCS area: pMTG or mPFC) factorial repeated-measures ANOVA to analyze the accuracy and the reaction times in the training task. Regarding the accuracy values, there was a main effect of the training task (*F* (1,18) = 30.30, $p < .0001$) such that accuracy in the tool task was greater than in the hand task (see Table 4.1). For the reaction times, we observed the same main effect of the training task (*F* (1,18) = 355.73, $p < .0001$) such that reaction times in the hand task were higher when compared to the tool task (see Table 4.1).

Table 4.1 – Training task results.

Session	Accuracy (%)		Reaction Times (ms)	
	Average	SD	Average	SD
$\text{pMTG}_{\text{tools}}$	91.61	2.36	447.91	39.70
$\text{mPFC}_{\text{tools}}$	92.04	3.34	453.60	40.20
$\text{pMTG}_{\text{hands}}$	75.37	15.92	726.51	100.67
$\text{mPFC}_{\text{hands}}$	75.48	14.84	739.81	80.05

pMTG – posterior middle temporal gyrus; mPFC – medial prefrontal cortex

fMRI results

Behavioral task. Participants viewed images of hands, tools, and places inside the scanner, and were instructed to press a button every time they saw an image of a place in order to maintain them awake and attentive to the stimuli. The results show a high hit rate (M = 99%, SD = 1.5) and a low false alarm rate (M = .6%, SD = .7), indicating that participants were, indeed, paying attention to the images.

ROI selection. The hands > animals contrast ($p < .001$, uncorrected) revealed increased BOLD signal change in bilateral posterior parietal cortices (extending across the superior parietal lobe (SPL) and anterior intraparietal sulcus (aIPS)), and bilateral pMTG. The tools > animals contrast ($p < .001$, uncorrected) revealed increased BOLD signal change in the posterior parietal cortices (SPL bilaterally, and extending to aIPS and supramarginal gyrus (SMG) in the left hemisphere), left pMTG, left dorsal occipital cortex (DOC), and medial fusiform gyrus (mFUG). Thus, we chose the following regions as ROIs for hand areas: left SPL (peak t-value = 4.46, MNI coordinates = [-24 -69 60]), right SPL (peak t-value = 5.93, MNI coordinates = [30 -63 60]), left aIPS (peak t-value = 5.23, MNI coordinates = [-30 -39 42]), right aIPS (peak t-value = 4.62, MNI coordinates = [30 -42 48]), left pMTG (peak t-value = 9.37, MNI coordinates = [-51 -66 6]), and right pMTG (peak t-value = 5.42, MNI coordinates = [51 -57 0]). As tool ROIs, we chose left SPL (peak t-value = 6.14, MNI coordinates = [-24 -69 60]), right SPL (peak t-value = 5.87, MNI coordinates = [21 -69 60]), left IPS (peak t-value = 5.62, MNI coordinates = [-24 -57 51]), left SMG (peak t-value = 3.86, MNI coordinates = [-45 -33 39]), left DOC (peak t-value = 6.05, MNI coordinates = [-30 -84 18]), left pMTG (peak t-value = 6.23, MNI coordinates = [-54 -69 -6]), left mFUG (peak t-value = 6.14, MNI coordinates = [-27 -51 -15]), and right mFUG (peak t-value = 4.57, MNI coordinates = [27 -48 -12]).

MVPA results. We used two factorial repeated-measure ANOVAs to analyze the accuracy values from our classifications. For the classification of hands vs. animals, we used a 2 (tDCS area: pMTG or mPFC) * 2 (training task: hands or tools) * 6 (hand-ROIs) ANOVA, whereas for the classification of tools vs. animals, we used a 2 (tDCS area: pMTG or mPFC) * 2 (training task: hands or tools) * 8 (tool-ROIs) ANOVA. We employed two separate ANOVAs because there were different ROIs per ANOVA.

As predicted, there was a significant interaction between tDCS area and training task such that the accuracies differed between the two tDCS areas for the classification between hands vs. animals (F (1,19) = 9.71, p = .006) and for the classification of tools vs. animals (F (1,19) = 6.88, p = .017). Specifically, post-hoc tests (FDR corrected; Benjamini & Hochberg, 1995) revealed that the accuracy for the classification of tool vs. animals was higher when tDCS was applied to pMTG and paired with the tool training task ($\mathrm{pMTG}_{\mathrm{tools}}$), than when tDCS was applied to mPFC and paired with the tool training task ($\text{mPFC}_{\text{tools}}$) ($t$ (19) = 2.55, adjusted p = .04, see Figure 4.2C). However, there was no difference when tDCS was applied to pMTG in tandem with the hand training task ($\text{pMTG}_{\text{hands}}$) nor when applied to mPFC in tandem with the hand training task ($\text{mPFC}_{\text{hands}}$) ($t$ (19) = 1.65, adjusted p = .12).

Surprisingly, the accuracy for the classification hands vs. animals did not show the expected pattern. That is, hands vs. animals accuracy was higher for $\text{pMTG}_{\text{tools}}$ than $\text{mPFC}_{\text{tools}}$ (t (19) = 4.02, adjusted p = .002, see Figure 4.2D), while there was no difference between $\text{pMTG}_{\text{hands}}$ and $\text{mPFC}_{\text{hands}}$ (t (19) = 1.11, adjusted p = .28).

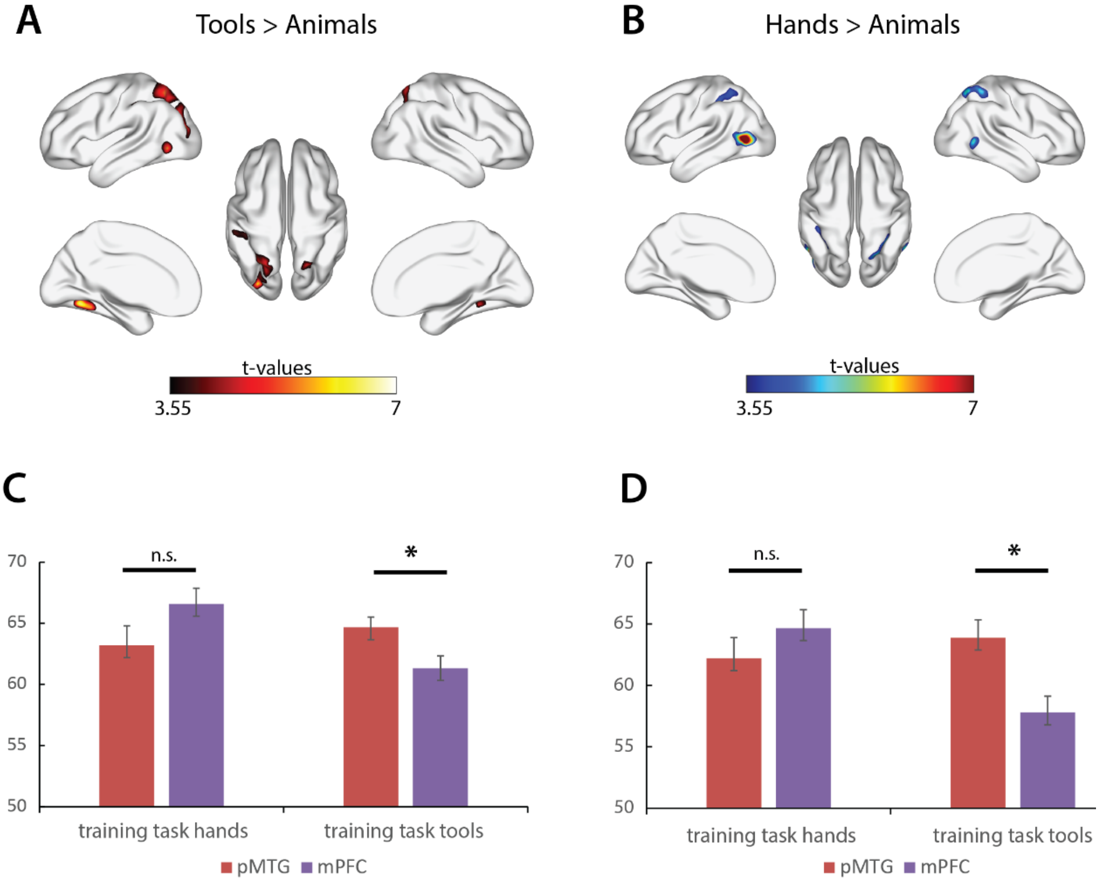

Figure 4.2 – Contrasts of interest and MVPA results.

Figure 4.2. The univariate results (p < .001, uncorrected) used to define regions of interest for the **(A)** tools > animals and **(B)** hands > animals contrasts; and classification accuracy (percentage) for **(C)** tools vs. animals and **(D)** hands vs. animals, for both tDCS areas (pMTG and mPFC) and training tasks (hands and tools), tDCS area

demonstrating an interaction. All error bars reflect one standard error of the mean across participants (* = adjusted p value < .05).

Because we already showed that the hand training task elicits significantly more errors and slower reaction times than the tool training task (see training task results), and that this training task did not show any significant difference for the two stimulation areas, we decided not to include this condition in the next analysis (i.e., we focused only on the tool training task; but see results for the hand task in Supplementary Figure 4.1).

In order to analyze the differences between stimulation sites for each ROI separately and see how stimulating pMTG concurrently with a tool training task changes classification accuracy, we compared the classifying accuracy for both classifications (tools vs. animals and hands vs. animals) between the conditions where we stimulated pMTG under a tool task (pMTG$_{\text{tools}}$), and where we stimulated mPFC under a tool task (mPFC$_{\text{tools}}$).

For the classification of tools vs. animals (Figure 4.3A and Figure 4.3B), pMTG$_{\text{tools}}$, when compared to mPFC$_{\text{tools}}$, led to higher accuracy values only in two tool ROIs (and no hand ROIs): the left pMTG (t (19) = 4.28, adjusted p = .0008) and left mFUG (t (19) = 2.75, adjusted p = .05).

For the classification of hands vs. animals (Figure 4.3C and Figure 4.3D), pMTG$_{\text{tools}}$ (when compared to mPFC$_{\text{tools}}$) led to significantly higher classification accuracies in three hand ROIs: left pMTG (t (19) = 5.72, adjusted p = .0006), right pMTG (t (19) = 3.66, adjusted p = .006) and left aIPS (t (19) = 2.78, adjusted p = .024). Moreover, it led to higher accuracy values in two tool ROIs and: tool -related regions: left pMTG (t (19) = 5.18, adjusted p = .0008) and left IPS (t (19) = 2.90, adjusted p = .036).

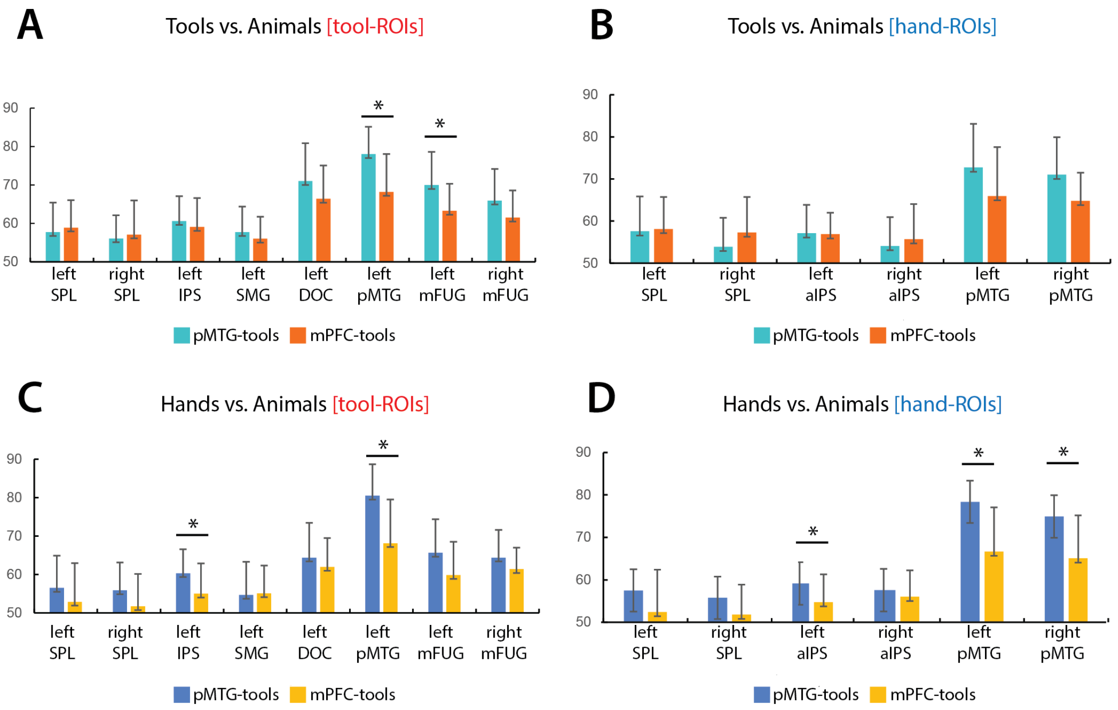

Figure 4.3 – ROI-specific MVPA results.

Figure 4.3. A comparison of the classification accuracy (percentage) between pMTG$_{tools}$ and mPFC$_{tools}$ for **(A)** tools vs. animals in each region identified as a tool ROI, **(B)** tools vs. animals in each region identified as a hand ROI, **(C)** hands vs. animals in each region identified as a tool ROI, and **(D)** hands vs. animals in each region identified as a hand ROI. P-values are FDR corrected for 8 tests in tool-ROIs and for 6 tests when analyzing hand-ROIs (* = adjusted *p* value < .05).

4.5. Discussion

Here we investigated whether two functionally different networks that share certain nodes – as is the case with the tool and hand networks that share pMTG among other areas – could be disentangled by exploring horizontal modulations and long-distance connections through the use of tDCS. To do so, we stimulated pMTG, while combining it with category-specific training tasks in order to enhance the effects of the tDCS stimulation and looked at how this affected classification accuracy between hands or tools (vs animals), when compared to a control stimulation site (mPFC). We showed that applying tDCS to an area where preferences for tools and hands overlap, such as pMTG (i) produced effects in distal brain regions, and (ii) partially facilitated the processing of categorical information in a way that was dependent on the training task prior and during tDCS stimulation.

Importantly, we were able to replicate previous studies (Lee et al., 2019; Ruttorf et al., 2019) by showing that tDCS stimulation modulates BOLD signal patterns in distal brain areas. Specifically, we demonstrated that classification accuracy for hands vs. animals and tools vs. animals was higher when pMTG was stimulated compared to mPFC in distal regions related to hand and tool processing. This result is in line with what previous studies showed (e.g., Lee et al., 2019; Ruttorf et al., 2019): object representations within a specific region can be causally modulated through horizontal modulations from a distal to a local region.

However, our results failed to fully confirm some of our predictions, especially for the training tasks that were coupled with tDCS. Here we predicted that there would be a category-specific effect of the task on the effects visible for the tool and hand networks – this prediction was not fully met.

On the one hand, we demonstrated that the classification between tools and animals benefited from the tDCS stimulation to pMTG only when this stimulation was paired with a tool training task, but not a hand training task, and only in tool ROIs. We showed that when classifying tools vs. animals, the $\text{pMTG}_{\text{tools}}$ condition (when compared to the $\text{mPFC}_{\text{tools}}$ condition), significantly improved the classification accuracy in left pMTG (as expected given that this was the tDCS stimulated area) and left mFUG. The effect on mFUG is an important one as it shows the importance of distal modulation on a functional network – stimulating a tool/hand overlap area under a tool training task led to an advantage in classifying tools vs. animals in a distal yet connected tool (but not hand) area – the left mFUG.

This is in line with our previous study (Amaral et al., 2021), where we showed that pMTG, when processing tools and in the process of conceptual integration, shares information with posterior parietal and dorsal occipital regions (associated to grasping – Almeida et al., 2008, 2010, 2014; Culham et al., 2003), and also communicates with mFUG (more related aspects of visual form and texture – Cant & Goodale, 2007; Cavina-Pratesi et al., 2010). Moreover, previous neuromodulation studies (Lee et al., 2019; Ruttorf et al., 2019) showed that interfering with the processing in a particular tool-region causally affects other distal regions of the tool-network. This suggests that despite the fact that pMTG is a tool/hand overlap region, it is possible to specifically target tool representations over hand representations, by combining the tDCS with a tool-task.

On the other hand, we were not able to obtain similar results for the hand training task over the classification of hands. Although this was an unexpected result, there may be some potential explanations for the failure to obtain results with the hand training task over hand classification. One possible explanation relates with the fact that the kind of task used for the hand training, unlike that for the tool training, was not necessarily related with recognition and processing of hands. Specifically, during the hand training task participants had to press a button every time the image changed from a right hand to a left hand (or vice-versa), whereas in the tool task, participants were instructed to look for a change in tool (e.g., from a hammer to a screwdriver). Thus, the task in the hand training condition could be more dependent on aspects related to mental rotation, rather than hand recognition and processing. In fact, as shown in the training result section, the hand task was clearly different from the tool task – accuracy during the tool task was above 90%, whereas it was around 75% for the hand task; reaction times for the hand task were, on average, about 300ms slower than for the tool training task. In part then, the lack of an effect for the hand training task may be related with the actual difficulty of the task, as well as its potential engagement of non-hand processes and networks. Moreover, the tDCS montage employed in this study, with the anodal electrode centered at pMTG and the two cathodal electrodes positioned both anterior and posterior to pMTG, may have inhibited the effect for the hand training task. The organization of the lateral occipitotemporal cortex (LOTC; Wurm et al., 2017) suggests that our tDCS montage, and specifically our most posterior cathodal electrode could have inhibited social and action representations important for the processing of hands (Bracci et al., 2010, 2018) and thus weakening, or completely overriding, the conjoint effect of the hand training and pMTG stimulation. These are two strong possible reasons for the lack of an effect of the hand tasks on the classification of hand stimuli, and we believe that future work will show that if these two aspects are taken care of, we will obtain a similar result for the hand training task as we did for the tool training task.

But our effects also show another potentially interesting but unexpected result – namely that the tool training task affected hand classification in certain tool and hand ROIs. In particular the areas where we show an effect of the tool training task on hand classification are areas typically associated with object grasping and manipulation, and object-related action (i.e., pMTG and left aIPS). For instance, aIPS is known to play an important role in the computation of hand-shapes for object grasping (Binkofski et al., 1998, 1999; Culham et al., 2003; Monaco et al., 2011), particularly in shaping the hand for the correct manipulation of the object (Buchwald et al., 2018). Perhaps then, the tool training task leads to an advantage for hand classification because it is distally engaging regions dedicated to the processing of grasping and manipulation properties. For instance, grasping a tool requires information about object structure and object volumetry (e.g., Brandi et al., 2014; Buxbaum et al., 2007) – when we want to manipulate a hammer, we need to adjust our hand based on the handle format and size. Thus, it is possible that the tool training task led to tool-related distal activations in grasping, manipulation and action areas, and by virtue of that, and of the fact that hand processing in those areas was intimately related with action, those distal tool-related effects percolated to hand processing, and hence hand classification. Moreover, the hand images used during our fMRI experiment were actually in grasping postures (power and precision grips) and this could produce an activation of the motor system. In fact, we have previously demonstrated shared tool-hand invariant (power vs. precision) grasp-type representations in the left posterior parietal cortex (Bergström et al., 2021). Additionally, several studies have shown that pictures of hand grasp postures can influence object categorization, such that visualizing a hand with a particular grasp posture activates motor information, affecting the processing of manipulable objects, like tools (e.g., Almeida et al., 2018; Borghi et al., 2007; Craighero et al., 2002).

Overall, then, our results (at least partially) show that overlapping functionally-specific networks can be disentangled by focusing on their category-specific horizontal modulations between neural nodes. Specifically, if we focus on how these horizontal long-distance modulations causally affect local processing, we will bring forth strong category-specific organizational dissociations.

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Chapter V.

SPATIAL OVERLAP, BUT TEMPORAL SPECIFICITY: TEMPORAL DYNAMICS DISSOCIATE HAND AND TOOL PROCESSING – STUDY 3

To be submitted: Amaral, L., Besson, G., Caparelli-Dáquer, E., Bergström, F., & Almeida, J. (2021). Spatial overlap, but temporal specificity: temporal dynamics dissociate hand and tool processing. *Unpublished Manuscript.*

5.1. Abstract

Object recognition is a complex process that is putatively dependent on how the brain organizes object-related information. Research has focused on the spatial principles that rule the organization of object knowledge, but temporal dynamics may also prove insightful in our efforts to understand this complex process. One case in which temporal dynamics may be most relevant, is when neural processing for different categories seem to overlap spatially – as is the case of the categories of hands and tools. Here we focus on the differences and/or similarities between the time-courses of hand and tool processing under electroencephalography (EEG). Using multivariate pattern analysis, we compared, for different timepoints, decoding accuracy for images of hands or tools when compared to images of animals. Our findings reveal that for particular time intervals (~168ms and ~264-320ms), decoding accuracy for hands and for tools differs. Furthermore, we show that classifiers trained to differentiate between tools and animals generalize their learning to decoding of hand stimuli at ~400ms after stimulus onset. Classifiers trained to distinguish between hands and animals, on the other hand, were unable to extend their learning to the classification of tools (as hands or animals). These findings demonstrate how the processing of these two functionally related categories differs in time at earlier-to-mid stages of processing and how these discrepancies may relate to distinct features that hands and tools have. Moreover, the findings point to processing similarities at a later stage, which is most likely related to the action processing shared by hands and tools.

Keywords: hands, tools, overlap, time-course, EEG, MVPA

5.2. Introduction

Our ability to recognize objects is crucial in our daily life in order to guide and adapt our behavior to our needs and the context in which we are in. Research in object recognition has been trying to unravel the neural processes behind object recognition using different approaches that go from studying neuropsychology patients to using brain imaging techniques (e.g., Grill-Spector & Malach, 2004; Mahon & Caramazza, 2009; Martin, 2007; Martin & Caramazza, 2003). A central aspect in object recognition is understanding how object knowledge is organized in the human brain: i.e., understanding not only where and how object knowledge is stored and it is organized, but also, and importantly, when different kinds of object-related information become available. Here, we will focus on the temporal dynamics of object knowledge.

Object recognition occurs in a fraction of a second, and it is a highly structured process. Several functional Magnetic Resonance Imaging (fMRI) studies have shown that specific categories of objects elicit higher responses (when compared to baseline categories) in different regions of the brain (e.g., faces, Kanwisher et al., 1997; places/scenes, Epstein & Kanwisher, 1998; tools, Almeida et al., 2013; Chao & Martin, 2000; Mahon et al., 2007; bodies, Downing et al., 2001; and hands, Bracci et al., 2012, 2016). But what drives this categorical organization? Different theories try to explain this object topography by appealing to modality-specific effects (e.g., Martin & Chao, 2001; Warrington & Shallice, 1984), domain-specific constrains (e.g., Caramazza & Shelton, 1998; Mahon & Caramazza, 2011), or constraints imposed by connections with distal regions that share the same categorial preference (e.g., Almeida et al., 2013; Amaral et al., 2021; Chen et al., 2017; Garcea et al., 2019; Lee et al., 2019; Walbrin & Almeida, 2021), among others.

These studies have all focused on a static spatial understanding of object processing. Nevertheless, the temporal layout of object processing is essential for a more complete understanding of how we recognize objects in order to navigate our environment. In fact, electrophysiological studies have been trying to identify the time correlates of object processing (e.g., Kaiser et al., 2016; Kiefer, 2001; Mollo et al., 2017; Proverbio et al., 2007; Simanova et al., 2010, for a review see Contini et al., 2017). A major property of visual processing and visual object processing is the hierarchical nature of this process. Many studies have shown how object representations are temporally stratified going from a fast and coarse categorization to a slower and more detailed representation (Carlson et al., 2013; Cichy et al., 2014, 2016; Clarke et al., 2013). For instance, in a study combining functional magnetic imaging (fMRI) and magnetoencephalography (MEG), Cichy and colleagues showed not only a temporally organized processing sequence underlying object recognition, but they also demonstrated that object representations are organized categorically (Cichy et al., 2016; see also Cichy et al., 2014). Using representational similarity analysis (RSA; Kriegeskorte et al., 2008) they fused fMRI and MEG signals and showed that early visual representations appear in the occipital lobe at around 50-80ms after stimulus onset. This neuronal activity then expands in time and space into ventral and dorsal visual stream regions, showing a clear temporal pathway from low- to high-level visual processing. They also showed that the effects observed within ventral stream were category-selective (Cichy et al., 2016). These findings support previous research on temporal dynamics that show object processing is category-selective (Carlson et al., 2013; Liu et al., 2009).

Obtaining a temporal layout of object processing is thus a promising avenue for understanding object-related computations, and it grounds our spatial understanding of how objects are processed in the brain. Importantly, though, a temporal understanding of object processing can go beyond just temporally tagging our spatial understanding of object knowledge and help adjudicating between different computational hypothesis about object-related neural processing. This may be particularly important for regions that seem to show spatially defined overlapping categorical preferences for more than one category or objects. One such example is the spatial overlap in categorical preferences for the categories of hands and tools. Despite their perceptual differences, hands and tools are functionally connected (Almeida et al., 2018) and show an overlap in neural response preferences in two cortical regions: left lateral occipitotemporal cortex (LOTC) and left inferior parietal lobule (IPL) (e.g., Bergström et al., 2021; Bracci et al., 2012; Peeters et al., 2013). According to Bracci and colleagues (2012), this overlap cannot be explained by shared visual features, and reflects the common specific set of features that hands and tools share during object manipulation – i.e., they both relate to visuomotor and action processing (Bracci et al., 2012).

Whether this response overlap is due to complete (or partial) similarity of the responses for hands and tools in those areas, and whether their responses in these areas can be disentangled has been the recent focus of research. It is possible that response overlap does not necessarily represent true neural overlap. In fact, hands and tools may engage separate neuronal populations and the putative overlap be a "by-product of fine-grained patchiness for tools and hands in the same neural region" (Almeida et al., 2018, p. 299). In fact, Bracci and colleagues (2016) found not only that both categories engage brain regions involved in action processing (as previously demonstrated, see Bracci et al., 2012), but also that the distribution of response patterns within those regions were different for the two categories (Bracci et al., 2016).

Can category-specific processing and computations about these two categories be disentangled within and from these overlap areas? In a previous study (Amaral et al., 2021), we showed that both hand/tool response overlap regions (left IPL and left LOTC) present different patterns of connectivity that are category-dependent. Specifically, when looking at tool responses, we observed: 1) connectivity from left LOTC was correlated with tool-preferences in regions like the left dorsal occipital cortex and the medial fusiform gyrus (mFUG) bilaterally; and 2) connectivity from left IPL was correlated with tool-preferences only in left mFUG. For hand representations, we showed: 1) connectivity from left LOTC was correlated with hand-preferences in the right superior temporal sulcus (STS); and 2) connectivity from left IPL was correlated with hand-preferences in the left postcentral gyrus and in the left STS. These results suggest that despite the overlap response in these regions, the connections established with these areas are dependent on the category that is being processed (Amaral et al., 2021), suggesting that the fingerprints of each of these neural networks is different despite sharing a particular similar node. More recently, these same authors also showed that applying a neuromodulation technique (e.g., transcranial direct current stimulation – tDCS) to left LOTC, and combining it with a tool related task, improves the processing of tools distally in nodes of the tool network (Amaral et al., 2021). These findings suggest that despite the overlap observed in left LOTC, it is possible to disentangle functionally-specific networks by applying tDCS combined with a category-specific task (Amaral et al., 2021).

One potential explanation for the putative response overlap, and for our ability to disentangle hand and tool computations through connectivity, is that these computations are implemented in different times points – that is, the time-course of hand and tool processing may be different. Here we will test how separable hand and tool processing are temporally. To do so we will use a multivariate approach where we will compare decoding accuracy (for the different time points of an object categorization task) for images of hands and for images of tools when compared to images of animals. The application of multivariate analyses to EEG data is rather recent, but it provides a robust methodology to access temporal neural dynamics (Cichy & Pantazis, 2017). Our results show that hands and tools present differences in their decoding accuracy against animals for specific time ranges (around 168ms and around 264-320ms). Moreover, when applying a cross-decoding scheme (i.e., train on tools vs. animals, test on hands, and vice-versa), we found that classifiers trained to discriminate between tools and animals generalized their learning to hands – this was true only around 400ms after stimulus onset. However, classifiers trained to discriminate between hands and animals were not able to generalize their learning to discriminate tools. These findings suggest that, while hand and tool processing differ temporally from each other, they also show specific similarities. Tool processing, in particular, appears to provide some key information for hand categorization, allowing the classifier to classify hands as tools at ~400ms after stimulus onset.

5.3. Methods

Participants

Fourteen participants (M = 28 years, SD =8.01, 6 males) took part in this study. All participants had normal or corrected to normal vision and were right-handed. Written informed consent was obtained from all participants prior to the beginning of the experiment and the study was approved by the Ethical Committee of the Faculty of Psychology and Educational Sciences of the University of Coimbra.

Stimuli and procedure

Participants were asked to categorize images of hands, tools, animals and feet (see Figure 5.1), following a paradigm that was partially used in a previous study (Almeida et al., 2018). Stimuli were greyscale, 200*200 pixels (subtending ~5° of the visual angle) and each category included 8 pictures of different objects/items (total = 32 pictures). Hand pictures were photographs of hands in grasp positions and tool pictures were photographs of different manipulable objects (tweezers, key, spring, scissors, wrench, hammer, screwdriver, and knife). Stimuli were presented using Matlab (The

MathWorks Inc., Natick, MA, USA) and Psychtoolbox (Brainard, 1997) using a refresh rate of 60Hz.

After setting up the EEG device and placing the electrodes, participants started the task. On each trial, a fixation cross was presented during 500ms, followed by the target picture (that stayed on screen for 3s or until the participant responded). The instructions were to press a button, as quickly and accurately as possible, with their left or right index, indicating category membership of the picture that was presented. The experiment was divided in two parts: one part where participants categorized tools vs. animals; and another part where participants categorized hands vs. feet. Response assignment for the buttons was counterbalanced across participants, as well as the order of the two categorization tasks. There were 128 trials for each category/condition and the number of repetitions of each stimulus was 16, for a total of 512 trials.

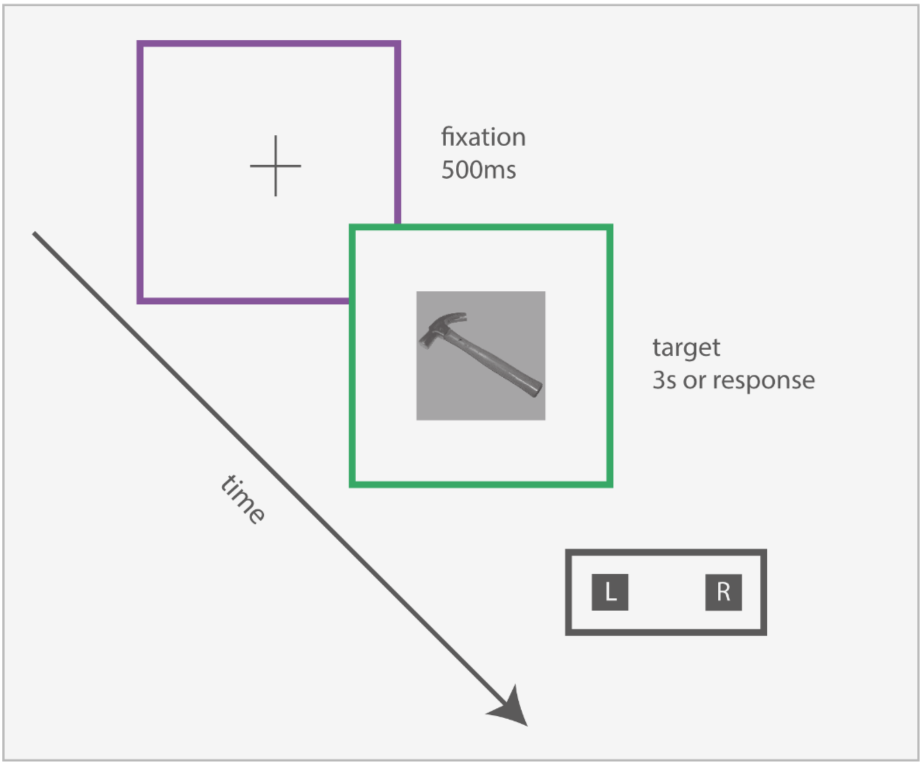

Figure 5.1 – Experimental procedure.

Figure 5.1. A fixation cross appeared for 500ms followed by the target image. The task of the participants was to press a button for one category (hand or tool) or the other button for the control category (foot or animal).

Data acquisition

Electrical brain activity was recorded using a wet-based elastic cap with 64 channels (eego™mylab, ANT Neuro, The Netherlands). Data was acquired with a sampling rate of 1000Hz. The impedance of all electrodes was kept below 5 KΩ. EEG signal was recorded using EEProbe recording software (ANT Neuro, The Netherlands) and was amplified using an ANT digital amplifier.

Data preprocessing

Preprocessing was performed in Matlab (The MathWorks Inc., Natick, MA, USA) using the open source EEGLAB toolbox (Delorme & Makeig, 2004), and custom-made scripts. EEG data was down-sampled to 250 Hz, digitally filtered using a bidirectional linear filter (EEGLAB FIR filter) that preserves phase information (pass-band 0.5–40 Hz), and then averaged-referenced offline on the average of both mastoids. EEG data underwent a custom-made sanity check and correction to control that the EEG triggers (sent from the task computer and recorded by the amplifier in EEG data) correctly matched the task triggers (sent from and recorded by the task computer). Triggers and corresponding EEG trials were removed when no correction could be ensured (2 trials of one participant were lost). EEG data was then epoched (from -500ms to 500ms post-stimulus onset) and baseline-corrected (by subtracting the EEG average from the window -200 to 0ms post-stimulus onset).

EEG automatic artefact rejection. An automatic artefact rejection algorithm (Jas et al., 2017) was then used to reject bad electrodes and/or trials. Briefly, considering a group of time signals (e.g., epochs of trials along one electrode), this algorithm reject those presenting a peak-to-peak value (a quantity commonly used for identifying bad trials in M/EEG) exceeding a (data-driven) threshold, automatically defined as the threshold yielding the minimum difference (i.e., sum of the squared difference) between the mean of the under-threshold signals and the overall median signal (Jas et al., 2017). For each participant, this algorithm was applied twice in the following order: 1) *across trials* for each electrode, in order to detect electrode-wise bad trials; and 2) *across electrodes* for each trial, in order to detect trial-wise bad electrodes. After each application of the algorithm, each trial was repaired by interpolation if less than half the electrodes were rejected or excluded from subsequent analysis otherwise. Overall, this two-steps procedure yielded a rejection rate of 8.10% (3.75%; mean and SD across participants) of the data (channels and/or trials); trial-wise electrode interpolation could then be applied to the extent that our final dataset missed 4.42% (3.31%) of the trials.

Multivariate pattern analysis

Decoding analyses were performed using the Matlab toolbox CoSMoMVPA (Oosterhof et al., 2016). We used a leave-one-fold-out cross-validation procedure to train a linear discrimination analysis (LDA) classifier to discriminate between z-score normalized EEG signals of two experimental conditions (hands vs. animals OR tools vs. animals). We used animals as the baseline category for both procedures to rule out differences depending on the baseline. The cross-validation procedure ensured that training and testing data was kept completely independent, and that partitions were balanced (i.e., each condition was presented equally in each fold/partition). In addition to this decoding approach, we also performed a cross-decoding approach: the classifier was trained to discriminate between hands vs. animals, and then tested on tools (and vice-versa). The decoding was executed using pseudo-trials (i.e., averaging across 5 trials – allowing a maximum of 3 resampling of each trial), to improve the signal-to-noise ratio (Grootswagers et al., 2017). In order to reduce dimensionality, we applied Principal Component Analysis (PCA) and kept components that explain 99% of variance. Finally, we used a temporal generalization (TG) method (King & Dehaene, 2014) over the cross-decoding approach – this allowed us to investigate the ability of the classifier to generalize across time, thus implying that the neural information identified at time t persisted at time t'. For this TG analysis, PCA and trial averaging were not performed.

For each participant, the decoding accuracy was computed across all electrodes (63 in total, excluding EOG), for each of the 126 time points following the stimulus onset (between 0 to 500ms). We then analyzed decoding accuracies at the group level using a two-tailed paired t-test (when comparing the results from decoding hands vs. animals with tools vs. animals) and a two-tailed one-sample t-test against chance level (50%) for the cross-decoding and TG approaches. Finally, we used threshold-free cluster-enhanced (TFCE; Smith & Nichols, 2009) Monte Carlo simulations with 10,000 iterations to correct for multiple comparisons, as implemented in the CoSMoMVPA Toolbox (Oosterhof et al., 2016).

5.4. Results

Behavioral results

We used a one-way repeated measures ANOVA to analyze the accuracy and the reaction times across the conditions. Accuracy results (i.e., pressing the correct button for the target image) show that the experimental conditions did not differ in difficulty (*F* (1,13) = 1.07, *p* = .37). Reaction times (RTs) analysis also showed that the four conditions did not differ in RTs (*F* (1,13) = 1.10, *p* = .36). For more details, please see Table 5.1.

Table 5.1 – Behavioral results.

Condition	Accuracy		Reaction Times (ms)	
	Average	SD	Average	SD
hands	.97	.02	603	42.99
tools	.97	.04	616	54.98
feet	.97	.03	593	34.47
animals	.98	.02	608	60.38

Multivariate decoding results

Are hands and tools differently processed over time?

One possible explanation for the overlap that hands and tools present in some regions of the brain, is that category-specific computations are carried out for each category at distinct times. To test this hypothesis, we employed a multivariate approach and compared the decoding accuracy between hands vs. animals and tools vs. animals. The use of the same baseline category (animals) for both classification procedures allow for a more balanced understanding of the differences in the processing of hands and tools across time. In this analysis we showed that decoding accuracy (acc) was significantly different between the two conditions during specific time ranges. The accuracy for tools (vs. animals) was significantly higher than hands (vs. animals) in an early time point around 168ms (peak z-value = -2.08, acc_{tools} = .60). The reverse outcome (hands accuracy higher than tools) was observed in two later time intervals: between 264 and 304ms (peak t-point = 268ms, peak z-value = 3.09, acc_{hands} = .65) and between 312 and 320ms (peak t-point = 316ms, peak z-value = 2.07, acc_{hands} = .64). These results suggest important differences in the time-courses of hand and tool processing (for more details see Figure 5.2).

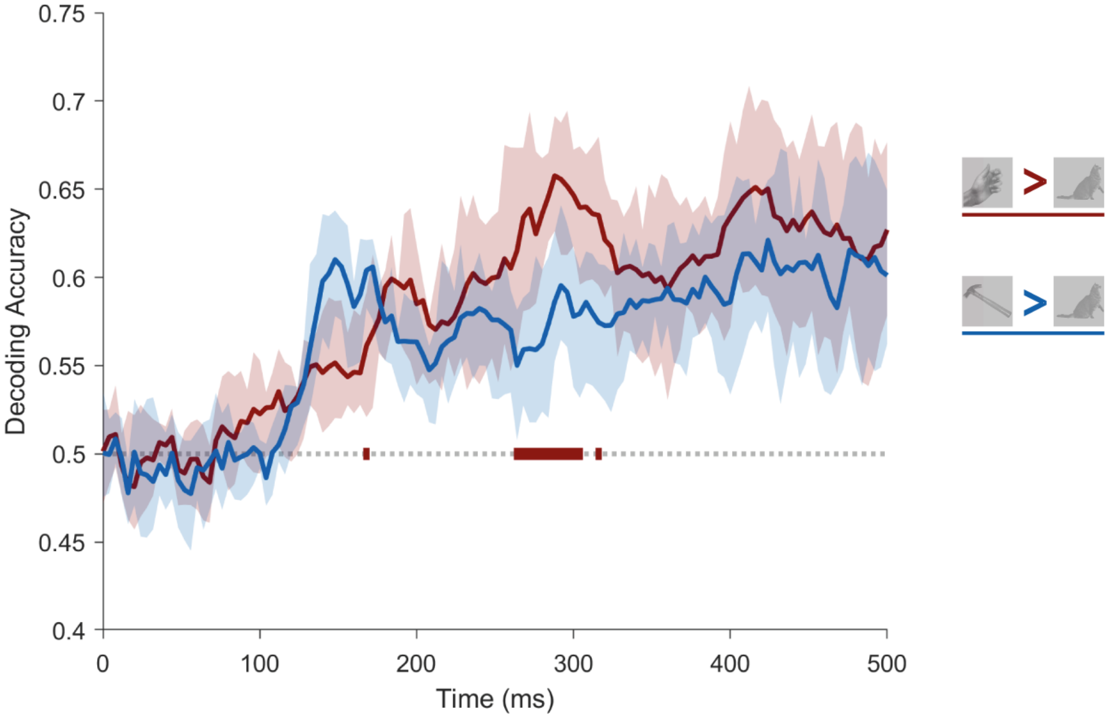

Figure 5.2 – Decoding accuracy results (paired analysis).

Figure 5.2. Decoding accuracy for hands vs. animals (red line), and tools vs. animals (blue line). The red points in the baseline (0.5) correspond to the significant time clusters (|z| > 1.96, cluster-wise corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016)) for the paired analysis between hands and tools accuracy.

Is the category-specific neural representation of tools/hands at different time points informative of the neural representation of hands/tools?

We then focus on whether category-specific information on tools (or hands) can be generalizable to the processing of hands (or tools). To address this question, we used a cross-decoding approach, and tested 2 classifiers: 1) one trained on decoding tools vs. animals; and 2) one trained on decoding hands vs. animals. Importantly, we tested these classifiers with the other category of interest (e.g., if a classifier was trained on tools vs. animals, it was tested with hands). For the classifier that was trained on tools and tested on hands (Figure 5.3A), we found significant generalization effects in a time window between 384 and 428ms (peak t-point = 400ms, peak z-value = 3.09, acc = .58). No significant effects were found for the classifier trained on hands and tested on tools (Figure 5.3B, all |z| values < .98).

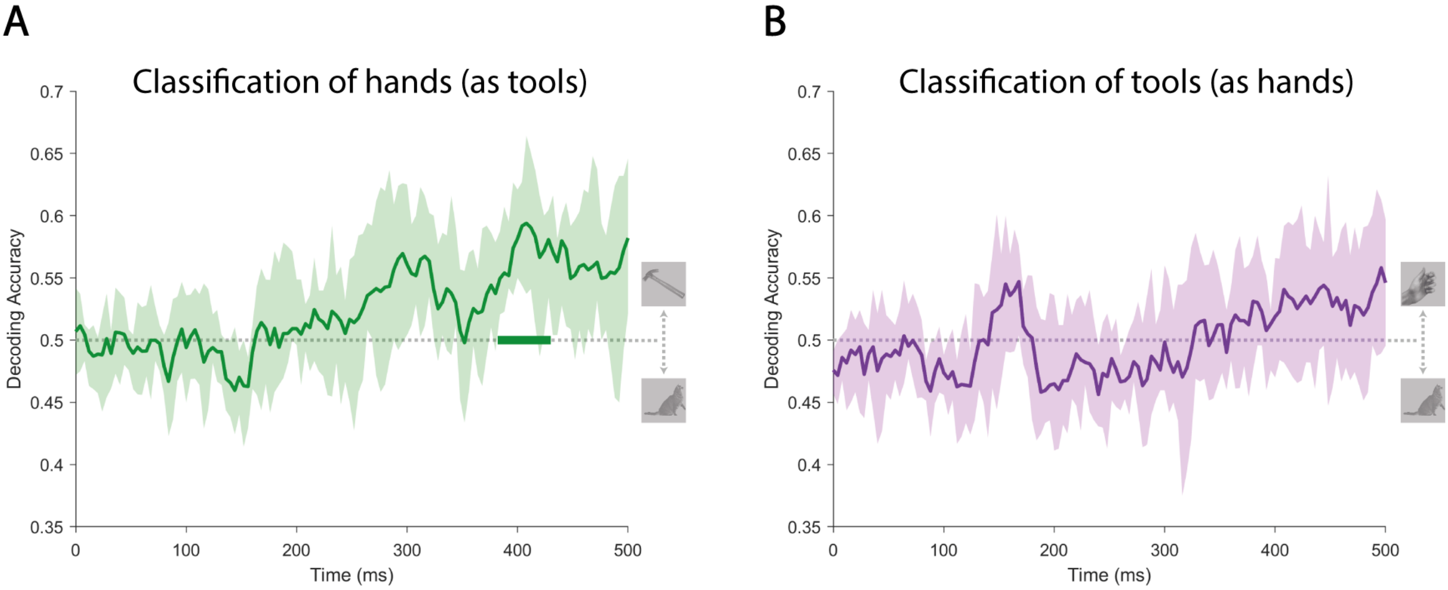

Figure 5.3 – Cross-decoding accuracy results.

Figure 5.3. (A) Decoding accuracy when the classifier trained on tools vs. animals was then tested to classify hands. Above-baseline accuracies shows that hands were classified more as tools, while beyond-baseline accuracies shows that hands were

classified more as animals, according to the classifier trained at the time point considered. The green points in the baseline (0.5) correspond to the time cluster significantly different from the baseline (|z| > 1.96, cluster-wise corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016)). **(B)** Decoding accuracy when the classifier trained on hands vs. animals was then tested to classify tools. No significant effects were observed in this analysis (|z| < 1.96).

Is the category-specific neural representation of tools/hands informative of the neural representation of hands/tools when generalizing across time?

We wanted to understand whether the generalization of tool/hand representations to the processing of hands/tools could be extended in time – that is, whether there was cross-time generalization of the processing of tools and hands. For such, we used a TG approach, and looked for timepoints where tool (when compared to animal) distinctive patterns could be used to categorize hands across time (and vice-versa). The results from this analysis are represented in a matrix, where each axis indicate the training and testing time. Results that lie on the diagonal of the matrix represent the same time point for training and testing (i.e., they correspond to the cross-decoding analysis presented above). In this analysis we did not use trial averaging or PCA because these are not typically in a TG approach (King & Dehaene, 2014). Nevertheless, and as a control for the feasibility of this approach, we observed that results from cross-decoding (Figure 5.3A and Figure 5.3B) are identical to the results obtained in the diagonal of the TG results (Figure 5.4A and Figure 5.4C).

As shown in Figure 5.4A, training on tools vs. animals (and testing on hands) revealed three mid clusters and two late clusters (i.e., classifying hands as tools more than as animals; all clusters with a z > 1.96). The first cluster (represented in white) shows that a classifier trained on tools vs. animals with data from around 280-330ms can be used to classify hands as tools in an earlier time interval (around 170-220ms). The other two mid clusters (represented in brown and pink colors) show that a classifier trained on tools vs. animals around 280-380ms classifies hands as tools both earlier (from ~220ms) and later (until ~440ms) in time. The late clusters demonstrate that a classifier trained on tools vs. animals around 380-450ms also allows for classification of hands as tools before (from ~230ms) and after that time interval (until ~500ms). When testing the opposite effect (training on hands vs. animals, testing on tools), no significant results were observed (all |z| values < 1.64, Figure 5.4C and Figure 5.4D).

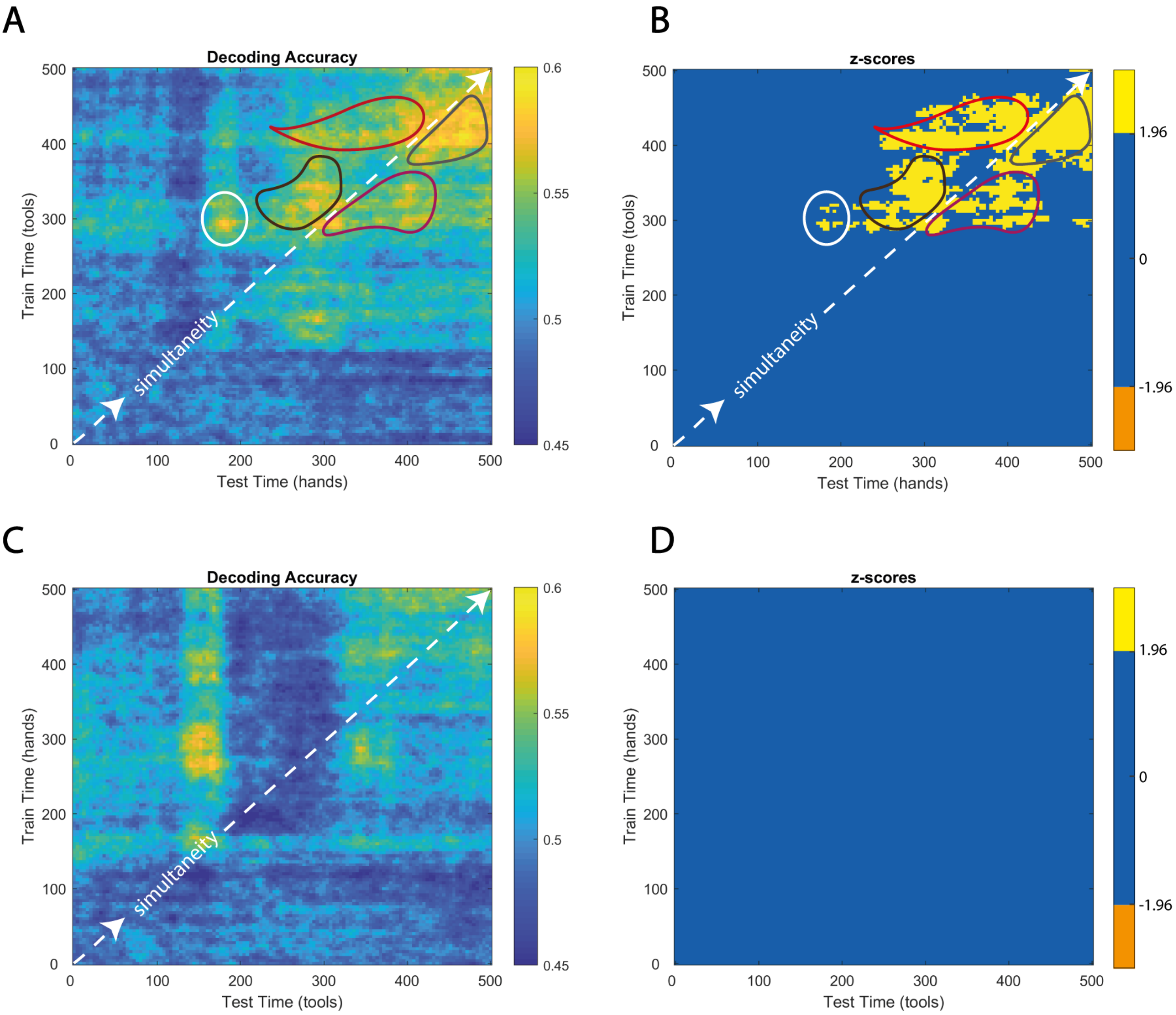

Figure 5.4 – Results from time generalization approach.

Figure 5.4. (A) Decoding accuracy across time when the classifier trained on tools vs. animals and was then tested on hands. **(B)** The yellow color represents the significant time points when classifying hands as tools (z > 1.96, cluster-wise corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016)), that were divided in three mid clusters (white, brown, and pink circles) and two late clusters (red and gray circles). **(C)** Decoding accuracy across time when the classifier trained on hands vs. animals and was then tested on tools. **(D)** No significant effects were observed in this analysis (|z| < 1.96).

5.5. Discussion

Understanding the temporal dynamics of object knowledge is essential for developing sophisticated models of visual object processing. Here we set out to investigate the timing of object knowledge by looking at two functional related categories: hands and tools. Specifically, we investigated whether there are temporal differences and/or similarities during the processing of these two related categories.

We first looked at whether neural patterns for tools and hands can be temporally discriminated. To this end, we used a decoding approach, where we compared the accuracy of decoding between hands and animals and between tools and animals during different time points after stimulus onset. Even though the decoding accuracy profiles for these two decoding conditions present some similarities through time, the accuracy pattern was clearly different during two time intervals (around 168ms and around 264-320ms).

In the first time interval (~168ms), the accuracy for decoding tools (vs. animals) was higher than that for decoding hands (vs. animals). This shows that during this earlier time point, tools are more easily distinguishable from animals than hands are – that is, category-specific tool responses seem to be more distinguishable and/or unique than category-specific hand responses. These results show that at that time, tools are more different from animals than hands are from animals. This could be due to larger domain-specific differences (e.g., living vs. non-living distinctions, Caramazza & Shelton, 1998) - for instance, it may be the case that domain membership (i.e., tools are non-living things, whereas animals and hands are living things) could be the driving force of the effect at this stage. In fact, in a MEG study, Carlson et al. (2013) used multidimensional scaling (MDS) and found that by ~120ms after stimulus onset, distinguishability between exemplars becomes possible, and from that time point onwards we can see the emergence of categories and subcategories (e.g., faces and animals are very close in the representational space). These results can help us to explain why tools and animals are more distinguishable at an earlier stage than hands (a body part) and animals. Moreover, the fact that animals and manmade objects differ in early perceptual features (Long et al., 2017) and that categorization between these two categories emerges at ~150ms (Proverbio et al., 2007) could potentially also be the basis of our results. Finally, tools and animals also immediately differ in their level of manipulability (a difference that is not immediately apparent when comparing hands and animals), which is another aspect that may lead to better classification between tools and animals than between hands and animals. In fact, Proverbio (2012) showed a desynchronization of the Mu (μ) rhythm around 140-175ms, when comparing tools vs. non-tools (i.e., non-manipulable objects). The Mu (μ) rhythm is a brain wave that appears most prominently over sensorimotor cortex during a relaxed state and its suppression is induced by motor action. These results suggest then that motor information (e.g., manipulability) can be extracted from visual objects at early stage of processing (Proverbio, 2012).

Later on in the processing of these categories – around 264-320ms after stimulus onset – we showed that hands were more dissimilar from animals than tools were from animals – i.e., accuracy for hands (vs. animals) was higher than tools (vs. animals). During this time window, this heightened discriminability between hands and animals could be related to later stages associated with semantic processing. In fact, this time window follows categorical processing (e.g., N1, N2, Zani et al., 2015) and precedes more integrative and conceptual components (e.g., P300, N400, De Sanctis et al., 2013). It may also be linked to differential processing associated with hands and animals in what respects biological motion and social representations that occur during hand processing. The N240 component, for example, has been shown to originate in the superior temporal sulcus (STS, Hirai et al., 2003), a region involved in aspects of social cognition as well as facial and body expression (Bonda et al., 1996; Grossman et al., 2000; Narumoto et al., 2001; Puce et al., 1998). Interestingly, we previously found that STS plays an important role during hand processing in the overlap regions (Amaral et al., 2021).

Another important test to the neural and cognitive overlap between hand and tool processing, is whether processing at a particular time point for one of the categories can be generalized to the processing of the other category. To test this, we employed a cross-decoding approach, where we tested the ability of a classifier trained on classifying tools vs animals (or hands vs. animals) to classify hands as tools (or tools as hands). We found that classifiers trained on classifying tools vs. animals were significantly biased to classify hands as tools (more so than as animals) around 400ms post-stimulus onset. These results suggest that category-specific information from tools is represented in a way that is sufficiently similar to how hand related information is coded around 400ms after stimulus onset in order to allow for generalization from tool processing to hand processing. However, we did not find a similar result for the processing of hands vs animals on decoding of tools. That is, the patterns of activation for hands (when compared to animals) used by our classifier do not seem to allow for generalizing to tools.

A possible interpretation of this result is that as a consequence of the processes at play (potentially automatically) when seeing a tool (Handy et al., 2003; Handy & Tipper, 2007), there is information (e.g., tool affordances – a tool's graspable status and its associated motor program) that percolates to hand-specific computations in order to implement those action programs. These kinds of interactions could potentially be responsible for the generalization effects seen here. Importantly, the processing of these kinds of tool-related information may be automatic (Grèzes et al., 2003; Tucker & Ellis, 2001; Tucker & Ellis, 1998). Interestingly, processing of certain grasp related information seems to happen exactly at ~400ms: De Sanctis and colleagues measured the EEG correlates during grasping movements and found grasp-specific activation peaking at 300ms over parietal regions that continued to the central and frontal electrodes at around 400ms (De Sanctis et al., 2013).

This effect could also be related to the ventro-dorsal pathway – critical for tool use (Binkofski & Buxbaum, 2013). For instance, in a study combining fMRI and EEG, Mizelle and Wheaton (2010) identified cortical regions, as well as temporal dynamics, associated to correct and incorrect use of tools. Correct use of tools led to occipitoparietal and frontal activations typically associated to the tool network. Additionally, source localization analysis of EEG showed that occipitotemporal regions were exclusively active to correct tool use between 300 and 400ms (Mizelle & Wheaton, 2010). In a MEG study, Suzuki and colleagues investigated the neural responses to visible and invisible images of tools. They found a strong neural response to visible images of tools in left parietal regions at 400ms (Suzuki et al., 2014). These results suggest that the ability for a classifier trained on categorizing tools vs. animals to classify hands at that time window is dependent on action related computations that connect hands and tools.

This result could also provide insight on why the spatial overlap shown in fMRI for the processing of hands and tools comes about, as occurs during the time window when these categories share action-related information. This may be particularly true for the spatial overlap in neural responses for hands and tools in the IPL because of the role of this area in accessing manipulation knowledge (e.g., Boronat et al., 2005; Buxbaum et al., 2000; Ishibashi et al., 2011; Kellenbach et al., 2003).

Importantly, our results also show that classification of hand stimuli (vs. animals) does not generalize to the categorization of tools. The classification of hands, and especially in comparison with animals, may not lean necessarily on action-related (or other high-level) aspects, and thus, the generalization to tools may not be as clear as it was for the case of hands. Importantly, the fact that training on the categorization of hands vs. animals does not generalize to the classification of tools may bring interesting insights into our understanding of the representation of information – this lack of reciprocity between tool and hand representations strongly suggests a processing contingency whereby action-related hand processing depends upon tool-related action processing.

Finally, in the TG analysis, we wanted to extend the previous results and test whether cross-decoding could be generalized across time. We showed above that training on tools vs. animals allows to classify hands as tools at ~400ms. With the TG method, we extended these results and demonstrated that the information that allows to classify hands as tools is maintained in the neural patterns over time. Specifically, we showed that training on tools vs. animals around ~300ms and later at ~400ms provides enough information to classify hands as tools both earlier (~200ms) and later (~500ms) than those time points. This suggests the kind of tool-related action processing on which hand (action-related) processing is contingent upon occurs at ~300ms and ~400ms. Although the effect at ~300ms did not reach statistical significance for cross-decoding, we can observe in Figure 5.3A a peak accuracy during that time. Importantly, it has been shown that tool-specific affordances are coded precisely around these temporal windows: for instance, in an EEG study, Proverbio and colleagues compared tools and non-tools and found that action affordance is computed at ~250ms (Proverbio et al., 2011). Note that, once again we found no generalization effects for tools when training on hands.

Overall, the results show both temporal differences and similarities between hand and tool processing. On the one hand, classical decoding results show that the temporal windows at which hands and tools are different and are suggestive of the kinds of information that are computed over time during the processing of each category that sets them apart. Cross-decoding and TG analyses, on the other hand, demonstrate when hands and tools are comparable, and suggest that there is specific processing contingency: training on tools vs. animals allows for hand decoding, but training on hands vs. animals does not allow for tool decoding. This dissociation may be related to action information computed for our interactions with tools that can trample to the processing of hands.

Note that the results presented here might have methodological limitations. For instance, we used a block-design that splits our experiment in two tasks: identifying tools and animals and identifying hands and feet. Although the order of the two tasks was counterbalanced across participants, when doing a cross-decoding analysis that trains on hands vs. animals, this implies that we trained on different blocks. However, we ran a supplementary analysis (training on hands vs. feet) for both cross-decoding and TG, and no significant effects were found (see Supplementary Figure 5.1 and Supplementary Figure 5.2).

In conclusion, our results show both differences and similarities between the time-course of hand and tool processing. We demonstrated that not only are the two categories processed differently over time, but that tool representations can also be informative (in specific time points) for hand processing. The fact this outcome was not established for hand representations clearly supports a processing contingency in which action-related hand processing is tied to the processing of action attributes during tool processing. Together these results shed new light on the respective stages of hand and tool processing and highlight how it is possible to disentangle their processing.

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Chapter VI.

GENERAL DISCUSSION

6.1. Summary

Our ability to rapidly and efficiently recognize an object is crucial for our daily life. The scientific community has been attempting to unravel the processes that underpins object recognition, but many questions remain unanswered. The work that I presented here tries to clarify some of these unaddressed questions and focus on the interaction between two categories of objects – hands and manipulable objects (i.e., tools) – as a handle to better understand brain dynamics in the process of object recognition and conceptual representation.

We easily recognize hands and tools as two (very) different visual categories. It is, however, equally simple to accept the notion that the two categories must share some common ground during their processing. In most situations, we need our hands to manipulate the tools and this manipulation requires considering a variety of sources of information. For instance, the shape of a tool, as well as its typical use will determine how I place my hand to maneuver it. The link between the two categories is so strong that they engage some of the same brain regions during their neural processing. Specifically, hands and tools are known for activating both left posterior middle temporal gyrus/lateral occipitotemporal cortex (pMTG/LOTC) and left inferior parietal lobule/intraparietal sulcus (IPL/IPS) (Bergström et al., 2021; Bracci et al., 2012, 2016; Peeters et al., 2013). But what does this overlap mean? Are hands and tools processed in the brain in a similar way? Or is it possible to disentangle hand from tool processing? To examine this question, I used functional magnetic resonance imaging (fMRI), transcranial direct current stimulation (tDCS), and electroencephalography (EEG) to study 1) if the connectivity constrains exhibited by regions where neural response to hands and tools overlap depend on the category being processed; 2) if we can isolate hand and tool processing within the overlap regions by priming the system to focus on one of the categories; and 3) if there are temporal differences during the processing of hands and tools.

In the first study, I used fMRI to measure the pattern of responses to different categories: hands, tools, and animals. Then, I correlated the voxel-wise category preferences across the brain with functional connectivity between those voxels and two overlap regions that respond both to hands and tools (left IPL/IPS and left pMTG/LOTC). I showed that functional connectivity fingerprints from the two overlap regions are related to categorical preferences for hands and tools in a distinct way within different areas of the brain. These findings demonstrate that areas that process both categories retain category-specific object topography, and that the processing of each category is dependent on the distal connections within the category-specific neural network.

In the second study, I used tDCS – a non-invasive neuromodulation technique – together with fMRI in order to investigate the effects of neuromodulation in the neural processing that is shared by hands and tools. Specifically, I combined tDCS with a training task that was either related to hands or tools. Stimulation was applied to one of the overlap areas (pMTG/LOTC). After the tDCS/training session, participants observed images of different categories inside the scanner (fMRI task). Using a decoding approach, I found that classification was more accurate at differentiating tools from animals only when the stimulation was on pMTG (and not on the control area – medial prefrontral cortex, mPFC) and only when combined with the tool training task. Unexpectedly, the combined version of tDCS on pMTG with the tool training task (and not the hand training task) also led to an enhanced accuracy when classifying hands vs. animals. These results suggest that it is possible (at least partially) to disentangle the two overlap networks, by increasing the specific category processing with tDCS combined with a cognitive task related to that category.

Finally, in the third study, I explored (possible) temporal differences between hand and tool processing. Using a multivariate approach, I compared classification accuracy (within different time points of the visual task) for hands and tools (vs. animals). I found that hands and tools present differences in their classification accuracy against animals for specific time intervals (~168ms and ~264-320ms). Moreover, when applying a cross-decoding scheme (i.e., training on tools vs. animals and then testing on hands, and vice-versa), I also found that training the classifier decoding tools versus animals was sufficient for the classifier to identify hands – this was true at ~400ms after stimulus onset. Inversely, the opposite effect was not found – training on hands vs. animals does not lead to an advantage in classifying tools. Overall, the findings shows both differences and similarities between the temporal processing of hands and tools. The findings not only reveal when hand and tool processing differed (and how those differences are related to different properties that hands and tools have), but also when neural representations of tools can generalize to the neural representations of hands.

In the next section, I further discuss the implications of this thesis for our understanding of the unique relationship between hands and tools, as well as to corroborate the role of functional connectivity in the organization of object knowledge.

6.2. Implications

Brain in action – when hands and tools meet

It is now established that representations for hands and tools widely overlap in specific regions of the brain located in both parietal and temporal cortices. The fact that these two categories do not share any visual similarity and are in fact categorizable into different large-scale categories – e.g., animate vs. inanimate – leaves open the question of what truly connects hands and tools. Bracci and colleagues (Bracci et al., 2012, 2016) argued that the functional link between the two categories is action-based. This means that the categorical preferences that we observe in the overlap regions are not based on the visual features of hands and tools, but instead on the action-related properties that these items hold (Bergström et al., 2021; Bracci et al., 2016, 2017; Bracci & Peelen, 2013).

Interestingly, left LOTC is known for being functionally connected to regions related to action planning and recognition such as those within the frontoparietal cortex (Bracci et al., 2012; Lingnau & Downing, 2015; for a review see Wurm & Caramazza, 2021). Moreover, IPL (that extends in study 1 to anterior IPS) is a region that has long been associated with tool-specific action processing. For instance, patients with lesions to IPL reveal ideomotor apraxia – an impairment in manipulating everyday objects (e.g., Almeida et al., 2018; Buxbaum, Giovannetti, et al., 2000; Buxbaum, Veramonti, et al., 2000; Garcea et al., 2013) – whereas the computation of hand-shapes for object grasping is known to be heavily influenced by aIPS (Binkofski et al., 1998, 1999; Buchwald et al., 2018; Culham et al., 2003; Monaco et al., 2011).

However, this does not mean that the representations within IPL and LOTC is the same. In fact, in Study 1, both overlap regions showed differences in their distal relationships, suggesting different roles for each overlap region when processing hands or tools. Interestingly, for tool processing, the distal connections from IPL appear to be linked to the transmission of information about manipulation, while the distal connections established by LOTC seem more related to material and surface properties of the tools supported by its preferential connectivity with the medial aspects of the fusiform gyrus. The differences in the patterns of distal connections conveyed by IPL and LOTC for hand processing can be attributed to motor and social factors. These patterns of connectivity seem to be related to aspects pertinent to the computations being performed locally and they can also be associated to the different processing computed over parietal (IPL) and occipito-temporal (LOTC) cortices. On the one hand, connectivity patterns between IPL and other regions of the brain may be related with computing and accessing aspects related to object-specific functional grasps and manipulation. On the other hand, the connections established from LOTC seem to be related to perceptual properties, crucial for ventral stream processing during object recognition. These results highlight the division of labor between the two streams, but they also emphasize the need of integration between the two systems implemented through distal connections with regions from both dorsal and ventral streams.

The results from Study 3 also underline the action-based interaction that exists between hands and tools. Using a cross-decoding analysis, I tested if hands were classified as tools (when training on tools vs. animals) and if tools were classified as hands (when training on hands vs. animals). I observed a dissociation effect that shows that training on tools vs. animals allows the classifier to categorize hands as tools (at ~400ms post-stimulus onset), but not the opposite. These findings can be interpreted based on action related processing, where the discrimination on tools vs. animals is achieved by action-related computations (e.g., manipulation) in a later stage.

Together these results bring evidence to the fact that hands and tools interact in terms of their action properties and, although both overlap regions may relate to this object-related action processing, they may play different roles during hand and tool perception.

The nature of the overlap

The strong overlap between responses to hands and tools begs the question of whether they reflect the same or separate neural populations being activated. If the two categories activate the same group of neurons similarly (within the overlap regions), this would imply that the responses of those neurons for the two categories would be indistinguishable – that is, effectively, tools and hands would be exactly the same or similar within these sets of neurons. For instance, hands and tools could jointly represent an action dimension and the representations coming from the overlap regions would not be discriminable. Alternatively, we may be looking at adjacent neurons and not to a true overlap. Then, the putative overlap response may be a result of distinct neural groups that are spatially overlapped but otherwise separate at a fine spatial scale (i.e., below the standard resolution of fMRI). In a previous study (Almeida et al., 2018), we showed interference effects in a priming task. That is, participants were slower to categorize a tool (after the unconscious presentation of a hand), and the same happen when categorizing hands – participants were also slower in the presence of a tool prime. If one assumed that overlap responses for hands and tools were the same, one would have to expect a facilitation effect (i.e., faster reaction times when pairing hands and tools). However, if the neural populations that respond to hands and tools are not the same, or their processing is different, then one would potentially interpret this interference effect as resulting from lateral inhibitory connections produced by the adjacent (but not overlapping) hand and tool patches (Almeida et al., 2018).

Importantly, a recent study (Bergström et al., 2021) showed that (hand-tool invariant) grasp information can be extracted from the left posterior parietal cortices – PPC (including IPL). Specifically, data from this area allows for decoding grasp type (power versus precision grasps) that generalize from tool images to hand grasping videos (and vice-versa). Moreover, hand-specific grasp representations (that are viewpoint-independent) are extracted from hand-related regions, such as bilateral PPC, left ventral premotor, and left LOTC (Bergström et al., 2021). These results point to differing stages of abstractness, where hand-tool invariant grasps rely primarily on the left PPC, and hand-specific grasp attributes are handled more broadly across the hand network (Bergström et al., 2021), and bring evidence of shared or similar patterns (at the fMRI scale) between hands and tools in parietal cortex.

A slightly different hypothesis, supported by the findings in this thesis, is that the same neurons respond to hands and tools, but they do it in a distinct way (i.e., they may perform different computations dependent on the category being processed). In Study 1, results show that both overlap regions present different patterns of connectivity when processing hands and tools. This indicates that in such areas, the same neurons (or at the very least neurons within the same voxels) receive and send category-relevant information to specific category-specific networks in a manner that is dependent on the stimuli being processed. These category-specific organization dissociations were validated by the results in Study 2. Finally, Study 3 shows that hand and tool processing present different time-courses, addressing the possibility that the neural population for the two categories could be the same, but the neurons respond to hands and tools at different time points. However, this EEG study also demonstrates a time period when neural representations for hands are similar to tool representations (~400ms after stimulus onset), possibly implying that neural overlap exists at this time point. The results from Bergström et al. (2021) could also help to explain this cross-decoding effect: PPC was shown to be central for the representation of abstract grasp information, and potentially for the conversion of item-specific grasp patterns to more item-invariant grasp representation. Thus, a possible interpretation of the EEG findings is that tools (when compared to animals) trigger this abstraction information coming from PPC (particularly in IPL), which then allows for the generalization to hand representations.

Nevertheless, the results described throughout the thesis do not unequivocally demonstrate the nature of the neural overlap. Thus, other techniques with higher spatial resolution should be used to assess possible neural differences at a micro scale (e.g., high-resolution fMRI; electrocorticography). Nevertheless, the previously described findings do not support the extreme view that there is absolute neural overlap in the responses for hands and tools – this extreme view would require that hands and tools are indiscriminate in the overlap regions, which me (and others) demonstrate is not the case. Alternatively, the same neurons (within the overlap regions) respond both to hands and tools, but that response will be different in terms of spatial and time dimensions. Depending on the category being processed, neurons receive and send information specifically related to that category, and with potential temporal dissociations different between the two categories. Despite of these computational differences within the same neurons, there seems to be particular time points when hand and tool representations are highly similar.

The role of functional connectivity in the organization of object knowledge

What principles are at play in the organization of object knowledge in the brain is one of the most debated questions in the field of cognitive neuroscience. According to a relatively new theory, local representations do not solely depend on the computations undertaken within a local region that shows preference for a particular category. These also depend on the distal connectivity with other regions that share the same categorical preferences (e.g., Almeida et al., 2013; Chen et al., 2017; Hutchison et al., 2014; Hutchison & Gallivan, 2018; Lee et al., 2019; Mahon et al., 2013; Mahon & Caramazza, 2011; Walbrin & Almeida, 2021). This means that visual object recognition (mainly attributed to ventral stream processing) is mediated by patterns of connectivity that integrate the visual information from the ventral stream with category-related information computed by other regions of the brain. For each object category, the functional relationship established between the various regions will be different. For example, during tool processing, motor information and visual features are expected to be integrated – but this is probably not the kind of integration that is going to be important for the processing of animal stimuli. Importantly, in this thesis I set out to test this theoretical proposal. Most of the research that led to the development of this theoretical proposal on the relationship between local computations and distal connectivity has been conducted on regions that respond preferentially to a single object category. However, this hypothesis could be strengthened by investigating regions that respond preferentially to more than one category – if two categories share a particular node, but there are domain-specific connectivity constraints at play that influence local computations in that node, then one should see different input/output connections for reach of the categories. So, in the case of the overlap regions for hands and tools, the distal connectivity patterns should be dependent on the category being processed (hands or tools). The findings of Study 1 support this idea: the functional connectivity to/from the overlap regions correlates with response preferences in distal regions in a category-specific way. These findings were further developed in Study 2: combining tDCS with a cognitive training task, I explored the possibility of enhancing this connectivity constraint separation effect between hand and tool processing within the same region, by biasing the processing towards one of the categories. On the one hand, results reported in Study 2 corroborate the results from Study 1 – distal effects were found due to the stimulation applied to pMTG/LOTC. On the other hand, results from Study 2 also expand the results from Study 1, allowing for causality inferences that could not been made in Study 1. Specifically, Study 2 shows how distal modulations causally affect local processing: enhancing the processing within pMTG/LOTC impacts neural representations in distal regions. This implies that hand and tool representations in hand and tool-preferring regions are causally dependent on distal computations from pMTG/LOTC.

Overall, our findings demonstrate the importance of distal connectivity patterns in the organization of object knowledge – that is, hand and tool neural representations within local regions are causally modulated by distal processing from the overlap regions.

6.3. Limitations

In both fMRI studies that are part of this thesis, I refer to one of the overlap regions as left pMTG/LOTC. However, this definition does not mean that pMTG and LOTC concern to the same region. The borders of LOTC have been proposed to be the middle portion of MTG (anterior), lateral occipital sulcus (posterior), STS (dorsal), and inferior temporal gyrus (inferior) (Lingnau & Downing, 2015). When identifying the regions-of-interest in fMRI studies, LOTC is usually defined using the peak coordinates next to the lateral occipital sulcus, using different contrasts like objects > scrambled (Hutchison et al., 2014), hands > chairs or tools > chairs (LOTC-hand and LOTC-tool, Bracci et al., 2012; Knights et al., 2021). These subdivisions of LOTC (LOTC-hand and LOTC-tool) are often overlapping with each other (Bracci et al., 2012). pMTG is a region located next to the anterior occipital sulcus and that shows an enhanced activation for tools (Chao et al., 1999; Hutchison et al., 2014; Knights et al., 2021; Martin et al., 1996). Nevertheless, the coordinates reported in studies referring to pMTG are often identical (or very close) to the coordinates of LOTC. This is probably because LOTC-hand and LOTC-tool are anterior subparts of the LOTC, so they are very close to pMTG. Since I did not control for these anatomical boundaries in any of the fMRI studies, it should be noted that in this thesis I do not distinguish between pMTG and LOTC. The same goes for left IPL, since in Study 1 I observed that this region extends into aIPS, and some authors attribute the overlap between hands and tools in the parietal cortex to the IPS (Bracci et al., 2016).

It is also worth to mention that throughout this thesis I have used the terms 'tool' and 'manipulable object' interchangeably and they do not (necessarily) represent the same content. A tool is always a manipulable object, but the opposite is not necessarily true. 'Tools' are manipulable objects that show a strong link between their physical attributes and their function/manipulation (e.g., hammer, scissors). 'Manipulable objects' refer to all objects that can be manipulated and that do not (necessary) show a clear relationship between their physical attributes and their function/manipulation – e.g., lamp, book (Mahon et al., 2007). The findings described in this thesis refer to the specific category of tools and they cannot be generalized to all manipulable objects.

6.4. Future Directions

The empirical studies reported in this thesis allow for a better understanding of the functional relationship between hands and tools, giving an important theoretical contribution to our understanding of the organization of object knowledge in the brain. Nevertheless, these studies also raise new questions that should be taken into consideration in future investigations. In this section, I consider some research ideas that I plan to implement in the future.

Primarily, and because our predictions for Study 2 were not completely met, I think one possible future research direction is to resolve this issue. Results from Study 2 do not show an effect of the hand training task. We put forth two possible reasons for the lack of an effect: 1) the hand task was too complex, and certainly not directed at promoting action processing; and 2) the type of montage chosen for the tDCS could have inhibited social and action representations important for the processing of hands. Based on this, I propose to create a different cognitive task that promotes action processing (e.g., a task where participants watch two videos of pantomimed actions related to the use of tools and then they must decide which video correspond to the correct use) and choose IPL as the target area (for a possible target region and montage see Almeida et al., 2017; Lee et al., 2019; Ruttorf et al., 2019). This new experiment will allow not only to test (again) the separation of the hand processing within an overlap region, but it will also examine the effects of tDCS in a different overlap region (IPL). An alternative possible approach could be to maintain pMTG/LOTC as the target area, but with a different montage that ensures neighboring hand regions are not affected.

Another aspect that I think should be further explored are the temporal dynamics of hand and tool processing. I have used various techniques in this thesis including fMRI, tDCS and even EEG. These different methods provided access to important results at the spatial and temporal level. However, an important step to interpret these results in a broader way, is to combine (in the same study) methods that have high spatial and high temporal resolution. Thus, I think it would be relevant to implement a study where we use both fMRI and EEG. This fMRI/EEG fusion approach (Cichy & Oliva, 2020) would allow us to understand where (fMRI) do the temporal differences (EEG) between hand and tool processing occur. For instance, this could be very useful to investigate if the overlap regions show the same temporal dynamics, or not.

Finally, perceiving hands and tools involves recognizing multiple features important during the action perception and execution. The activity of the motor and somatosensory cortex (during action execution, or observation) causes a desynchronization of the Mu (μ) band, a spontaneous oscillatory human rhythm with a frequency of 8–13 Hz that appears most prominently over the sensorimotor area during a relaxed state. Several EEG studies have been showing that the suppression of this rhythm occurs during the processing of both hands and tools (Kumar et al., 2013; Muthukumaraswamy et al., 2004; Proverbio, 2012), but they have not addressed the possible differences between hands and tools. Particularly, what I want to investigate is if the suppression of μ rhythm occurs at different time points for hands and for tools.

6.5. Conclusion

The work described in this thesis focus on how conceptual knowledge is organized in the brain through the lens of two related categories (hands and tools). Particularly it focuses on how connectivity and temporal contingencies disentangle the neural processing shared by them. The main findings of the current thesis can be summarized in the following points: 1) functional connectivity has a crucial role in shaping the representations within regions that show overlap in neural responses to hands and tools; 2) the separation of the overlapping networks can be achieved by targeting distal connected regions; and 3) temporal dynamics of neural processing also allow for dissociating hand and tool processing.

Overall, the data presented here reflect the emergence of different brain mechanisms dedicated to hand and tool processing. They suggest that regardless of how hands and tools interact, our brain devotes different mechanisms during the processing of the two related categories. Nevertheless, and although all the studies focused on the segregation of hand and tool representations, the functional bonds shared between hands and tools remain clear.

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GENERAL INTRODUCTION AND DISCUSSION

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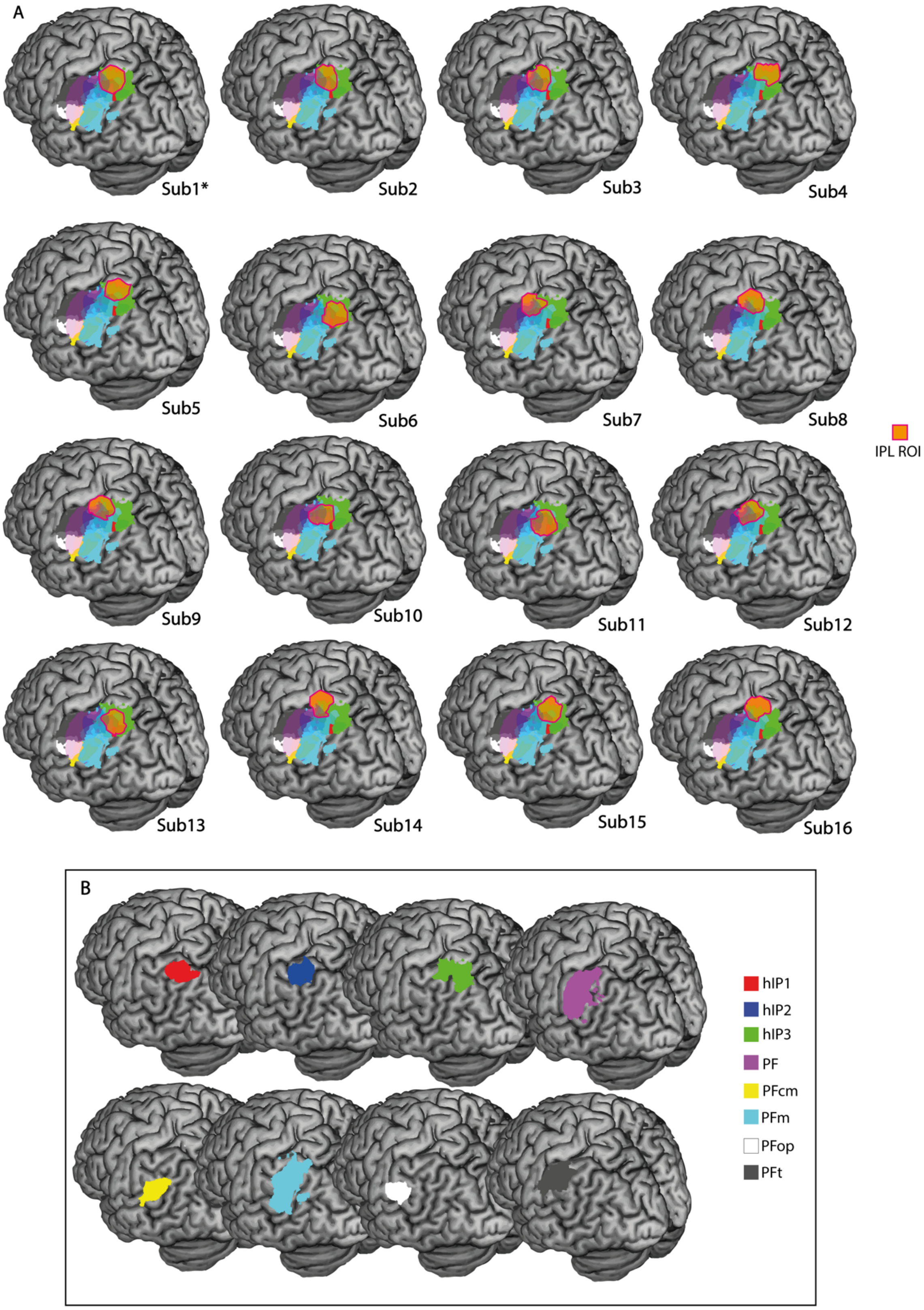
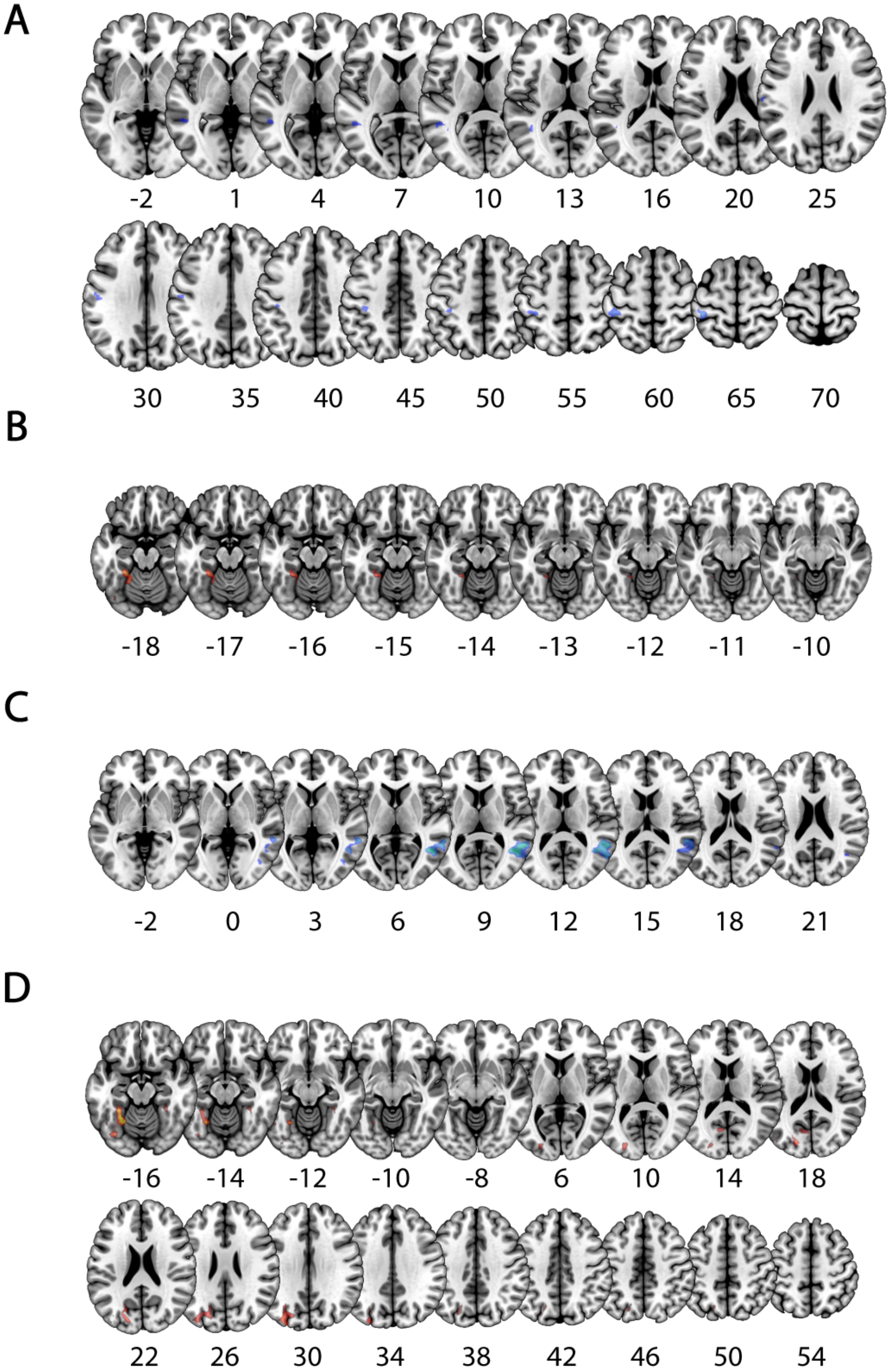
Supplementary Material.

FIGURES



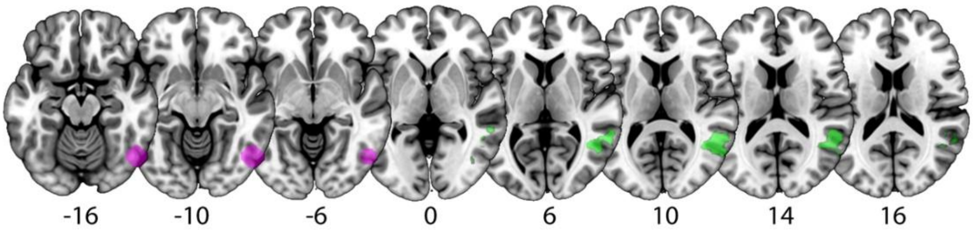
Supplementary Figure 3.1 – Location of the individual IPL/aIPS ROIs.

Supplementary Figure 3.1. (A) Location of the individual IPL/aIPS ROIs overlapped with the parcellations of the IPL (Supramarginal Gyrus) and intraparietal sulcus. **(B)** The different regions/parcel included in the left IPL (Supramarginal Gyrus) and left intraparietal sulcus as proposed in Caspers et al. (2006) and by Choi et al. (2006). *Because subject 1 did not have enough data to define the individual ROIs, we used the group peak to create them.



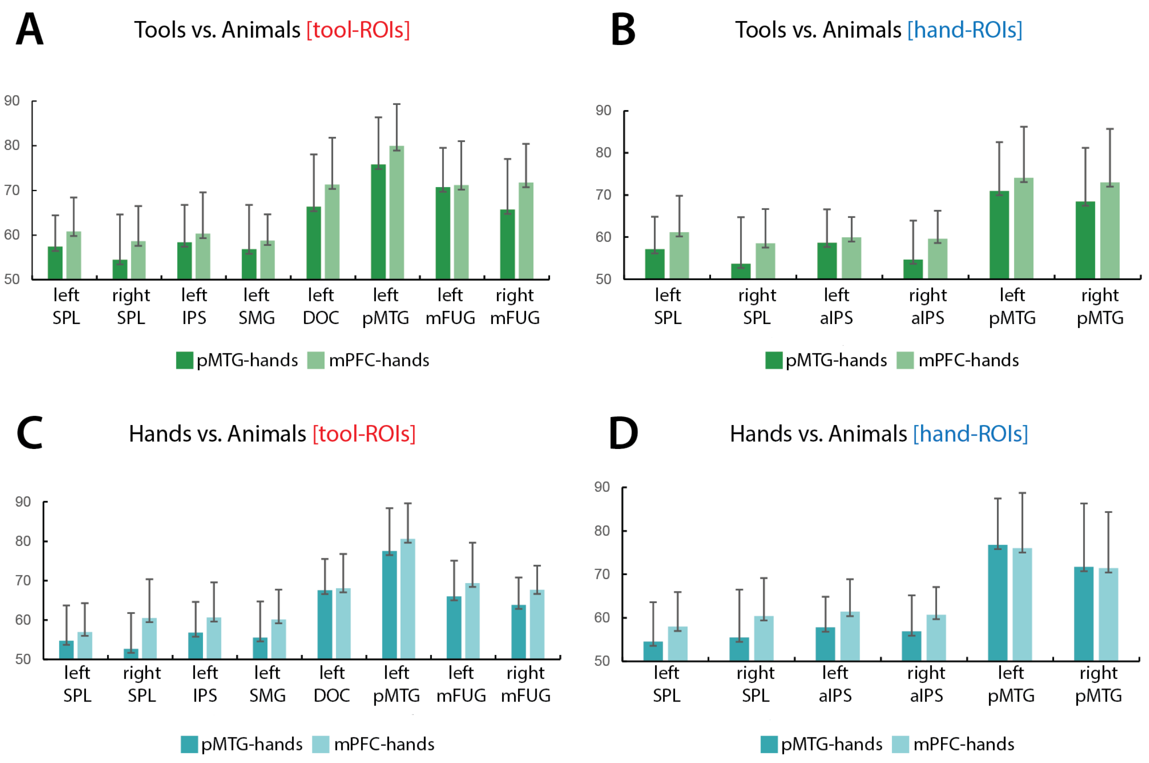
Supplementary Figure 3.2 – Whole-brain searchlight correlation between category-preferences and functional connectivity (volume maps).

Supplementary Figure 3.2. (A) cold colors indicate higher voxel-wise correlations between hand-preferences and functional connectivity to IPL/aIPS (compared to tool-preferences). **(B)** warm colors indicate higher voxel-wise correlations between tool-preferences and functional connectivity to IPL/aIPS (compared to hand-preferences). **(C)** cold colors indicate higher voxel-wise correlations between hand-preferences and functional connectivity to pMTG/LOTC (compared to tool-preferences). **(D)** warm colors indicate higher voxel-wise correlations between tool-preferences and functional connectivity to pMTG/LOTC (compared to hand-preferences).



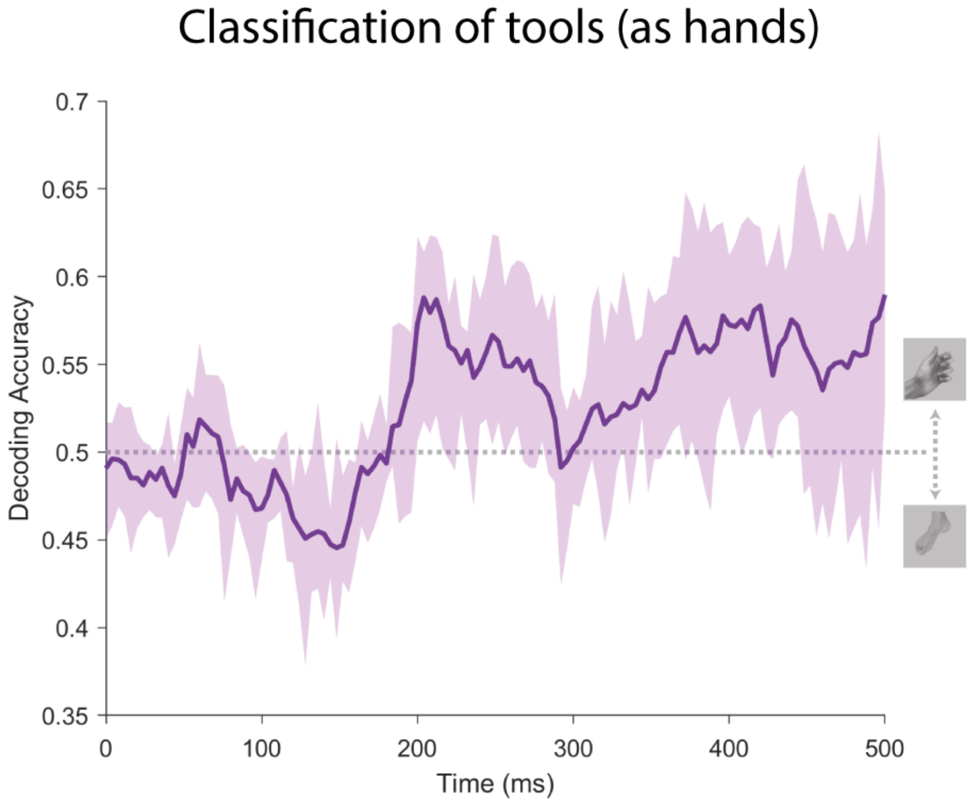
Supplementary Figure 3.3 – Location of the right STS cluster from the searchlight in relation to tool and hand right pMTG/LOTC.

Supplementary Figure 3.3. The right STS cluster (green) obtained in the whole-brain searchlight analysis for the correlation between connectivity coming from the left pMTG/LOTC and hand-preferences does not overlap with a functionally defined right pMTG/LOTC hand/tool overlap region (purple).



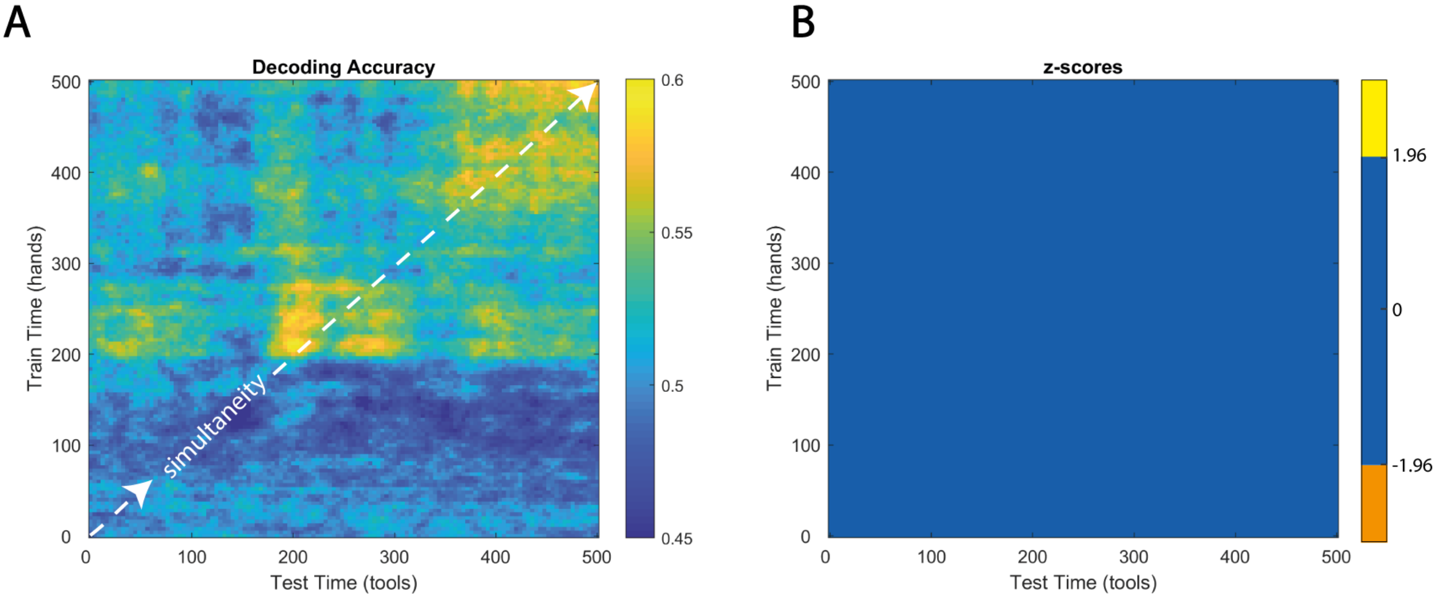
Supplementary Figure 4.1 – ROI-specific MVPA results (hands training session).

Supplementary Figure 4.1. A comparison of the classification accuracy (percentage) between pMTG$_{\text{hands}}$ and mPFC$_{\text{hands}}$ for **(A)** tools vs. animals in each region identified as a tool ROI, **(B)** tools vs. animals in each region identified as a hand ROI, **(C)** hands vs. animals in each region identified as a tool ROI, and **(D)** hands vs. animals in each region identified as a hand ROI. P-values are FDR corrected for 8 tests in tool-ROIs and for 6 tests when analyzing hand-ROIs and show no significant results (all adjusted *p* values > .1).



Supplementary Figure 5.1 – Cross-decoding accuracy results (using feet as control category).

Supplementary Figure 5.1. Decoding accuracy when the classifier trained on hands vs. feet was then tested to classify tools. No significant effects were observed in this analysis (|z| < 1.96, cluster-wise corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016)).



Supplementary Figure 5.2 – Results from the Time Generalization Approach

(using feet as control category).

Supplementary Figure 5.2. (A) Decoding accuracy across time when the classifier trained on hands vs. feet and was then tested on tools. **(B)** No significant effects were observed in this analysis (|z| < 1.96, cluster-wise corrected for multiple comparisons using TFCE Monte Carlo simulation with 10,000 iterations (Oosterhof et al., 2016)).

Supplementary Material.

TABLES

Supplementary Table 3.1 – Overlap between each individual IPL/aIPS ROI.

	a) intraparietal sulcus			**b) inferior parietal lobule (Supramarginal Gyrus)**				
	hIP1	**hIP2**	**hIP3**	**PF**	**PFcm**	**PFm**	**PFop**	**Pft**
Sub1	x	x	x	x		x		
Sub2	x	x	x	x		x		
Sub3	x	x	x	x		x		
Sub4	x		x			x		
Sub5	x	x	x			x		
Sub6	x	x	x			x		
Sub7	x	x	x	x		x		x
Sub8	x	x	x	x		x		
Sub9	x	x	x	x		x		
Sub10	x	x	x	x		x		x
Sub11	x	x	x	x				
Sub12	x	x	x	x		x		x
Sub13	x	x	x			x		
Sub14	x	x	x	x		x		
Sub15	x	x	x			x		
Sub16	x	x	x	x		x		

(a) *Parcellations of the intraparietal sulcus proposed by Choi et al. (2006);* ***(b)*** *Parcellations proposed by Caspers et al. (2006) of the left inferior parietal lobule (Supramarginal Gyrus).*