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**Neuronalne podstawy planowania różnych interakcji  
z narzędziami: badanie z wykorzystaniem funkcjonalnego  
rezonansu magnetycznego**

**Neural underpinnings of planning different interactions  
with tools: a functional magnetic resonance imaging study**

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## Introduction

(...) the ultimate reason we have brains is not so much to perceive the world as it is to act upon it. (Goodale, Króliczak, & Westwood, 2005, p. 269)

In almost every moment of our daily activities we are surrounded by handy, manipulable objects. They enhance our physical capabilities, like pliers strengthening the power and precision of a grip, provide us with new skills, like scissors cutting neatly a sheet of paper, or serve as essential means of interacting with other objects, like a key opening a door lock. Most of these objects are associated with multiple ways of handling, depending on the goal of the intended action. When grasping a corkscrew in order to pull a cork from a bottle, we would adopt a specific, function-appropriate hand posture, that would not necessarily be our first choice when lifting the same tool from a table and putting it back to a drawer. Indeed, the mere goal of our action seems to affect the processing of relevant visual features of the target object, as well as the selection of information that need to be retrieved from memory and implemented during the preparation of the motor plan. Surprisingly, although the neural underpinnings of both functional interactions with tools and a variety of actions directed at non-functional objects are relatively well understood, little is still known about the involvement of parieto-frontal action networks in the control of differently motivated actions directed at common tools. Hence, in the present study I set out to investigate the neural bases of preparing disparate functional and non-functional goal-oriented interactions involving familiar manipulable objects.

The first chapter of this thesis will focus on providing an up-to-date overview of research on cognitive and neural processes involved in different interactions with tools and will conclude with a presentation of the current project. In the second chapter, a detailed description of the experimental materials and methods will be presented. The third and fourth chapters provide descriptions and discussions of the results of two functional magnetic resonance imaging experiments conducted in the current project. The last, fifth chapter is devoted to a general discussion of the obtained results in the light of hypotheses put forward in the first chapter.

# Chapter 1. Background of the study

Consecutive sections of this chapter focus on a brief summary of the research on the neural basis of tool use skills and the differences between functional and structure-based object-directed actions. Subsequently, a review of recent behavioral, neuropsychological, and neuroimaging studies that focused on different goal-oriented interactions involving tools is provided. The last part of the chapter is devoted to the presentation of the current project.

## 1.1. Neural underpinnings of tool use skills

The most stereotyped and well-learned manual interactions with tools involve their functional use. In comparison to actions directed at simple objects with no built-in functional identity, skillful use of manufactured tools puts much greater demands on the brain's systems underlying the visuomotor transformations essential for action control. In order to acquire and manipulate a tool in a functional way, the brain needs to integrate, among others, the perceived visual structure and location of the object with the stored knowledge of its function and the corresponding learned motor routines of function-appropriate handling. Today, due to a large number of neuropsychological and functional neuroimaging studies that were conducted in the last two decades and focused on how the brain mediates the control of tool use skills, the neural bases of these processes are relatively well understood.

A crucial contribution to this knowledge was provided by research on planning and/or execution of tool use pantomimes (Bohlhalter et al., 2009; Choi et al., 2001; Fridman et al., 2006; Johnson-Frey, Newman-Norlund, & Grafton, 2005; Króliczak & Frey, 2009; Rumiati et al., 2004; Vingerhoets et al., 2012), planning and/or execution of real tool use (Brandi, Wohlschläger, Sorg, & Hermsdörfer, 2014; Hermsdörfer, Terlinden, Mühlau, Goldenberg, & Wohlschläger, 2007; Tsuda et al., 2009; Valyear, Gallivan, McLean, & Culham, 2012), imagined tool use (Imazu, Sugio, Tanaka, & Inui, 2007; Moll et al., 2000; Wadsworth & Kana, 2011), and recognition of tool use gestures (Buxbaum, Kyle, & Menon, 2005; Tarhan, Watson, & Buxbaum, 2015; Villarreal et al., 2008). Taken together, the results of these studies point to a distributed, predominantly left-lateralized network of frontal, parietal, and occipito-temporal areas as the cortical locus of the control of learned acts of transitive (tool-related) actions (for reviews, see Ishibashi, Pobric, Saito, & Ralph, 2016; Johnson-Frey, 2004; Lewis, 2006; Orban & Caruana, 2014; Reynaud, Lesourd, Navarro, & Osiurak, 2016; Vingerhoets, 2014). As the network has been also implicated in the processing of other

meaningful hand movements, such as intransitive (communicative) gestures (Króliczak & Frey, 2009; Króliczak, Piper, & Frey, 2016; Kubiak & Króliczak, 2016; Villarreal et al., 2008), it was termed the praxis representation network (PRN; Frey, 2008).

The principal role of PRN is to dynamically integrate and transform multiple components of action distributed across a set of interconnected brain areas into purposeful acts of praxis (Frey, 2007, 2008; Króliczak & Frey, 2009). Lateral occipito-temporal cortex (LOTC), including the caudal part of middle/inferior temporal gyri (cMTG/cITG), provides conceptual knowledge of objects, their visual features, and associated meaningful actions (Almeida, Fintzi, & Mahon, 2013; Andres, Pelgrims, & Olivier, 2013; Beauchamp & Martin, 2007; Goldenberg & Spatt, 2009; Vannuscorps, Dricot, & Pillon, 2016). This knowledge, together with contextual inputs specified by rostral middle frontal gyrus (rMFG; Bach, Peelen, & Tipper, 2010; Buccino et al., 2004), informs the selection of goal-appropriate motor response. Anterior divisions of intraparietal sulcus and supramarginal gyrus (aIPS/aSMG) are thought to calculate/store the representations of skilled hand postures (see the next section of this Chapter), but also to integrate the conceptual and motor representations into meaningful actions (Buxbaum, Kyle, Grossman, & Coslett, 2007; Kristensen, Garcea, Mahon, & Almeida, 2016; Króliczak et al., 2016; Randerath, Goldenberg, Spijkers, Li, & Hermsdörfer, 2010). Sensorimotor computations underlying the planning, programming, and execution of these acts are performed by ventral and dorsal premotor cortices (PMv and PMd, respectively), as well as the caudal superior parietal lobule (Cavina-Pratesi et al., 2010; Davare, Andres, Cosnard, Thonnard, & Olivier, 2006; Króliczak, McAdam, Quinlan, & Culham, 2008). Such a division of labor corresponds intuitively with the hypothesis of two functionally and neuroanatomically distinct streams of visual processing coexisting in the human brain. Both streams emerge from primary visual cortex but project to different cortical areas in the temporal and parietal lobes. While the ventral stream runs to the inferior temporal cortex and extracts the relevant visual information to construct and maintain a detailed perceptual representation of the environment and the objects within it, the dorsal stream projects to the posterior parietal cortex and uses the same visual input for the automatic control of skilled actions regardless of object function (Goodale et al., 2005; Goodale & Milner, 1992; Milner & Goodale, 2008). Importantly, close cooperation of both streams within the PRN is necessary on multiple stages of action preparation and execution for the successful performance of such complex tasks as grasping and using familiar tools (Frey, 2007; Króliczak, Cavina-Pratesi, & Large, 2012; van Polanen & Davare, 2015). For instance, the processing of visual information within the dorsal stream areas has been shown to influence object recognition by providing information about its motor-relevant features, i.e.,

whether or not the seen object is graspable and how it may be grasped given its current spatial properties such as location and orientation of the handle (Almeida, Mahon, & Caramazza, 2010). Computations carried by the ventral stream areas, on the other hand, have been observed to support the identification of errors during functional actions with objects (Mizelle, Kelly, & Wheaton, 2013), and brain damage restricted to the ventral stream may result in inappropriate grasping of familiar objects presented in non-canonical orientations (Carey, Harvey, & Milner, 1996; see also: Dijkerman, McIntosh, Schindler, Nijboer, & Milner, 2009; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000).

In sum, a well-studied network of left-hemispheric frontal, parietal, and occipito-temporal areas – the praxis representation network – has been indicated in many tasks related to the processing of meaningful hand movements, including the functional use of familiar tools. The main task of PRN is to integrate distributed object- and action-related information into a coherent motor plan that guides the acting hand in line with the prospective action goal.

## **1.2. Function- and structure-based object-oriented actions**

Kinematic studies have shown that the goal of the grasping agent, i.e., the action that he or she intends to accomplish subsequent to object contact, influences the macroscopic features of manual actions such as movement parameters of reaching (Armbrüster & Spijkers, 2006; Johnson-Frey, McCarty, & Keen, 2004; Marteniuk, MacKenzie, Jeannerod, Athenes, & Dugas, 1987) and hand pre-shaping during grasping (Ansuini, Giosa, Turella, Altoè, & Castiello, 2008; Ansuini, Santello, Massaccesi, & Castiello, 2006). The influence of action goal on early stages of movement is so prepotent, that even if the initial hand posture adopted during the first contact with object is uncomfortable or biomechanically awkward but offers a goal-appropriate final grasp after a simple wrist rotation, it is usually chosen over the posture that is initially comfortable, but requires further adjustments in order to complete the intended action (Rosenbaum & Jorgensen, 1992; Seegelke, Hughes, Knoblauch, & Schack, 2013; Zhang & Rosenbaum, 2008). These observations are important for the current project because the skilled and natural action of using a tool in accordance with its function is but one of numerous ways in which we interact with manipulable objects. On different occasions, we may grasp this same tool and hand it to another person or simply displace the object as a transient obstacle<sup>1</sup>. Taking into account such disparate action goals opens a new avenue

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<sup>1</sup> Yet another kind of interaction involving a tool is manipulating it in a non-conventional way, e.g., when lacking a hammer and using pliers instead to knock a nail. Actions of this kind were nevertheless outside the scope of the current project.

for investigations of neural and cognitive processes engaged in performance of differently motivated hand-object interactions.

It has been recently proposed by several researchers that different manual actions directed at tools are subserved by functionally and neuroanatomically distinct substreams/action systems rooted in the dorsal stream (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Daprati & Sirigu, 2006; Johnson & Grafton, 2003; Pisella, Binkofski, Lasek, Toni, & Rossetti, 2006; Vingerhoets, Acke, Vandemaele, & Achten, 2009). In agreement with the two visual-streams proposal, wherein the dorsal stream provided a dynamic on-line control of motor acts, the role of bilateral dorso-dorsal stream is mediating the visuomotor coding of object-directed hand movements on the basis of currently available information, i.e., the visually encoded structural (shape, size) and spatial (orientation, location) properties of an object. Perceptual processing of these features is necessary, and in some cases may be sufficient, to perform structure-based interactions with tools, such as reaching towards an object, grasping it with a stable grip, and moving it to a chosen location.

The left-lateralized ventro-dorsal stream, on the other hand, is devoted to skillful function-based manipulation of objects that are associated with long-term representations of object use. A crucial node of the ventro-dorsal stream – the supramarginal gyrus of the left inferior parietal lobule (IPL) – has been associated with the storage and retrieval of tool-related manipulation knowledge in the form of functional hand postures (for evidence from neuroimaging studies, see: Canessa et al., 2008; Elk, 2014; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007; Vingerhoets, 2008; for evidence from virtual lesion studies, see: Andres, Pelgrims, & Olivier, 2013; Ishibashi, Lambon Ralph, Saito, & Pobric, 2011; Pelgrims, Olivier, & Andres, 2011). Direct damage and/or impaired access to these representations after left IPL lesions are indicated as the possible causes of deficits observed in ideomotor apraxia (Buxbaum et al., 2007, 2005; Buxbaum & Saffran, 2002; Niessen, Fink, & Weiss, 2014), wherein the performance of skilled, learned movements, such as pantomiming the functional use of tools, is degraded despite the spared sensory and lower-level motor functions (Haaland, Harrington, & Knight, 2000; Leiguarda & Marsden, 2000). Indeed, apraxic patients have been shown to abnormally rely on the visual object structure (i.e., the features processed by the dorso-dorsal stream) while learning hand postures associated with the use of novel tools (Barde, Buxbaum, & Moll, 2007). An alternative hypothesis concerning the role of the left IPL in tool-related actions proposes that this area supports primarily the ability to reason about the physical properties of objects, which is supposed to be the reason why some apraxic patients demonstrate impaired ability to infer function from the structure of novel or

unfamiliar tools (Goldenberg & Hagmann, 1998; Goldenberg & Spatt, 2009; Osiurak, 2013; Osiurak, Jarry, & Le Gall, 2011; Reynaud et al., 2016).

On the cognitive level, action representations associated with manipulable objects – their *affordances* (Gibson, 1979; Kourtis & Vingerhoets, 2015; Michałowski & Króliczak, 2015; Mizelle et al., 2013) – have been shown to affect the perceptual processing of tools (Bub & Masson, 2012; Bub, Masson, & Cree, 2008; Lee, Middleton, Mirman, Kalénine, & Buxbaum, 2012). For example, Bub et al. (2008) have demonstrated that viewing pictures of familiar tools as primes was associated with activation of the related functional and structural grasp representations. When they were in conflict with the required manual response, i.e., grasping differently shaped elements of a neutral response device, participants' performance was degraded. Importantly, such a conflict may be induced during the interaction with multiple common tools that are associated with different manual responses depending on action goal (recall the example of a corkscrew from Introduction). Within-object conflict of competing responses has been shown to interfere with planning tool-directed actions (Jax & Buxbaum, 2010), and to affect perceptual judgements on objects located in peripersonal space (Kalénine, Wamain, Decroix, & Coello, 2016). Some researchers have also suggested that a defect in a brain mechanism responsible for resolving similar conflicts may play a role in apraxic disorders (Jax & Buxbaum, 2013; Rounis & Humphreys, 2015).

Along with the research on conflicting affordances, there has been a related debate on whether or not the action representations associated with tools are evoked automatically even if task-irrelevant. Although there is a plethora of studies suggesting that the answer to this question is positive (Ellis & Tucker, 2000; Grèzes & Decety, 2002; Grèzes, Tucker, Armony, Ellis, & Passingham, 2003; Proverbio, 2012; Tucker & Ellis, 2001), there is also a growing body of evidence for the hypothesis that the selection of a particular subset of object-related action features that are evoked depends on the context of the action in which the object is perceived, the task to be performed, and/or the goal of the acting person (Girardi, Lindemann, & Bekkering, 2010; Kalénine, Shapiro, Flumini, Borghi, & Buxbaum, 2014; Pellicano, Iani, Borghi, Rubichi, & Nicoletti, 2010; Randerath, Martin, & Frey, 2013; Rey, Roche, Versace, & Chainay, 2015).

An attempt to reconcile both perspectives – the neural and the cognitive one – can be found in the works of Borghi and Riggio (2009, 2015), who proposed to distinguish affordances into *stable* and *variable*. In this view, stable affordances are related to invariant object properties, such as the hand posture appropriate for functional use of tools, and are mediated by the ventro-dorsal stream areas. Variable affordances, on the other hand, are concerned with temporary object characteristics, such as the current location of the object and

the orientation of its graspable part. Extracting this information from the visual input is associated with dorso-dorsal stream activity (Sakreida et al., 2016). The authors suggested that although manipulable objects indeed do potentiate multiple motor responses towards them, the action that is finally selected depends crucially on behavioral goals of the actor (Borghetti & Riggio, 2015; see also: Cisek & Kalaska, 2010).

In conclusion, numerous objects that we encounter during our daily activities are associated with disparate manipulations contingent on our goals. These action goals seem to affect the selection of object features that would be incorporated in the goal-appropriate motor plan. Different object-oriented interactions are thought to be mediated by distinct pathways of the dorsal processing stream, with dorso-dorsal stream being associated with actions depending on object structure (linked to variable affordances), and ventro-dorsal stream associated with overlearned, skillful object manipulations (related to stable affordances).

### **1.3. Previous research on cognitive and neural processes involved in different interactions with tools**

In what follows, I present an overview of the recent studies that focused on different manual actions undertaken with functional objects, and the conclusions relevant for the current study.

#### **1.3.1. Behavioral studies**

Behavioral studies wherein participants performed different manual actions with tools focused primarily on the influence of long-term object-related representations (such as knowledge of the proper functional hand posture or the social context of handing an object to a different person) on the planning and execution of motor responses directed at tools, as measured by the difference in response initiation times associated with disparate actions. For instance, in the study by Jax and Buxbaum (2010) participants positioned their hands on familiar tools with one of the two intentions: to functionally use them or to pass them to another person. The task consisted exclusively of the reaching and grasping phase of the movement, with no subsequent action required. The authors reported that initiating *grasp-to-use* actions took significantly longer than initiating *grasp-to-pass* actions. Importantly, similar results were observed by Valyear, Chapman, Gallivan, Mark, and Culham (2011) and Squires, Macdonald, Culham, and Snow (2015) in priming studies where volunteers grasped and actually demonstrated the typical use of real tools or simply grasped and transported them to target locations. The authors associated longer initiation times for function-based actions with the

need to retrieve and incorporate relevant conceptual information (i.e., the manipulation knowledge) into the motor plan.

Nevertheless, structure-based actions may also be supported by stored object representations, and in the face of certain task requirements, the aforementioned pattern of differences in initiation times can be reversed. As shown by Osiurak, Roche, Ramone, and Chainay (2013), when participants had to grasp a familiar tool and actually use it or hand it to the experimenter, *grasp-and-pass* actions were initiated slower than *grasp-and-use* actions. According to the authors, passing an object to another person or transporting it to a certain location may be associated with activation of long-term social and/or object representations in order to determine (prior to movement onset) whether or not the receiver's hand/surface would provide appropriate support for the transmitted object. In a more recent study, Chainay, Brüers, Martin, and Osiurak (2014) examined the influence of object weight and the type of task to be performed (reaching and grasping objects as if to use or transport them vs. real using and transporting) on action planning. While there were no significant differences in initiation times between use and transport tasks or heavy and light objects when the action was only pretended, initiating actual lift and transport actions took faster than initiating lift and use actions, and real actions directed at lighter objects were started significantly slower than actions concerning heavier objects. Such an outcome suggests that potentially simpler responses to overall object structure may also require an access to the long-term object representations, but this effect may be observed only under specific task requirements concerning action execution.

Together, the results of the studies reviewed above converge on the notion that both the goal of the acting person and the context in which the action is performed affect the extent of conceptual and/or motor representations that are retrieved and incorporated in the motor plan.

### **1.3.2. Neuropsychological studies**

Case studies in neuropsychological literature have provided crucial insights into the organization of different object-oriented action representations in the human brain by demonstrating that both function-based and structure-based grasping actions may be selectively impaired in patients with bilateral or exclusively left-hemisphere damage (Daprati & Sirigu, 2006). Jeannerod, Decety, and Michel (1994) reported a patient with bilateral posterior parietal lesion, whose performance in a grasping task differed depending on the type of object to be grasped. Namely, her grasping movements were severely impaired when

directed at simple plastic cylinders for which no conceptual knowledge to support the action guidance was available, but improved when the cylinders were replaced with familiar objects. Conversely, the apraxic patient studied by Sirigu et al. (1995) was able to correctly reach and grasp the presented objects in order to hand them to the examiner, but failed to grasp these same objects in a way appropriate for their subsequent use, irrespective of the tested hand. These cases of selective deficits indicate that the neural bases of processes specifically engaged in functional interactions involving tools are anatomically distinct from that of actions based solely on object structure.

Another line of research investigated the ability of left brain-damaged (LBD) patients to recognize and/or produce goal-appropriate hand postures or actions. A study on a group of nine apraxic patients with left inferior parietal lesions revealed their impaired ability to recognize and produce functional hand postures associated with the use of familiar objects, in contrast to normal performance in the case of postures appropriate to interaction with novel objects for which only the visual information about object structure was available (Buxbaum, Sirigu, Schwartz, & Klatzky, 2003). This result is consistent with the putative role of the left IPL in storing learned associations between objects and hand postures appropriate for their skillful usage.

In a study on grip selection by Osiurak et al. (2008), left and right brain-damaged patients had to perform two grasping-related tasks: grasp a simple dowel and transport it to one of the target locations (two final postures – comfortable and uncomfortable – were distinguished on the basis of the position of the thumb on the dowel) and grasp a familiar tool to demonstrate its functional usage with a provided recipient (again, two postures – thumb toward the functional part of the tool and thumb away from the functional part – were distinguished). Both patient groups differed from the control group in the *grasp-and-transport* task by selecting and performing significantly less comfortable final postures. Conversely, in the tool demonstration task, a vast majority of patients from both groups executed a correct, *thumb-toward-the-functional-part* grasp. Importantly, there was no significant correlation between the scores obtained in either task and more general praxis tests (e.g., tool use pantomime) administered to all the participants. Such a pattern of results is consistent with the notion that functional grasp and tool use representations may be organized independently in the brain (Randerath et al., 2010; Randerath, Li, Goldenberg, & Hermsdörfer, 2009; cf. Przybylski & Króliczak, 2017). However, because of the fact that the *grasp-and-transport* actions were not directed at tools, but simple dowels, and the task itself tested primarily the ability to anticipate the most comfortable hand posture at the end of the movement, these

results did not shed any new light on the issue of neural mechanisms engaged in performing differently motivated actions with functional objects.

In a similar study by Randerath et al. (2009), the dowels were replaced by familiar tools and the task was to grasp an object (in a goal-appropriate manner) by the handle oriented towards or away from the participant and either transport it to the nearby container or demonstrate its functional usage. In the latter task, when the handle was oriented away and a substantial hand rotation was required, LBD patients with moderate to severe apraxia have been found to produce significantly less function-appropriate (rotated) grasps than healthy controls, LBD-patients without apraxia, or right brain damage patients. Importantly, when the task was to grasp an object and transport it to the container, the proportion of function- and structure-based grasps did not differ significantly between the groups. A follow-up study revealed that the production of inappropriate hand posture in a tool-use demonstration task was associated with lesions in the left angular (ANG) and inferior frontal (IFG) gyri (Randerath et al., 2010).

Together, the results of the abovementioned studies indicate that multiple cognitive and/or sensorimotor processes are engaged in the retrieval, preparation, and execution of disparate interactions involving tools, and many of these processes are associated with separable neural loci.

### **1.3.3. Neuroimaging studies of healthy participants**

Most functional magnetic resonance imaging (fMRI) reports concerning tool-directed manual skills have focused primarily on functional interactions (Chen, Garcea, & Mahon, 2015; Hermsdörfer et al., 2007; Króliczak & Frey, 2009; Przybylski & Króliczak, 2017; Valyear et al., 2012; Vingerhoets et al., 2011; but cf. Brandi et al., 2014). When actions motivated by disparate goals were taken into account, they usually involved non-functional objects (Cavina-Pratesi et al., 2010; Gallivan, Johnsrude, & Randall Flanagan, 2015; Gallivan, McLean, Flanagan, & Culham, 2013; Króliczak et al., 2008; Monaco et al., 2011). So far, only a handful of neuroimaging studies investigated familiar tools and different actions oriented towards them.

Buxbaum, Kyle, Tang, & Detre (2006) examined the neural underpinnings of knowledge of hand postures appropriate for object use and object transport. It was predicted that the recognition of functional hand postures (especially those that are devoid of the prehensile component, such as palming or poking) would specifically engage the left IPL, relative to the prehensile postures programmed solely on the basis of overall object structure.

Compared to trials in which participants made decisions about transport-appropriate grasps, judging use-appropriate non-prehensile hand postures was associated with significantly greater activation in the left IFG/MFG, STG/MTG, and IPL. No differences were found between prehensile use-appropriate postures and transport-appropriate postures. Nevertheless, it remains an open question whether such a pattern of activity would also be revealed if participants had to actually engage in the preparation and execution of both types of actions.

Vingerhoets et al. (2009) investigated the influence of distinct motor goals (intentions) on imagined actions directed at familiar tools, unfamiliar tools, and graspable neutral shapes. Here, the task was to imagine performing one of the four actions with the dominant (right) hand: (1) pointing to an object, (2) grasping an object, moving it, and putting it back down, (3) grasping a tool with an intention to use it, or (4) grasping a tool and using it. The comparison of crucial importance for the present overview revealed that relative to grasping and moving, grasping and using familiar tools significantly increased activity in the left SPL and IPL. Similarly to the study by Buxbaum et al. (2006), an unresolved issue concerns the role of these areas in preparing such disparate actions for their subsequent execution.

Valyear et al. (2012) utilized an fMRI repetition suppression method to investigate changes in neural activity associated with the preparation and demonstration of familiar (tool-specific) vs. arbitrary (non-functional) actions directed at common tools. The reduction of BOLD signal specific to functional actions was observed in the left PMv, PMd, and aIPS, as well as in the right SPL. These results indicated that functional affordances associated with the visual features of well-known objects are represented within the network of areas related to tool use manual skills. The remaining question is whether a similar effect would be detected if the control task involved non-arbitrary, well-learned action that is not use-related.

In a recent fMRI study on real interactions with objects, Brandi et al. (2014) instructed participants to prepare and/or execute functional *grasp-and-use* or structural *grasp-and-transport* actions directed at real tools and neutral bars. Both dominant right and non-dominant left hands were tested. The authors reported increased activity in the left PMd, LOC, MTG, and bilateral SPL, when participants executed *grasp-and-use* actions relative to *grasp-and-transport* actions (irrespective of the type of the target object), with clusters of significant activity in the left PMd and SPL found also in the planning phase of the movement ( $p < 0.001$ , uncorrected). Importantly, clusters within the left PMv, SMG, MTG, postcentral gyrus, middle occipital gyrus, and medial superior occipital gyrus exhibited significantly greater activation for functional tool use actions than for functional actions with neutral bars (defined as grasping them and placing one of their ends in a special opening) or transport actions with either type of object. However, as the data for the dominant right and non-

dominant left hand were combined, the question of hand-dependent engagement of the identified areas in tool-directed actions has not been posed. Moreover, as the study considered real actions with recipient objects provided, the need for the retrieval of stored action representations to inform the motor plan was limited.

In sum, although both behavioral and neuroscientific studies indicate that the intention to properly use, transmit, or displace a tool may engage different mechanisms in the brain, no study to date has directly compared activation patterns associated with planning tool-oriented actions motivated by disparate functional and non-functional goals.

#### **1.4. Current project**

This study aimed to fill the abovementioned gap by examining the modulations of cortical neural activity related to distinct interactions with common tools contingent on action goals. To this end, functional magnetic resonance imaging (fMRI) was used to measure the blood oxygen level dependent (BOLD) signal changes associated with planning and the subsequent execution of pantomimed reaching and/or grasping movements directed at tools with different intentions in mind.

As each of the investigated actions was undertaken towards the same set of familiar tools, the stimuli were presented in non-canonical orientations (with the functional part of the tool pointing towards the participant) in order to ensure that different action goals would be coupled with distinct biomechanical demands for grasp kinematics. An additional condition wherein tools were presented in canonical orientations and required to be grasped in a functional way was introduced to isolate the rotation-related activity, and to compare grasps with similar kinematic demands guided by different goals.

To isolate the network or areas engaged primarily in preparing the hand posture component of the action, and not the reach/arm transport component, a control condition requiring participants to reach towards an object in order to move it with the back of the hand was introduced.

To test the influence of action goal on the preparation of the corresponding motor plan instead of explicitly indicating the appropriate hand posture and the precise positioning of fingers on the to-be-grasped object (cf. Makuuchi, Someya, Ogawa, & Takayama, 2012), the intention cue was each time presented before the target stimulus. This way, while the goal of the action was set externally, the motor plan for each particular trial had to be generated internally (Ariani, Wurm, & Lingnau, 2015) and the visual attention of participants was guided to the action-relevant visual features of target objects.

Finally, to test whether or not the same network is involved in preparing tool-directed grasps irrespective of the hand involved, both the dominant right and the non-dominant left hand were examined (cf. Króliczak & Frey, 2009; Króliczak et al., 2016; Przybylski & Króliczak, 2017).

Based on earlier studies I expected that:

**Hypothesis 1:** Compared to *reach-and-move* actions, planning both functional (i.e., *grasp-to-use*) and structural (i.e., *grasp-to-pass*) actions would involve the left-lateralized praxis representation network (Frey, 2008; Marangon, Jacobs, & Frey, 2011; Przybylski & Króliczak, 2017).

**Hypothesis 2:** A subset of areas within the PRN – namely, the areas of the ventro-dorsal stream: the inferior parietal, ventral premotor, and middle lateral prefrontal cortices – would be invoked more in the planning of functional as compared to structural grasps of tools (Brandi et al., 2014; Buxbaum et al., 2006; Króliczak & Frey, 2009; Vingerhoets et al., 2009).

**Hypothesis 3:** The left-lateralized PRN activity associated with planning function- as compared to structure-based grasps would be very similar independent of the tested hand (Johnson-Frey et al., 2005; Króliczak & Frey, 2009; Przybylski & Króliczak, 2017; Vingerhoets et al., 2012).

## **Chapter 2. Materials and methods**

### **2.1. Participants**

Twenty healthy adult individuals (age range = 20-29, mean age = 24.7, 10 women) with no history of neurological or psychiatric disorders participated in two fMRI sessions. All participants had normal or corrected-to-normal visual acuity and were strongly right-handed, as determined by the revised version of the Edinburgh Handedness Inventory (mean Laterality Quotient = 96.6,  $SD = 9.2$ ; Dragovic, 2004; Oldfield, 1971). An informed written consent was obtained from each participant before testing. At study conclusion, they were all compensated financially for their time and efforts, and debriefed. The study was approved by the Bioethics Committee at the Poznan University of Medical Sciences and was carried out in accordance with the principles of the 2013 WMA Declaration of Helsinki.

### **2.2. Setup and apparatus**

Participants were positioned head first and supine in the magnet bore with both their arms laid alongside the body. A pair of MRI-compatible two-button response devices (Lumina LU400-PAIR manufactured by Cedrus, San Pedro, CA, USA) was attached to the scanner table with Velcro stripes, one response pad on each side of the body. To reduce scanner noise, participants were provided with headphones. Head movements were restricted by fixing the head in place with foam cushions. Stimulus presentation and response recording were controlled by SuperLab ver. 4.5.2 software (Cedrus, San Pedro, CA, USA) digitally synchronized with the MRI scanner. The stimuli were projected onto a 32-inch NordicNeuroLab LCD monitor (NordicNeuroLab, Bergen, Norway) positioned at the back of the scanner and viewed via a tilted mirror attached to the head coil.

### **2.3. Main experiments**

Every participant took part in two separate experiments on consecutive days; one testing the dominant right hand, and the other testing the non-dominant left hand. Even though the order of the tested hands was counterbalanced across participants, including gender, the experiment testing the right hand will be nevertheless referred to as Experiment 1, and the experiment testing the left hand as Experiment 2.

### 2.3.1. Stimuli

The stimuli consisted of 72 high-resolution, greyscale photos of 12 different graspable common objects such as mechanical tools, garden implements, office or kitchen utensils, and personal care items. Each object was photographed with a Sony DSC-H50 digital camera on a white background, in six different orientations (i.e., 0, 45, 135, 180, 225, and 315 degrees), and presented during the experiment in its foreshortened view, emulating the perspective of a person standing by the table on which the tool was placed. Examples of the objects used in this study are presented in **Figure 2.1**, and a list of all the objects can be found in the Appendix.



**Figure 2.1. Examples of stimuli used in Experiment 1 and Experiment 2.** Top row, from left to right: tools presented in 45°, 0°, and 315° orientations. Bottom row, from left to right: tools presented in 135°, 180°, and 225° orientations.

### 2.3.2. Procedure

To establish the neural underpinnings of different interactions with tools, BOLD fMRI signal was measured while participants planned and executed tool-oriented pantomimed actions arranged in an event-related design (Króliczak & Frey, 2009).

Each Experiment consisted of 6 functional runs with 24 trials each. At the beginning of each run, participants were asked to press one of the buttons of the response pad with the index finger of the tested hand and maintain the pressing throughout the whole run, except for the execution of the planned actions. This manipulation made it possible to control the exact moment of movement onset and thereby to reject from analyses the trials wherein participants

erroneously initiated the movement during the planning phase. Each trial comprised six consecutive phases (see **Figure 2.2**):

1) **Oversampling Interval:** a variable length delay of 0, 0.25, 0.5, or 0.75 s was time-locked to the acquisition of a volume of fMRI data in order to improve the accuracy of estimating the hemodynamic response associated with the performed task (Miezin, Maccotta, Ollinger, Petersen, & Buckner, 2000).

2) **Goal Cue:** one of three geometrical shapes of different colors was presented centrally for 1 s and denoted an action goal for the present trial. A tan square indicated that the to-be-seen object should be grasped with an intention to functionally use it (the *USE* cue), a pink circle indicated that the object should be grasped with an intention to pass it to another person (the *PASS* cue), and a blue rectangle specified that the object should be reached and simply moved with the back of the tested hand (the *MOVE* cue).

3) **Stimulus Picture:** an image of the target object was presented centrally for 1.5 s. Participants were instructed to prepare to pantomime the action identified by both the Goal Cue and the Stimulus Picture (i.e., grasp the object to use it, grasp the object to pass it, move the object) with the tested hand as soon as the Stimulus Picture appeared and throughout the subsequent delay period.

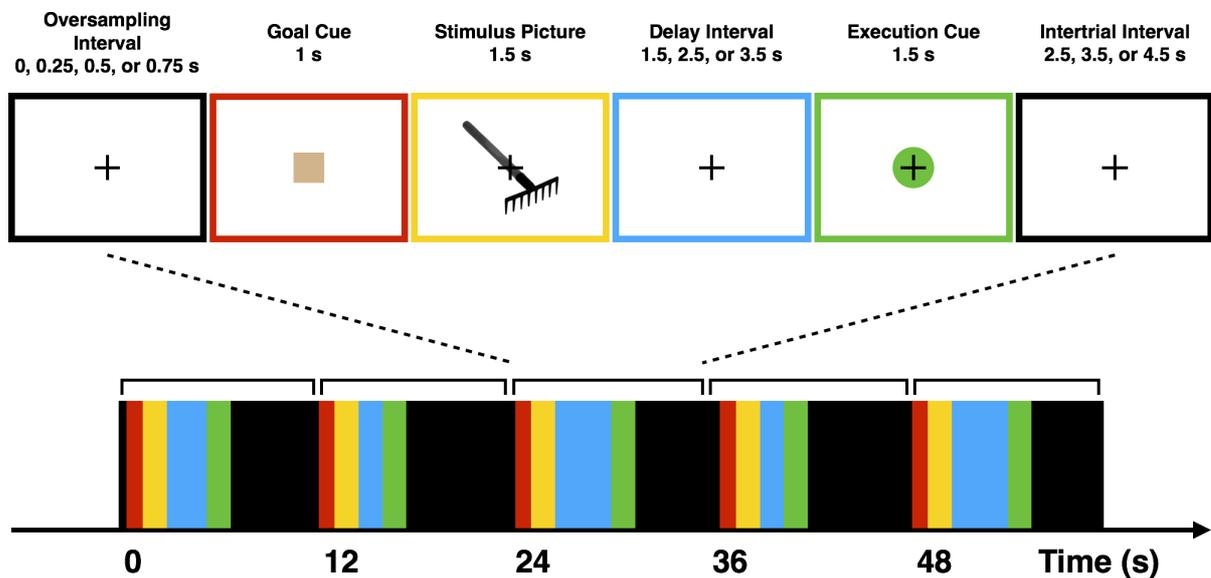
4) Variable length **Delay Interval:** 1.5, 2.5, or 3.5 s.

5) **Execution Cue:** a bright green circle was presented in the middle of the screen for 1.5 s and prompted participants to release the pressed button and to simulate the preplanned action with the tested hand. They were instructed to use only the fingers, hand and forearm, with the upper arm remaining still. Because of the supine position in the scanner, all actions were performed without visual feedback. At the offset of the Execution Cue participants returned their hands to the initial position and resumed pressing the button with the index finger.

6) **Inter-Trial Interval (ITI):** each trial concluded with a variable interval of 2.5, 3.5, or 4.5 s, and, if necessary, an additional short period for synchronization with the scanner trigger. In each run, 4 additional 9.5-s rest intervals were introduced pseudorandomly at the end of the trials with the longest ITIs, providing four 14-s periods serving as resting baseline.

During each run participants were instructed to fixate on a centrally presented cross. Manual performance was monitored by the experimenter. Trials in which the executed action did not match the specified action goal, the presented target object, and/or its orientation (e.g., functional grasp performed instead of reaching and moving the object, precision grip performed instead of a power grip, no wrist rotation performed in a case when a substantial

rotation was necessary) were rejected from analyses. In total, due to the errors in action execution or action timing, 66 out of 2880 trials (2.9%) completed with the right hand and 87 out of 2880 trials (3.8%) completed with the left hand were rejected from further analyses.

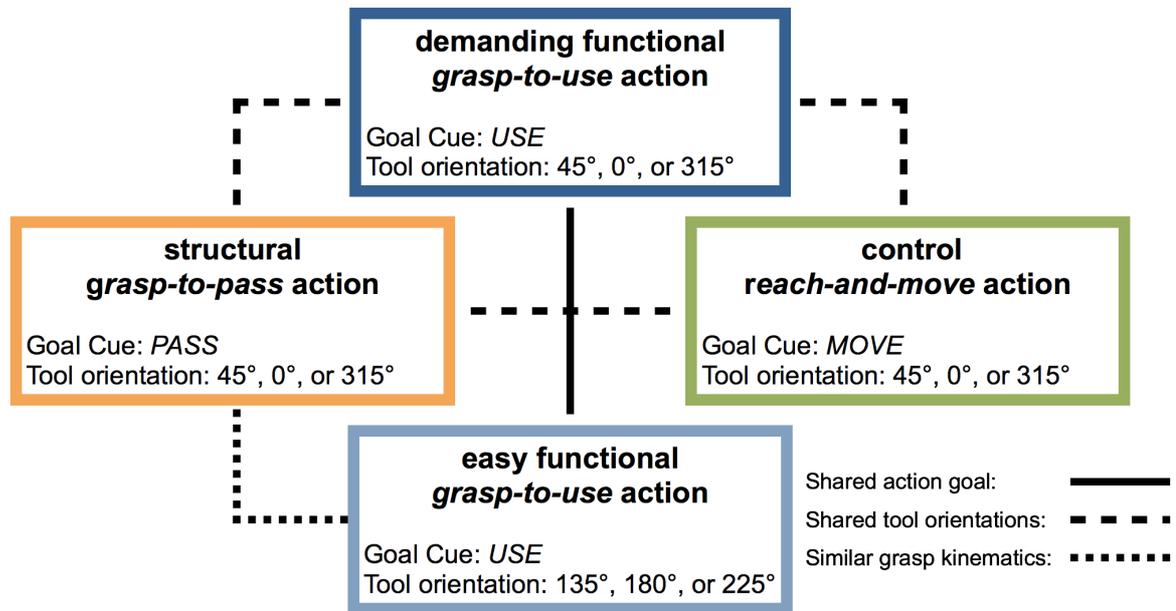


**Figure 2.2.** Trial structure and timing (top) with a portion of a sample trial sequence within a functional run of the experimental paradigm (bottom). After an initial Oversampling Interval (0, 0.25, 0.5, or 0.75 s), a 1-s Goal Cue was followed by a 1.5-s Stimulus Picture, and a variable (1.5, 2.5, or 3.5 s) Delay Interval for action planning. Next, an Execution Cue was presented for 1.5 ms. ITIs were 2.5, 3.5, or 4.5 s in length.

There were four testing conditions distinguished based on Goal Cues and/or the subset of orientations at which the target objects were presented (see **Figure 2.3**):

1. demanding functional *grasp-to-use* action (in short: demanding functional grasp): the *USE* cue accompanied by an object presented in one of three different orientations – 0°, 45°, or 315° – that required the inclusion of a substantial hand rotation in the action plan;
2. easy functional *grasp-to-use* action (in short: easy functional grasp): the *USE* cue accompanied by an object presented in one of three different orientations – 135°, 180°, or 215° – that required the inclusion of a minor (if any) hand rotation in the action plan;
3. structural *grasp-to-pass* action (in short: structural grasp): the *PASS* cue accompanied by an object presented in 0°, 45°, or 315° orientation;
4. control *reach-to-move* action (in short: control action): the *MOVE* cue accompanied by an object presented in 0°, 45°, or 315° orientation.

It is of note that trials in the demanding and easy functional grasp conditions shared an action goal. Trials in the demanding functional grasp and structural grasp conditions shared tool orientations. Finally, trials in the easy functional and structural grasp conditions shared similar grasp kinematics.



**Figure 2.3.** Four conditions of the study resulting from the combination of three different action goals (indicated by Cues) and two sets of stimulus orientations.

Throughout the experiment, each of the 12 target objects was presented 3 times in every condition, each time in a different orientation. Such object-orientation-intention/goal triplets were distributed pseudorandomly across 6 complementary orders of trials in a counterbalanced manner so that every order consisted of 24 trials (6 trials in each condition) presented in a pseudorandom sequence. Targets from each condition had an equal likelihood of being followed by either of the 3 delay intervals and ITIs. The sequence of presentation of the 6 orders was pseudorandomized across participants and testing sessions so that each participant was assigned each order twice, once during each testing session, and each assigned sequence was unique within the whole study.

One day prior to the first fMRI testing session, each participant took part in a training session. First, participants were familiarized with the scanning procedures, completed a pre-scan MRI-safety questionnaire and the Edinburgh Handedness Inventory. Subsequently, each participant completed a minimum of two series of 24 training trials of the experimental paradigm, presented on a computer screen and administered separately for each hand. For every participant, the order in which the hands were trained was the same as the order in

which they were subsequently tested during the fMRI sessions. It was strongly emphasized that all the manual movements should be performed precisely but in a calm manner, and the head motion during the scanning must be eschewed. All participants performed faultlessly before being advanced to the testing sessions.

## 2.4. Functional Grasp Localizer

All the 20 participants were also tested twice (once per session) in two functional localizers: Functional Grasp Localizer (FGL) and Tool Use Localizer (TUL).

FGL served to identify brain areas associated with the retrieval of conceptual knowledge regarding tool use and/or selection of functional hand postures associated with the prototypical usage of common tools. Participants were instructed to pantomime grasping the presented tool with an intention to subsequently use it according to its function (Function-based condition), or to put it aside (Structure-based condition). It is of note that in contrast to structural *grasp-to-pass* actions performed in the main experiment, the pantomime of structure-based grasps in the FGL did not require our participants to consider the more distant context of the action, i.e., the information about the recipient of the handed object. There were twelve 18-s blocks of pantomimed tool grasps (six blocks of function-based grasps and six blocks of structure-based grasps) in response to pictures of tools displayed for 1.5 s each (6 stimuli in each block, 1.5-s interstimulus interval). The stimuli for the FGL were selected to induce “action conflict” whereby different hand pre-shaping and postures are required for using and for moving the same object (Buxbaum et al., 2006; Watson & Buxbaum, 2015). Six different tools were used, 3 different exemplars of each tool, with each exemplar presented at 3 different orientations: 135°, 180°, and 225°. A list of the stimuli used in FGL can be found in the Appendix. Each task block began with an instructional cue - a Polish word “UŻYJ” (Eng. *use*) in the case of Function-based condition, and “PRZEŁÓŻ” (Eng. *displace*) in the case of Structure-based condition - displayed for 1 s above the central cross, which remained on the screen during the whole functional run and served as a fixation point. Participants were told that they should start to pantomime the task-appropriate grasp as soon as a new photo appeared, maintain the final hand posture as long as the photo was displayed, and return to the resting position during the interstimulus interval. All actions were performed with the same hand (dominant right or non-dominant left) that was tested in the main experiment during the same fMRI session. Additional six 18-s blocks of rest periods were introduced pseudorandomly between task blocks. A schematic diagram of the block structure and timing is displayed in **Figure 2.4**. Two different pseudorandom orders of task and rest blocks were

prepared and administered to each participant. The assignment of the two orders was counterbalanced across the tested hands.

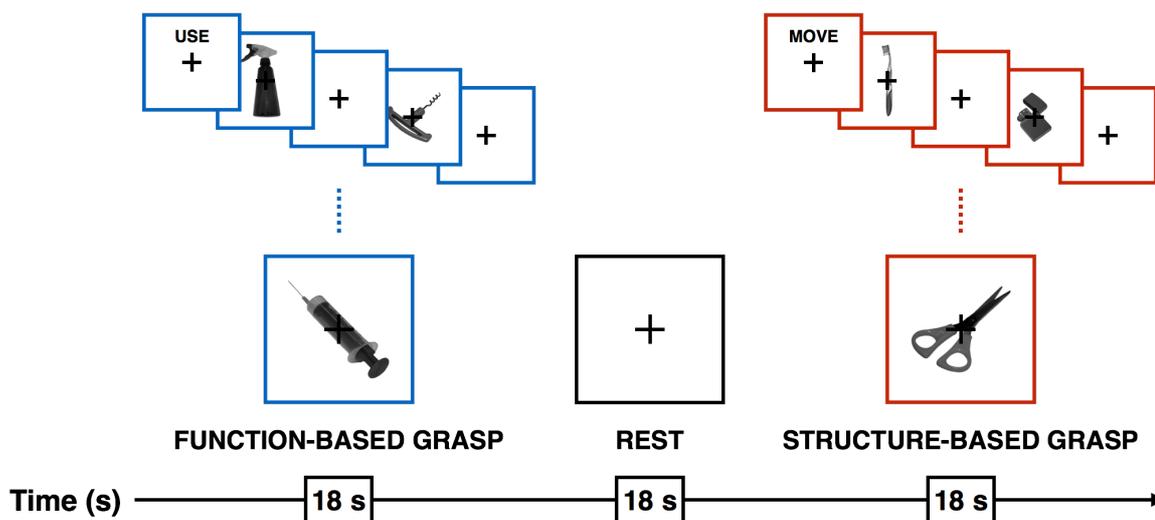


Figure 2.4. Trial structure, timing, and examples of stimuli used in the Functional Grasp Localizer.

## 2.5. Tool Use Localizer

TUL was used to identify brain areas associated with pantomiming the functional use of familiar tools in contrast to a control task wherein repetitive, pre-learned hand and finger movements were required. There were four 18-s blocks of pantomimed tool use in response to pictures of tools displayed for 3 s each (6 stimuli in each block) and four 18-s blocks of abstract hand and finger movements in response to pictures of walking, flying, and swimming animals presented for 3 s each (6 stimuli in each block; a list of the stimuli used in TUL can be found in the Appendix). In the latter case, the required manual movement depended on the way the presented animal usually moves, and the three possible responses were presented and rehearsed during the training session and immediately prior to each of the testing sessions. In both tasks, participants were instructed to start the movement as soon as a new picture (a tool or an animal) appeared and to maintain its execution as long as the picture was displayed. All actions were performed with the same hand (dominant right or non-dominant left) that was tested in the main experiment during the same fMRI session. Additional four 18-s blocks of rest periods were introduced pseudorandomly between task blocks. A black cross remained in the center of the screen during the whole functional run and served as a fixation point. A schematic diagram of the block structure and timing is displayed in **Figure 2.5**. Two different pseudorandom orders of task and rest blocks were prepared and administered to each participant. The assignment of the two orders was counterbalanced across the tested hands.

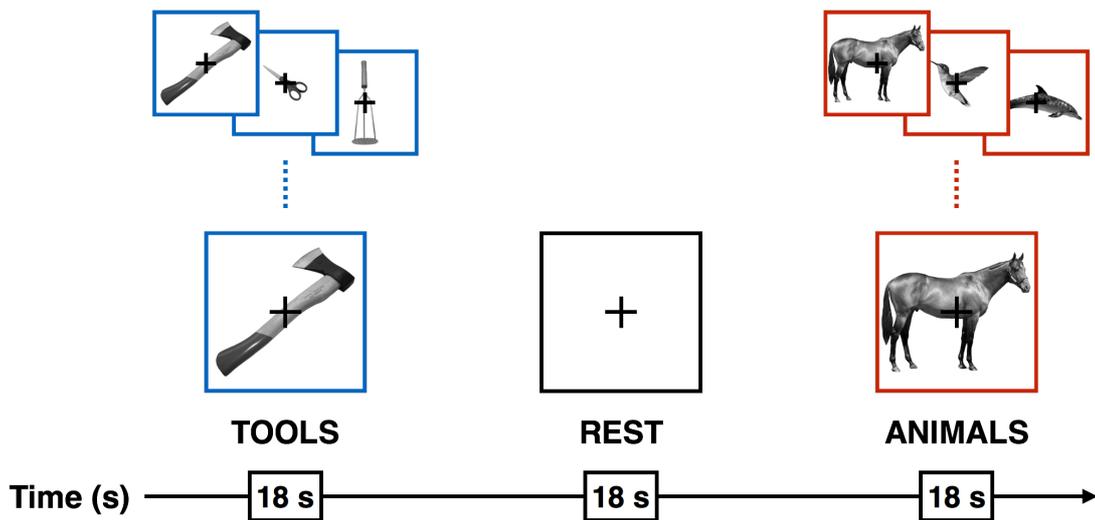


Figure 2.5. Trial structure, timing, and examples of stimuli used in the Tool Use Localizer.

## 2.6. Imaging parameters

All scanning was performed in the Rehasport Clinic (Poznan, Poland) on a 3-Tesla Siemens MAGNETOM Spectra MRI scanner (Siemens Healthcare, Germany) using a 16-channel head coil for radio frequency transmission and signal reception. The BOLD echoplanar (EPI) images were collected using a T2\*-weighted gradient echo sequence with the following parameters: time to repetition (TR) = 2000 ms, time to echo (TE) = 30 ms, flip angle (FA) = 90°, voxel matrix = 58 x 64, Field of View (FoV) = 181.25 x 200 mm, 35 axial slices with in-plane resolution of 3.125 x 3.125 mm and slice thickness of 3.1 mm. High-resolution T1-weighted structural images were acquired using a 3D magnetization-prepared rapid gradient echo (MP-RAGE) pulse sequence: TR = 2300 ms, TE = 3.33 ms, inversion time (TI) = 900 ms, FA = 9°, voxel matrix = 240 x 256, FoV = 240 x 256 mm, 176 contiguous sagittal slices, 1.0-mm isotropic voxels. To improve the accuracy of functional-to-anatomical data co-registration, fast spin echo T2-weighted structural images were also collected: TR = 3200 ms, TE = 417 ms, FA = 120°, voxel matrix = 256 x 256, FoV = 256 x 256 mm, 192 contiguous sagittal slices, 1.0-mm isotropic voxels. Raw image data were converted to NIfTI-1 format using MRI-Convert software (<http://lcn.uoregon.edu/downloads/mriconvert>).

## 2.7. Data analyses

The collected data were analyzed using two approaches: 1) a whole brain analysis and 2) an ROI analysis. The aim of the whole brain analysis was to identify and to compare the networks of areas that mediate planning of different interactions with tools. The principal goal

of the ROI analysis was to investigate the patterns of activity related to planning different interactions with tools within areas typically implicated in the preparation and/or execution of complex manual actions (Brandi et al., 2014; Jacobs, Danielmeier, & Frey, 2010; Króliczak & Frey, 2009; Marangon et al., 2011; Vingerhoets & Clauwaert, 2015). Both types of analysis were performed separately for the dominant right (Experiment 1) and the non-dominant left hand (Experiment 2). Data from Tool Use Localizer were analyzed separately for each hand and served to create hand-dependent ROIs independently of the main experiments to avoid *double dipping* in the data (Kriegeskorte, Simmons, Bellgowan, & Baker, 2009). Data from Functional Grasp Localizer, instead, were analyzed irrespective of the tested hand (i.e., the results of analysis represent an average calculated across the two hands) to increase the chances of identifying brain areas associated specifically with functional grasps. This was because the differences between the two tasks of FGL were very subtle – participants had to pantomime function- or structure-based grasps of the same target objects presented in the same orientations which required only a minor (if any) wrist rotation. The results of FGL analysis served to inform the interpretation of the main experiments results.

### **2.7.1. Whole brain analyses**

All structural and functional images were analyzed using FSL (FMRIB's Software Library, <http://fsl.fmrib.ox.ac.uk/fsl/>) version 5.0.7 (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). First, two high-resolution T1-weighted structural images acquired for each participant were averaged using FLIRT (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001) and subjected to the removal of non-brain tissue using BET (Smith, 2002). Subsequently, functional images were analyzed with FEAT (FSL's FMRI Expert Analysis Tool) version 6.00. Preprocessing procedures included: the removal of non-brain tissue using BET; motion correction using MCFLIRT; spatial smoothing using a Gaussian kernel of full width at half-maximum (FWHM) = 6.2 mm; grand mean intensity normalization of the whole 4D data set by a single scaling factor; and high-pass temporal filtering ( $\sigma = 25$  s). Before statistical analyses, autocorrelation in the data was corrected using a pre-whitening procedure (Woolrich, Ripley, Brady, & Smith, 2001). Hemodynamic responses were modeled using a double-gamma function.

For spatial normalization, functional (EPI) images were first co-registered to the T2-weighted anatomical image with 6 degrees of freedom (DOF). Next, T2- and T1-weighted (MP-RAGE) images were aligned with the use of Boundary-Based Registration (Greve &

Fischl, 2009). Finally, registration of the T1-weighted image to the standard Montreal Neurological Institute (MNI-152) 2-mm template brain was performed using 12 DOF.

For a given participant, each fMRI run was analyzed separately at the first level. Next, within-subjects analyses of the main experiments were implemented using a fixed effects model implemented in the FSL's FEAT. Group analyses were performed using FLAME (FMRIB's Local Analysis of Mixed Effects) Stage 1 (Beckmann, Jenkinson, & Smith, 2003) to model and estimate random-effects components of mixed-effects variance. The resulting Z (Gaussianized t/F) statistic images were thresholded with a cluster-forming threshold of  $Z > 3.1$  and a family-wise error rate (FWER) controlled at  $\alpha = 0.05$  (Eklund, Nichols, & Knutsson, 2016).

Planning-related activity in each condition was modeled as the 3-s period beginning with the onset of the target stimulus (presented for 1.5-s) and lasting throughout the end of the shortest delay interval (1.5 s). Execution-related activity was modeled as the 1.5-s period during which the execution cue was displayed. Resting baseline was modeled as the 14-s period starting with the offset of the execution cue through the longest ITI and additional 9.5 s interval. As a result, whole brain analyses were based on a general linear model (GLM) with the following nine predictors:

1.  $_{PLAN}USE\ R+$ : planning demanding functional *grasp-to-use* actions;
2.  $_{EXE}USE\ R+$ : pantomimed execution of demanding functional grasps;
3.  $_{PLAN}USE\ R-$ : planning easy functional *grasp-to-use* actions;
4.  $_{EXE}USE\ R-$ : pantomimed execution of easy functional grasps;
5.  $_{PLAN}PASS$ : planning structural *grasp-to-pass* actions;
6.  $_{EXE}PASS$ : pantomimed execution of structural grasps;
7.  $_{PLAN}MOVE$ : planning control *reach-and-move* actions;
8.  $_{EXE}MOVE$ : pantomimed execution of control actions;
9. REST: resting baseline.

In order to identify brain areas whose activation in the planning phase of grasp-related conditions was modulated by the tested hand, activity associated with planning tool-directed grasps irrespective of action goal and tool orientation (as compared to planning control *reach-and-move* actions) with the dominant right hand was contrasted with activity associated with the same task performed with the non-dominant left hand, and vice versa.

To directly compare planning-related neural activity across hands for different action goals, a 2 (Hand: right, left)  $\times$  4 (Action: demanding functional *grasp-to-use* action, easy

functional *grasp-to-use* action, structural *grasp-to-pass* action, control *reach-and-move* action) repeated-measures analysis of variance (ANOVA) was run.

Anatomical localization of brain activation was undertaken with help from the Juelich Histological, and Harvard-Oxford probabilistic atlases implemented in the FSL. Clusters of significant activity were visualized by overlying activation maps on the Population- Average, Landmark- and Surface-based (PALS) atlas of the human cerebral cortex (Van Essen, 2005) using CARET software version 5.65 (Van Essen et al., 2001). Multi-fiducial mapping procedure was used wherein the obtained volumetric group average data were initially mapped to individual atlas surfaces, and then re-averaged to account for individual differences in brain anatomy.

### **2.7.2. Region-of-interest (ROI) analyses**

Six areas were chosen for the ROI analyses: rostral Middle Frontal Gyrus (rMFG), ventral Premotor Cortex (PMv), dorsal Premotor Cortex (PMd), caudal Superior Parietal Lobule (cSPL), anterior Supramarginal Gyrus (aSMG), and lateral occipito-temporal cortex (LOT) including caudal Middle and Inferior Temporal Gyri (cMTG/ITG).

All regions of interest were created separately for the dominant right and non-dominant left hand as spheres of 5-mm radius centered on maximally activated voxels from clusters involved in pantomiming the use of familiar tools (vs. performing repetitive, abstract hand movements) with the respective hand in the Tool Use Localizer paradigm.

Within each ROI, mean percent signal change relative to the resting baseline was calculated separately for each participant and each condition with the use of FSL's FEATQuery. The obtained data were submitted to separate repeated-measures Analyses of Variance (ANOVAs) for each ROI with Task (Planning, Execution) and Action (Demanding functional *grasp-to-use* action, Easy functional *grasp-to-use* action, Structural *grasp-to-pass* action, Control *reach-and-move* action) as two within-subjects factors. The adopted level of significance was  $\alpha = 0.05$ , and the required post-hoc tests were Bonferroni corrected (P-value corrected for multiple comparisons marked as Bf-p). When the assumption of sphericity was violated, Greenhouse-Geisser correction of the degrees of freedom was used.

## Chapter 3. Experiment 1: Planning tool-directed actions with the dominant right hand

### 3.1. Results

#### 3.1.1. Whole brain analysis

##### *Planning grasping of tools vs. reaching towards tools with the right hand*

A balanced contrast of planning tool-directed grasps irrespective of action goal and tool orientation vs. planning control *reach-and-move* actions was run to identify brain areas involved in grasp planning. This comparison revealed a widespread bilateral network of parieto-frontal and occipito-temporal areas, including all the crucial nodes of the PRN (Frey, 2008; Przybylski & Króliczak, 2017). Namely, significant BOLD signal increases were observed in the rostral middle frontal gyrus (rMFG), ventral and dorsal premotor cortices (PMv and PMd, respectively), supramarginal gyrus (SMG), intraparietal sulcus (IPS), and the lateral occipito-temporal cortex (LOTc), but also in anterior division of the insular cortex (aIC; cf. Biduła & Króliczak, 2015). Bilaterally increased activity was also detected in the superior parietal lobule (SPL), extending caudally into the antero-dorsal divisions of the precuneus (adPreCun; cf. Hutchison, Culham, Flanagan, Everling, & Gallivan, 2015). On the medial surfaces, there were also bilateral clusters of significant activity in the visual cortices, as well as in the supplementary and pre-supplementary motor areas (SMA complex; cf. Picard & Strick, 2001). Finally, sensorimotor and fusiform cortices were modulated only in the left hemisphere. These results are presented in **Figure 3.1**.

##### *Planning functional grasp-to-use actions vs. structural grasp-to-pass actions*

As shown in **Figure 3.2A**, a direct contrast of planning demanding functional *grasp-to-use* actions vs. structural *grasp-to-pass* actions (i.e., the two conditions sharing tool orientations) revealed increased activity in the left primary sensorimotor cortices, extending caudally towards the anterior division of the SPL (aSPL), and rostrally towards the left PMd, which was active also in the right hemisphere. Additionally, increased activity was observed in the left visual cortices and the right temporo-parietal junction (TPJ; cf. Astafiev, Shulman, & Corbetta, 2006)

Surprisingly, when the to-be-pantomimed actions had similar demands for grasp kinematics – i.e., when planning easy functional *grasp-to-use* actions was contrasted with planning structural grasps – a different pattern of results emerged, wherein none of the areas from the PRN was more engaged. Indeed, planning easy functional grasps was associated with bilaterally increased activity within the visual cortices, extending into the ventro-caudal division of the (primarily left) precuneus (see **Figure 3.2B**).

*Planning structural grasp-to-pass actions vs. functional grasp-to-use actions*

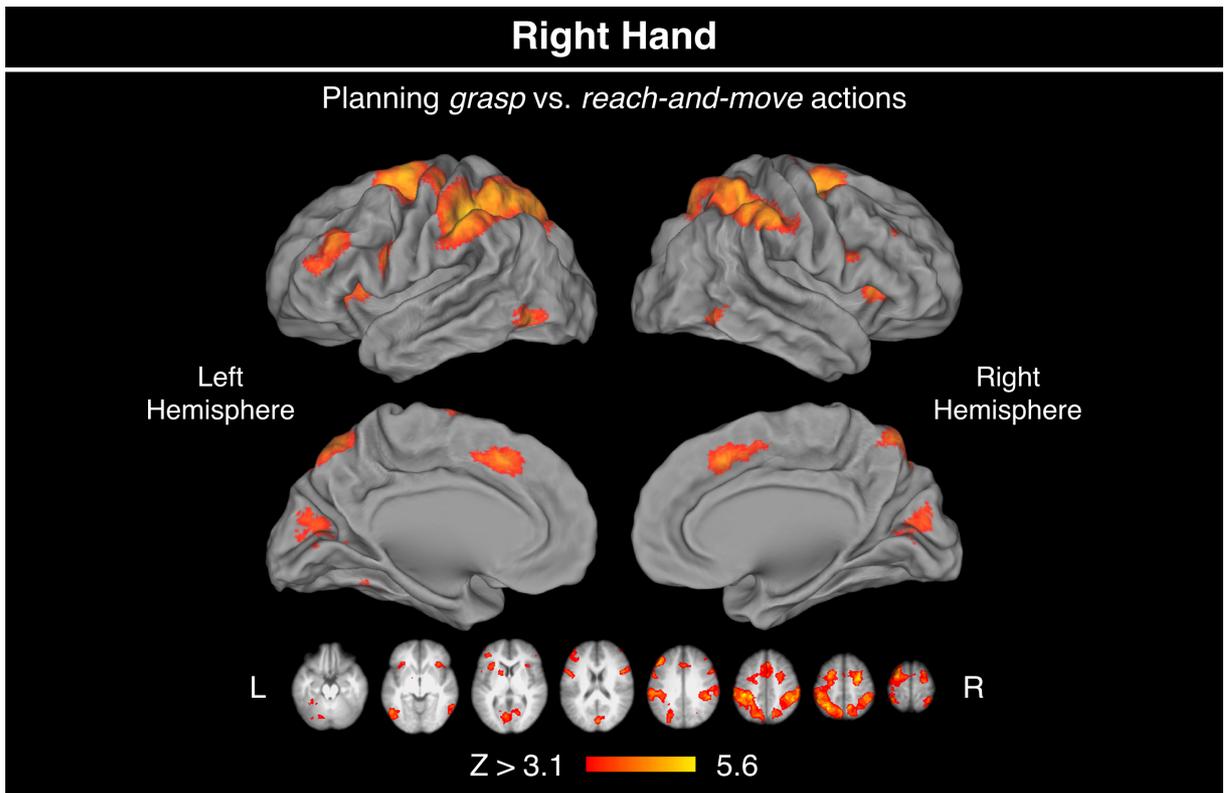
No areas were significantly more involved in planning structural *grasp-to-pass* actions as compared to demanding functional *grasp-to-use* actions, when the orientations of tools were shared. Surprisingly, though, when grasp kinematics were accounted for, the contrast of planning structural grasps vs. easy functional *grasp-to-use* actions revealed exclusively left-lateralized engagement of the rMFG, caudal SPL (cSPL), and aSMG, from where it extended into the anterior IPS (aIPS), as can be seen in **Figure 3.2C**.

*Planning demanding vs. easy functional grasp-to-use actions*

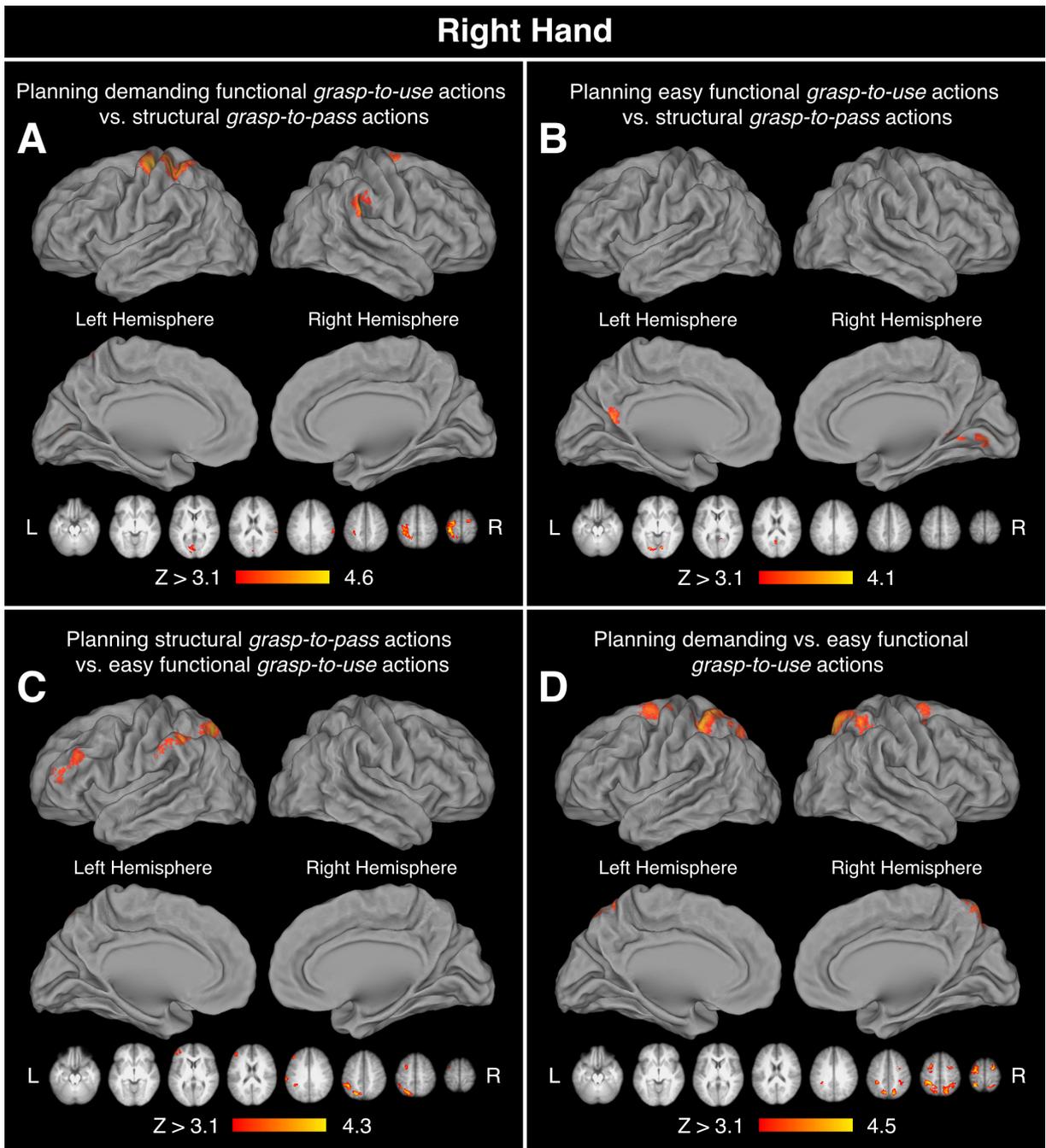
When planning demanding and easy functional *grasp-to-use* actions were directly contrasted, increased activity was localized bilaterally in the PMd and SPL, from where it extended ventrally towards aIPS (see **Figure 3.2D**).

*Execution of tool-directed grasps*

No significant differences between the networks involved in the execution of pre-planned demanding functional *grasp-to-use* actions, easy functional *grasp-to-use* actions, or structural *grasp-to-pass* actions were found.



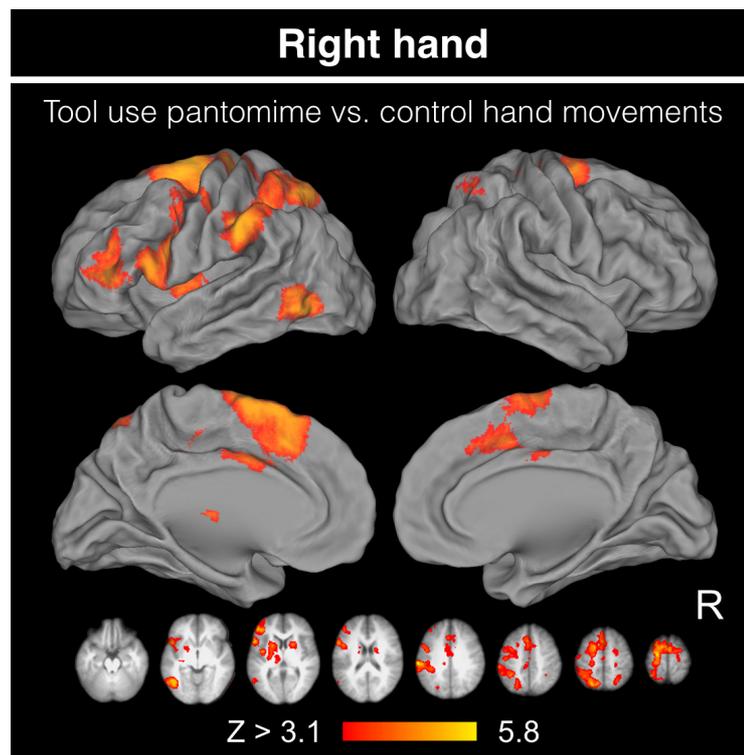
**Figure 3.1. Brain areas showing significantly increased activity during the planning of tool-directed grasp pantomimes (irrespective of action goal and tool orientation) as compared to the planning of control *reach-and-move* actions with the dominant right hand.** In Figures 3.1-3.3, the surface renderings presented in the upper panels demonstrate group average effects overlaid on the PALS atlas (see Chapter 2. Materials and methods), while the axial slices presented in the lower panels illustrate group mean statistical parametric maps projected onto a mean high-resolution T1-weighted anatomical image.



**Figure 3.2.** Brain areas showing significantly increased activity during the planning of: (A) demanding functional *grasp-to-use* actions as compared to structural *grasp-to-pass* actions, (B) easy functional *grasp-to-use* actions as compared to structural *grasp-to-pass* actions, (C) structural *grasp-to-pass* actions as compared to easy functional *grasp-to-use* actions, (D) demanding as compared to easy functional *grasp-to-use* actions. All actions were planned with the dominant right hand.

### 3.1.2. ROI analysis

Spherical ROIs for Experiment 1 were centered on maximally activated voxels from PRN-related clusters involved in pantomiming the use of familiar tools with the right hand in the Tool Use Localizer paradigm. The results of tool use pantomime vs. simple abstract hand movements contrast from TUL are presented in **Figure 3.3**, and the MNI coordinates of the centers of ROIs for Experiment 1 are given in **Table 3.1**, along with their Z values in the above-mentioned contrast.



**Figure 3.3.** Brain areas showing significantly increased activity during the pantomimed tool use as compared to simple repetitive hand movements. Both actions were performed with the right hand.

**Table 3.1. Regions of interest - spherical ROIs of 5-mm radius – for Experiment 1.** ROIs were based on maximally-activated voxels from clusters involved in tool use pantomime vs. simple repetitive hand movements performed in an independent localizer task with the dominant right hand. MNI coordinates of the peak voxels and their Z values are reported.

Left hemisphere region	MNI coordinates			Peak Z value
	x	y	z	
rostral Middle Frontal Gyrus (rMFG)	-44	38	24	4.11
ventral Premotor Cortex (PMv)	-46	8	16	4.57
dorsal Premotor Cortex (PMd)	-20	-14	68	5.48
Superior Parietal Lobule (SPL)	-14	-66	60	5.10
anterior Supramarginal Gyrus (aSMG)	-64	-26	34	5.89
Lateral Occipito-Temporal Cortex (LOTc)	-44	-60	-6	5.28

In the **rMFG ROI**, a 2 (Task)  $\times$  4 (Action) ANOVA revealed no main effect of Task [ $F_{(1,19)} = 2.5, p = 0.13$ ], but a significant main effect of Action [ $F_{(1,9,36,2)} = 15.7, p < 0.001$ ]. Namely, performing tasks involving structural *grasp-to-pass* actions was associated with significantly stronger activity than performing tasks involving demanding functional *grasp-to-use* actions (Bf- $p < 0.01$ ), easy functional *grasp-to-use* actions (Bf- $p < 0.001$ ), and control *reach-and-move* actions (Bf- $p < 0.001$ ). Additionally, performing tasks involving demanding functional grasps resulted in significantly higher activity than performing tasks involving control actions (Bf- $p < 0.05$ ). Nevertheless, all these results should be interpreted with caution because there was also a significant Task by Action interaction [ $F_{(3,57)} = 4.8, p < 0.01$ ] which revealed that the aforementioned effects were driven mostly by different levels of activity associated with planning actions, and not their execution. Indeed, responses associated with planning demanding functional grasps and structural grasps exceeded those evoked by control actions (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively). Moreover, planning structural grasps engaged the rMFG more than planning easy functional grasps (Bf- $p < 0.001$ ), while there was no significant difference between planning structural grasps and demanding functional grasps (Bf- $p = 0.19$ ). No significant differences between actions were found in the execution phase (Bf- $p > 0.86$  in all cases). The observed effects are shown in **Figure 3.4A**.

A somewhat similar pattern of activity emerged in the **PMv ROI**, but in contrast to rMFG, the main effect of Task was now significant [ $F_{(1,19)} = 10.9, p < 0.01$ ] and revealed that planning actions was associated with significantly weaker activity than their execution. There was a significant main effect of Action [ $F_{(3,57)} = 9.4, p < 0.001$ ], such that performing any task

concerning structural grasps resulted in higher activity than performing tasks concerning both easy functional grasps (Bf- $p < 0.01$ ) and control actions (Bf- $p < 0.01$ ). Performing tasks involving demanding functional grasps resulted in significantly higher activity than performing tasks involving control actions as well (Bf- $p < 0.05$ ). However, the familiar Task by Action interaction effect was revealed again [ $F_{(3,57)} = 3.6, p < 0.05$ ]. Specifically, planning demanding functional grasps and structural grasps evoked larger responses than planning control actions (Bf- $p < 0.001$  in both cases), and planning structural grasps employed the rMFG more than planning easy functional grasps (Bf- $p < 0.05$ ), but not demanding functional grasps (Bf- $p = 1.00$ ). Again, no significant differences between actions were found in the execution phase (Bf- $p = 1.00$  in all cases). These results are displayed in **Figure 3.4B**.

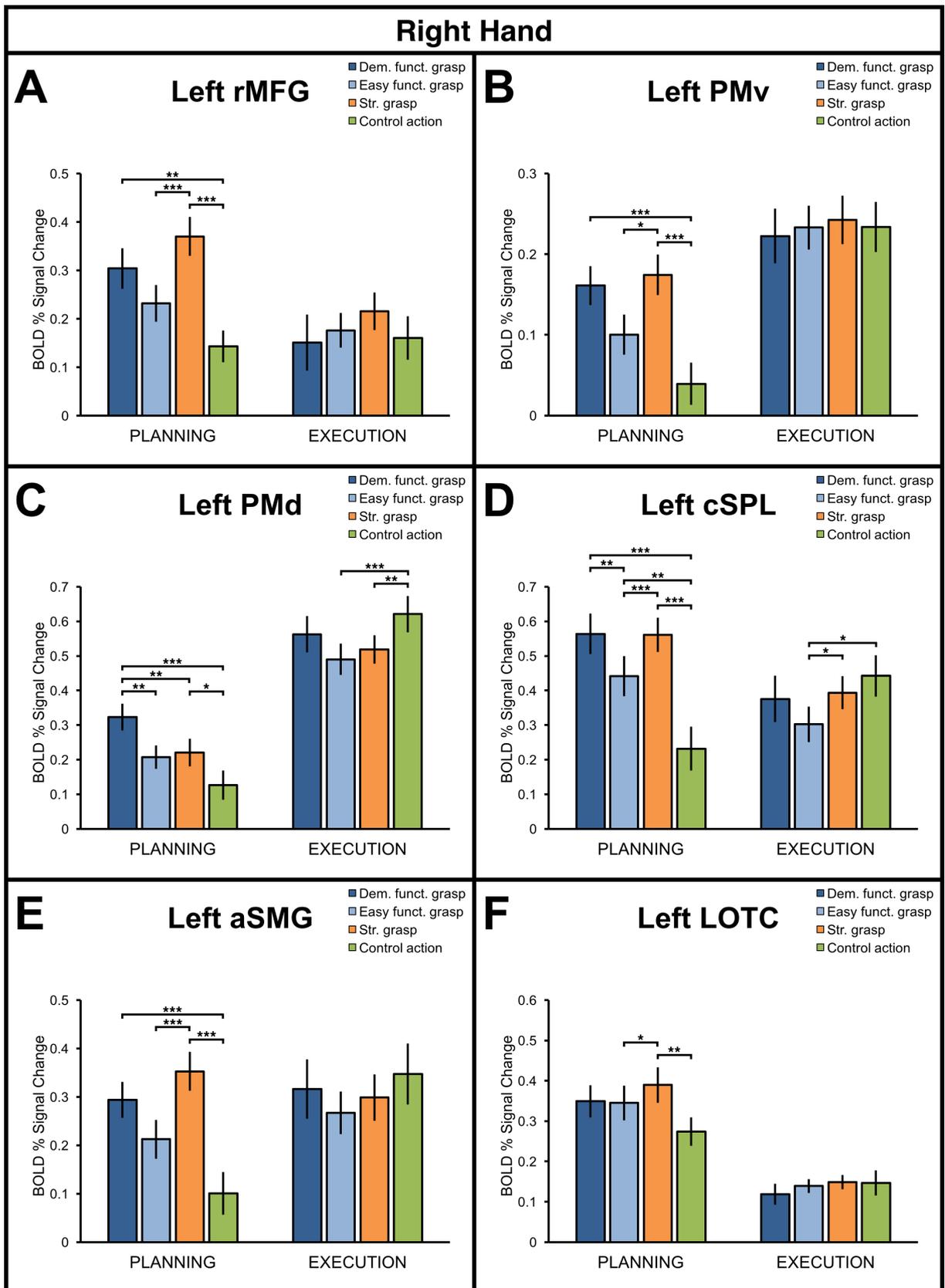
The **PMd ROI** showed a rather different pattern. The analysis revealed a main effect of Task [ $F_{(1,19)} = 94.3, p < 0.001$ ], such that planning actions was associated with significantly weaker activity than their execution. A main effect of Action was also significant [ $F_{(3,57)} = 8.5, p < 0.001$ ] and revealed that performing any task involving demanding functional grasps engaged the region more than performing tasks involving easy functional grasps (Bf- $p < 0.01$ ), structural grasps (Bf- $p < 0.01$ ), or control actions (Bf- $p < 0.05$ ). Finally, the Task by Action interaction was revealed as well [ $F_{(3,57)} = 13.8, p < 0.001$ ]. As shown in **Figure 3.4C**, both demanding functional grasps and structural grasps evoked larger responses in the planning phase than control actions (Bf- $p < 0.001$ , Bf- $p < 0.05$ , respectively), and planning demanding functional grasps was associated with significantly higher activity than planning easy functional grasps or structural grasps (Bf- $p < 0.01$  in both cases). Noteworthy, responses associated with the latter two conditions did not significantly differ from one another (Bf- $p = 1.00$ ). In the execution phase, on the other hand, performing control actions evoked significantly larger responses than performing easy functional grasps or structural grasps (Bf- $p < 0.001$ , Bf- $p < 0.01$ , respectively).

In the **cSPL ROI**, no main effect of Task was observed [ $F_{(1,19)} = 1.0, p = 0.33$ ]. There was a significant main effect of Action [ $F_{(2,2,41.4)} = 13.0, p < 0.001$ ]. Namely, performing any task concerning demanding functional grasps or structural grasps resulted in higher activity than performing tasks concerning easy functional grasps (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively) or control actions (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively). The familiar interaction effect was significant again [ $F_{(1.8,34)} = 15.4, p < 0.001$ ] and revealed that the responses for the three conditions concerned with planning tool-directed grasps exceeded those associated with planning control actions (Bf- $p < 0.001$  in the cases of demanding functional grasps and structural grasps; Bf- $p < 0.01$  in the case of easy functional grasps). Moreover, both planning demanding functional grasps and planning structural grasps

increased activity in the SPL significantly more than planning easy functional grasps (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively). In the execution phase, performing easy functional grasps resulted in significantly lower activity than performing structural grasps or control actions (Bf- $p < 0.05$  in both cases). The results are shown in **Figure 3.4D**.

In the **aSMG ROI**, there was no main effect of Task [ $F_{(1,19)} = 1.2$ ,  $p = 0.28$ ]. A significant main effect of Action [ $F_{(3,57)} = 13.3$ ,  $p < 0.001$ ] revealed that performing tasks involving demanding functional grasps or structural grasps resulted in higher activity than performing tasks concerning easy functional grasps (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively) or control actions (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively). A significant Task by Action interaction [ $F_{(3,57)} = 8.4$ ,  $p < 0.001$ ] showed that planning demanding functional grasps and structural grasps evoked larger responses than planning control actions (Bf- $p < 0.001$  in both cases), and planning structural grasps employed the aSMG more than planning easy functional grasps (Bf- $p < 0.001$ ), but not demanding functional grasps (Bf- $p = 0.21$ ). There was also a strong trend towards greater engagement of the region when the planning of demanding functional grasps was compared to the planning of easy functional grasps (Bf- $p = 0.051$ ). No significant differences between actions were found in the execution phase (Bf- $p > 0.39$  in all cases). The observed effects are shown in **Figure 3.4E**.

In the **LOTc ROI**, a significant main effect of Task was found [ $F_{(1,19)} = 18.8$ ,  $p < 0.001$ ]. In contrast to the PMv and PMd, planning actions was associated with significantly stronger activity than their execution. A main effect of Action was also significant [ $F_{(3,57)} = 7.2$ ,  $p < 0.001$ ] and revealed that performing tasks concerning structural grasps employed the region more than performing tasks concerning control actions (Bf- $p < 0.01$ ). A significant Task by Action interaction effect [ $F_{(2,38.4)} = 3.4$ ,  $p < 0.05$ ] demonstrated that planning structural grasps increased activity in the LOTc more than planning easy functional grasps or control actions (Bf- $p < 0.05$ , Bf- $p < 0.01$ , respectively). There was also a strong trend towards greater engagement of this region for planning easy functional grasps as compared to control actions (Bf- $p = 0.08$ ). The differences between actions in the execution phase were not significant (Bf- $p = 1.0$  in all cases). The results can be seen in **Figure 3.4F**.



**Figure 3.4. ROI analysis for Experiment 1.** Mean percent signal change within each ROI (A-F) is plotted relative to the resting baseline separately for two tasks (planning, execution) and the following actions: demanding functional *grasp-to-use* actions, easy functional *grasp-to-use* actions, structural *grasp-to-pass* actions, and control *reach-and-move* actions. Asterisks indicate differences with Bonferroni-corrected  $P$  values of at least 0.05 (\*), 0.01 (\*\*), or 0.001 (\*\*\*).

### 3.2. Discussion of Experiment 1

Compared to planning simple *reach-and-move* actions, planning both functional *grasp-to-use* actions and structural *grasp-to-pass* actions for subsequent production was associated with increases of activity in bilateral parieto-frontal and occipito-temporal areas. These results are in agreement with the recent results of Przybylski and Króliczak (2017) on the neural underpinnings of functional grasps of simple tools, as well as with the previous neuroimaging research on pantomimed or real tool use actions (Brandi et al., 2014; Króliczak & Frey, 2009; Króliczak et al., 2016; Vingerhoets et al., 2012, 2009), or complex manual actions directed towards neutral objects (Creem-Regehr, Dilda, Vicchilli, Federer, & Lee, 2007; Creem-Regehr & Lee, 2005; Jacobs et al., 2010; Marangon et al., 2011). In line with these reports, when study conditions involving grasping tools motivated by different action goals were directly compared, the crucial goal-specific differences were observed in the left hemisphere. This suggests that the engagement of the right hemisphere in planning distinctly motivated grasps as compared to control actions is not specific for interacting with tools in a meaningful way, but it rather reflects the more challenging nature of grasping actions associated with higher requirements for attentional processes and/or visuospatial transformations (Astafiev et al., 2006; Króliczak, Cavina-Pratesi, Goodman, & Culham, 2007).

As indicated by the whole brain analysis, the comparison of planning functional grasps and structural grasps directed at tools presented in the same orientations revealed increased activity primarily within the areas of the dorso-dorsal stream, including bilateral dorsal premotor cortex (left PMd engagement unveiled by the ROI analysis) and anterior division of the left superior parietal lobule. The possible reasons for the engagement of these areas in the task in question will now be discussed.

Recent neuroimaging studies utilizing an fMRI adaptation paradigms implicated PMd in coding hand and wrist rotation during grasping actions (Króliczak et al., 2008; Monaco et al., 2011, 2014; see also Begliomini, Caria, Grodd, & Castiello, 2007; Monaco et al., 2014; Begliomini, Nelini, Caria, Grodd, & Castiello, 2008). It is not surprising, therefore, that in the current study bilateral PMd was significantly more involved in planning actions that required an uncomfortable wrist rotation and adaptation of the functional hand posture to an object presented in a non-canonical way, with a business/functional part of the tool oriented towards the participant.

There is now strong evidence that SPL plays a crucial role in representing hand movements associated with reaching actions/transport component of the *reach-to-grasp* movements (Cavina-Pratesi et al., 2010; Filimon, Nelson, Hagler, & Sereno, 2007; Rizzolatti,

Matelli, Rizzolatti, & Matelli, 2003; Barany, Della-Maggiore, Viswanathan, Cieslak, & Grafton, 2014; Striemer, Chouinard, & Goodale, 2011). Importantly, anterior part of the SPL has been recently implicated in the dynamic representation of the reachable space (Macuga & Frey, 2014), but also in the integration of information about the transport and grasp components during prehensile actions (Fabbri, Strnad, Caramazza, & Lingnau, 2014). Thus, greater aSPL engagement in planning demanding functional vs. structural grasps is in line with these results, as planning a major hand rotation associated with grasping tools in a functional way required participants to expand the action space in order to accommodate the movement of the hand approaching the tool from behind.

Taken together, the observed greater involvement of the dorso-dorsal stream areas in planning demanding functional grasps as compared to structural grasps may reflect a greater biomechanical complexity of the former actions in this study. This interpretation is consistent with the observation that a similar network of dorso-dorsal stream areas was invoked when demanding functional grasps were contrasted with easy functional grasps sharing the action goal, but differing in target tool orientation and grasp kinematics. Indeed, when functional and structural grasps were matched with respect to grip kinematics and the required wrist rotation, none of the aforementioned dorso-dorsal stream areas showed greater engagement in planning functional grasps than planning structural grasps. Moreover, the observed greater activation of the ventro-caudal division of the precuneus in the case of easy functional grasps could have been associated with greater inhibition of the default mode network (Yeo et al., 2011) in the case of planning structural grasps, as this area was not activated when both conditions in question were compared to the resting baseline. Thus, planning structural grasps may have been more cognitively demanding for participants than planning functional grasps of similar grasp kinematics.

This interpretation gains further support from the observation of greater engagement of the left-hemispheric ventro-dorsal stream areas, including ventral premotor cortex (as indicated by ROI analysis) and anterior divisions of intraparietal sulcus and supramarginal gyrus (as indicated by both whole brain and ROI analyses), in planning structural as compared to easy functional grasp pantomimes. This results are discussed in detail below.

Anterior IPS and PMv constitute a human homologue of the monkey AIP-F5 circuit crucially involved in the visuomotor control of grasping actions (Davare, Rothwell, & Lemon, 2010; Jeannerod, Arbib, Rizzolatti, & Sakata, 1995; Rizzolatti et al., 2003). Activation of both areas is commonly reported in studies concerning visually-guided grasping of objects and/or task related to the functional manipulation of tools (Binkofski et al., 1999; Bohlhalter et al., 2009; Davare, Andres, Clerget, Thonnard, & Olivier, 2007; Johnson-Frey et al., 2005;

Króliczak & Frey, 2009; Rice, Tunik, & Grafton, 2006; Rumiati et al., 2004; Tunik, Lo, & Adamovich, 2008). In this tandem, aIPS is thought to compute possible grasps of objects on the basis of their spatial and perceptual features (Verhagen, Dijkerman, Medendorp, & Toni, 2012; Watson & Buxbaum, 2015; Schubotz, Wurm, Wittmann, & von Cramon, 2014), whereas PMv is associated, among other functions, with the selection of the appropriate hand posture on the basis of the information specifying possible configurations coming from the aIPS, conceptual action knowledge provided by lateral occipito-temporal cortex, and the current task instructions represented in the prefrontal cortex (Makuuchi et al., 2012; Vingerhoets, Nys, Honoré, Vandekerckhove, & Vandemaele, 2013; Castiello & Begliomini, 2008; Króliczak et al., 2012; Cavina-Pratesi et al., 2010; Króliczak et al., 2008). Additionally, both aIPS and PMv have been implicated in encoding goals of the observed or performed actions, with the goals understood as the object selected for action, the relation between the grasping hand and the object, or the final state wherein the object is acquired irrespective of the effector used (Hamilton & Grafton, 2006; Jacobs et al., 2010; Johnson Frey et al., 2003; Martin, Jacobs, & Frey, 2011; Tunik, Frey, & Grafton, 2005; Tunik, Ortigue, Adamovich, & Grafton, 2008; Umiltà et al., 2008; Vingerhoets et al., 2010). Lesions to either area disrupts hand preshaping when grasping an object (Binkofski et al., 1998; Davare et al., 2006), and damage to the left PMv has been shown to specifically affect the functional grasping of tools (Randerath et al., 2010). All in all, greater engagement of this circuit in the aforementioned contrast of planning structural vs. easy functional grasps may reflect higher demands placed on the visuomotor system by the task concerning the preparation of a grasp that would be appropriate for passing a tool to another person. Possible reasons for this increase in difficulty relative to easy functional grasps will be discussed in the General discussion.

As indicated in Chapter 1, left SMG has been linked with storing information about learned hand configurations related to the skillful use of functional objects (Andres et al., 2013; Pelgrims et al., 2011; Vingerhoets, 2008). In fact, some researchers have postulated that it encompasses a human-specific region – anterior SMG – devoted to observation and execution of tool-use actions (Orban & Caruana, 2014; Peeters et al., 2009; Peeters, Rizzolatti, & Orban, 2013). However, recent neuroimaging study expanded its putative role to representing a broader range of praxis skills, including both object-related and communicative gestures independent of handedness and the hand involved (Króliczak et al., 2016). Moreover, it has been suggested that left SMG may also play a role (similarly to the left PMv) in resolving action competition between competing object-directed hand postures (Watson & Buxbaum, 2015). Consistent with these proposals, the engagement of aSMG here may

support the hypothesis of an additional cognitive load associated with a selection of hand posture appropriate for passing an object.

As indicated and/or confirmed in the ROI analysis, planning structural vs. easy functional grasps was also associated with increased activity in the left rMFG, cSPL, and LOTC. Activation of the rMFG has been reported in tasks concerning the preparation of functional hand postures and/or tool pantomimes (Johnson-Frey et al., 2005; Króliczak & Frey, 2009; Przybylski & Króliczak, 2017; Vingerhoets & Clauwaert, 2015), as well as in studies on prospective grasp planning with a hand or a tool (Jacobs et al., 2010; Marangon et al., 2011; Martin et al., 2011). Consistent with these findings, damage to the left rMFG usually results in ideomotor apraxia (Goldenberg & Spatt, 2009; Haaland et al., 2000). The exact role played by this area seems to concern higher-level aspects of cognitive and motor control, spanning from the monitoring of information held in working memory (Miller & Cohen, 2001; Petrides, 2000) to the selection of the motor response appropriate for the current task (Buccino et al., 2004; Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000), and understanding the observed action within a given action context (Balconi & Vitaloni, 2012). As suggested by Bach et al. (2010), left rMFG may be involved in processing high-level action representations concerning both the goal of the object-related action and the way it has to be manipulated in order to achieve the desired outcome. In light of these findings, then, the greater engagement of the left rMFG in planning structural vs. easy functional grasps in the current study may be associated with maintaining information about the goal of the grasping action and the associated need to substantially change a motor strategy and select the goal-appropriate hand posture processed by aSMG and PMv. After all, preparing a structural grasp was required in 25% trials within each functional run and was embedded among more automatic – i.e., functional – interactions with tools and/or less demanding tasks of moving the tools away with the back of the hand.

Bilateral cSPL activation during planning structural vs. easy functional grasps revealed the engagement of the dorso-dorsal stream in preparing the task in question. Importantly, this activation was located more posteriorly than the dorso-dorsal stream activation associated with planning demanding functional as compared to structural grasps. Moreover, although the ROI analysis revealed that planning both demanding functional and structural grasp pantomimes involved this area more than planning easy functional grasps, these differences in activation could have had different causes. Specifically, cSPL activation during the preparation of demanding vs. easy functional grasps is consistent with numerous neuroimaging studies that have pointed to the engagement of this area in grasping actions (Cavina-Pratesi et al., 2010; Gallivan, McLean, & Culham, 2011; Króliczak et al., 2008), and

especially in the coding of appropriate hand orientation relative to the grasp-relevant dimensions of the target object (Monaco et al., 2011, 2014). In turn, one possible interpretation of the higher engagement of cSPL in planning structural as compared to easy functional grasps in this study is that during the preparation (but not execution) of hand posture that would be appropriate for passing an object to another person, participants could have unintentionally extended the action plan so that it included also the arm transport action that would follow grasping an object if it was actually to be handed. Such interpretation is consistent with the postulated role of cSPL in the control of reaching actions (Cavina-Pratesi et al., 2010; Prado et al., 2005), representing the peripersonal, reachable space (Gallivan, Cavina-Pratesi, & Culham, 2009; Macuga & Frey, 2014), as well as updating the location of hand in space based on predictive information (Granek, Pisella, Blangero, Rossetti, & Sergio, 2012).

Left LOTC, including cMTG/cITG, has been traditionally implicated in representing conceptual knowledge about familiar tools and/or their associated actions (Andres et al., 2013; Kellenbach, Brett, & Patterson, 2003; Vingerhoets, 2008; Weisberg, Van Turenout, & Martin, 2007; Gallivan, McLean, Valyear, & Culham, 2013; Schubotz et al., 2014; Lingnau & Downing, 2015). Consistent with this view, damage within this area is associated with impairments in both tool-related action production and recognition (Tarhan et al., 2015). Interestingly, recent neuroimaging study on left hemisphere stroke patients using voxel-based symptom-lesion mapping technique has highlighted the putative role of LOTC in storing the information about the typical posture (so far associated primarily with aSMG) and movement of the hand during skilled functional actions with manipulable objects (Buxbaum, Shapiro, & Coslett, 2014; see also Valyear & Culham, 2010; Watson & Buxbaum, 2015). Greater engagement of the left LOTC in planning structural grasps than functional grasps of similar kinematics, revealed by the ROI analysis, may therefore suggest that conceptual and/or motor representations concerning tool-related actions were substantially involved in the preparation of grasps with an intention to pass an object to a different person. It may be speculated that planning such an action may involve grasping an object in such a way that would enable the person to whom it is passed acquiring it with a functional grasp, as if he or she intended to subsequently use it. In such case, the involvement of action representations concerning function-appropriate hand postures, putatively stored in the left LOTC, would be very likely. The retrieval of task-related conceptual knowledge necessary for action planning could also explain why this area was the only one, as revealed by the ROI analysis, that was engaged significantly more during the planning phase than the execution phase of the action.

Finally, the observation that within-task differences between the four conditions of the study were detected almost exclusively in the planning phase suggests that all the critical aspects of the action plan were already prepared when the action itself was executed (Garofeanu, Króliczak, Goodale, & Humphrey, 2004; Goodale et al., 2005; Przybylski & Króliczak, 2017).

## Chapter 4. Experiment 2: Planning tool-directed actions with the non-dominant left hand

### 4.1. Results

#### 4.1.1 Whole-brain analysis

##### 4.1.1.1. Left hand planning and execution

###### *Planning grasping of tools vs. reaching towards tools with the left hand*

The network invoked in planning tool-directed grasps irrespective of action goal and tool orientation (as compared to the control *reach-and-move* actions) with the non-dominant, left hand was very similar to the one observed in the same balanced contrast for the dominant right hand. Grasp planning was again associated with significant BOLD signal increases in bilateral rMFG, PMv, PMd, aIC, SMG, IPS, SPL, adPreCun, LOTC, SMA complex, and visual cortices. Yet, the sensorimotor cortex was engaged almost exclusively in the right hemisphere, while the activity within the fusiform cortex was observed only on the left. These outcomes are shown in **Figure 4.1**.

###### *Planning functional grasp-to-use actions vs. structural grasp-to-pass actions*

When planning demanding functional *grasp-to-use* actions was contrasted with planning structural *grasp-to-pass* actions to be performed with the left hand, the pattern of significant increases of activity was strongly lateralized to the right hemisphere, as presented in **Figure 4.2A**. Significantly increased activity was observed in the right PMd, from where it extended medially to the SMA, and caudally into sensorimotor cortex, aSPL, and into the aIPS. Visual cortices were invoked almost exclusively in the left hemisphere.

In contrast to Experiment 1, when demands for grasp kinematics were matched, no brain areas were significantly more involved in planning easy functional grasps than structural grasps.

###### *Planning structural grasp-to-pass actions vs. functional grasp-to-use actions*

Again, no brain areas were more engaged in planning structural *grasp-to-pass* actions as compared to demanding functional *grasp-to-use* actions. However, when grasp kinematics

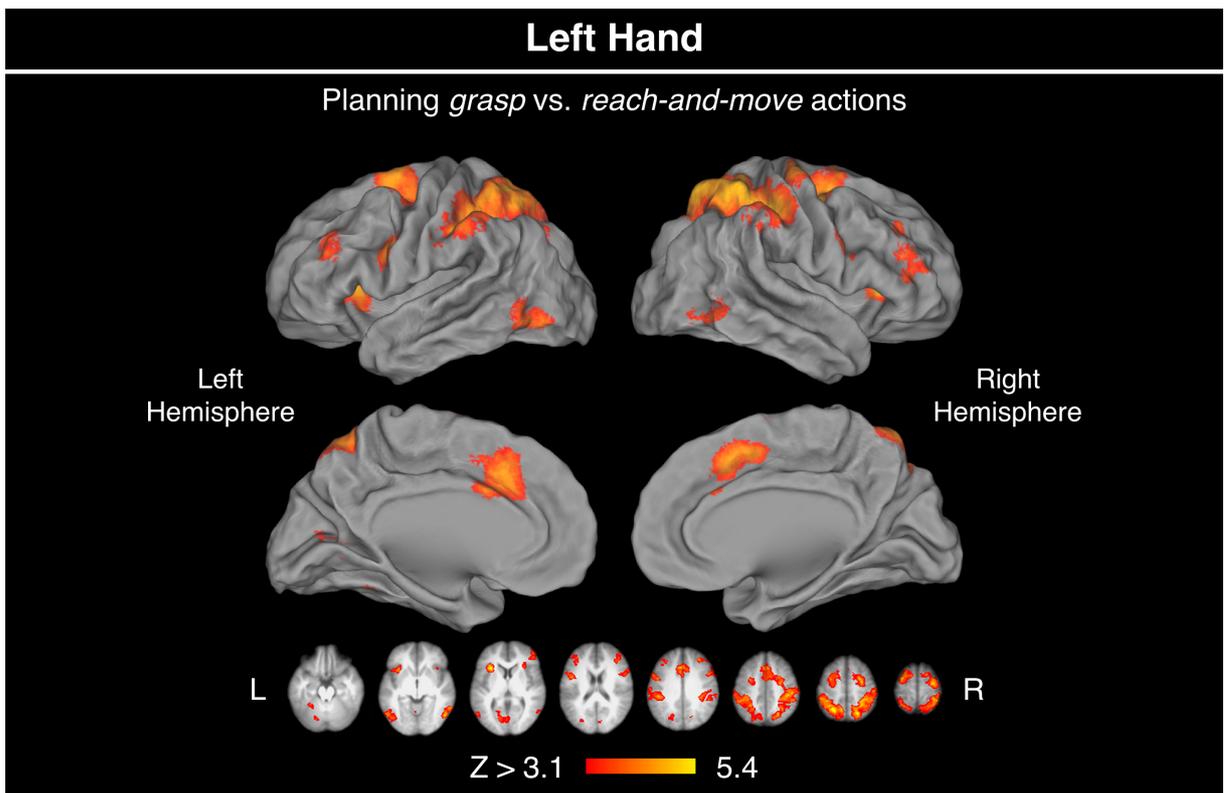
were matched, the contrast of planning structural grasps vs. easy functional *grasp-to-use* actions revealed increased activation in the left rMFG, cSPL, and a cluster at the junction of posterior SMG, angular gyrus (ANG), and adjacent IPS. Modulations of signal observed in the left PMd extended rostrally into pre-PMd, the putative homologue of monkey area F7 (cf. Picard & Strick, 2001). These results are shown in **Figure 4.2B**.

#### *Planning demanding vs. easy functional grasp-to-use actions*

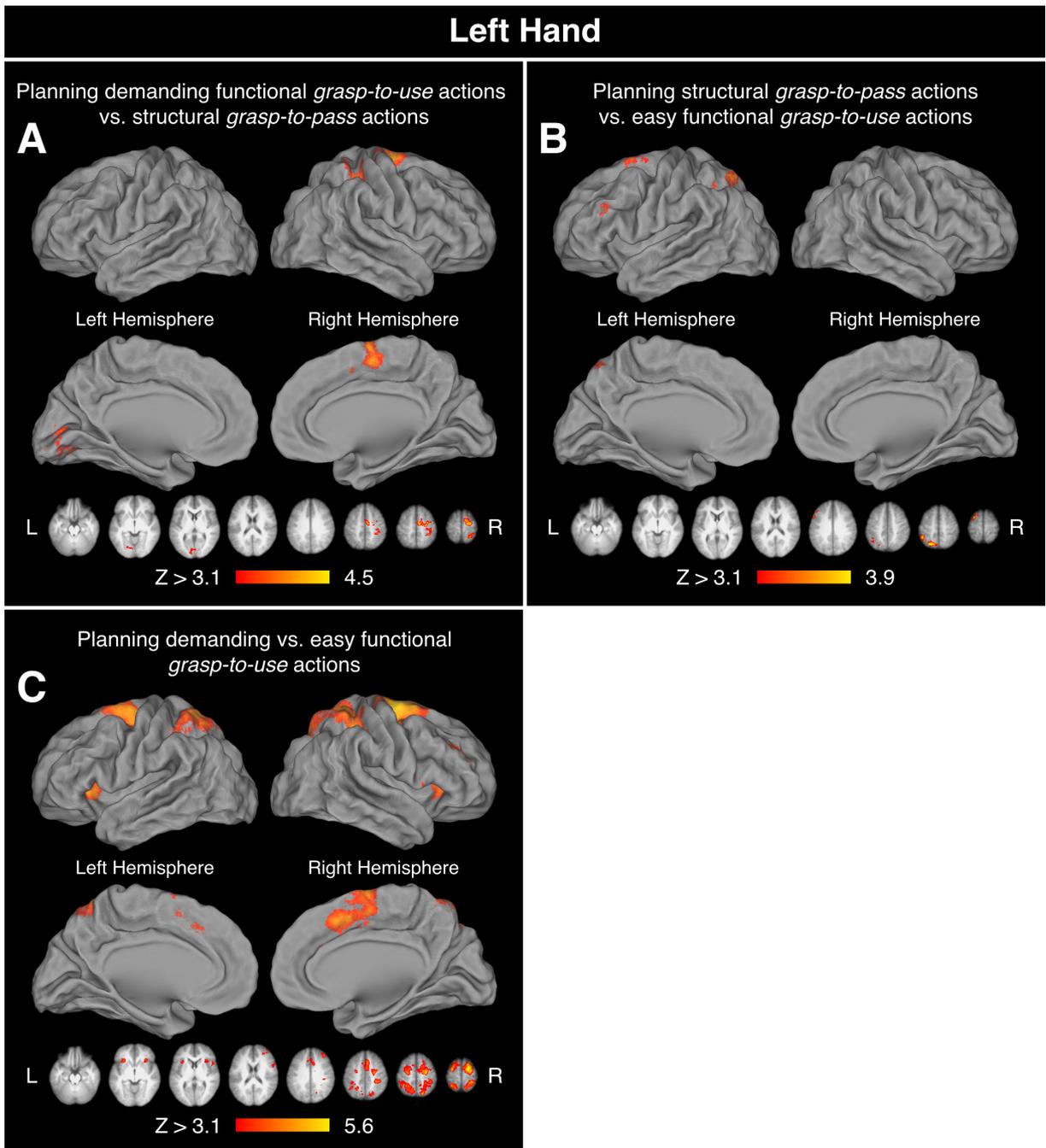
The contrast of planning demanding vs. easy functional *grasp-to-use* actions revealed a bilateral network of areas including PMd, aIC, aIPS, aSPL, and cSPL. SMA complex was invoked primarily in the right hemisphere, and the increased activity of sensorimotor cortices and the rMFG was exclusively right-lateralized (see **Figure 4.2C**).

#### *Execution of tool-directed grasps*

Executing pre-planned structural *grasp-to-pass* actions vs. demanding functional *grasp-to-use* actions revealed increased activation in the bilateral visual cortices, left rMFG and left IPS. Visual cortices of the left hemisphere were also significantly more engaged in the execution of easy vs. demanding functional grasps. No other significant differences between demanding functional grasps, easy functional *grasp-to-use* actions, or structural grasps were found in the execution phase for the non-dominant left hand.



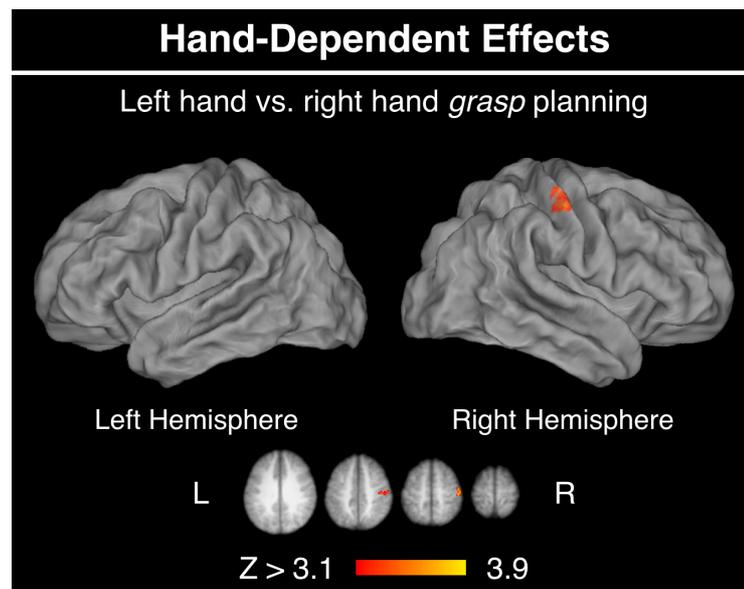
**Figure 4.1. Brain areas showing significantly increased activity during the planning of tool-directed grasp pantomimes (irrespective of action goal and tool orientation) as compared to the planning of control *reach-and-move* actions with the dominant right hand.** In Figures 4.1-4.6, the surface renderings presented in the upper panels demonstrate group average effects overlaid on the PALS atlas (see Chapter 2. Materials and methods), while the axial slices presented in the lower panels illustrate group mean statistical parametric maps projected onto a mean high-resolution T1-weighted anatomical image.



**Figure 4.2.** Brain areas showing significantly increased activity during the planning of: (A) demanding functional *grasp-to-use* actions as compared to structural *grasp-to-pass* actions, (B) structural *grasp-to-pass* actions as compared to easy functional *grasp-to-use* actions, (C) demanding as compared to easy functional *grasp-to-use* actions. All actions were planned with the non-dominant left hand.

#### 4.1.1.2. Hand-dependent planning

Direct contrasts of activity associated with planning tool-directed grasps (irrespective of action goal and tool orientation) for the right hand and the left hand revealed greater engagement of the contralateral somatosensory areas exclusively in the case of the non-dominant left hand (see **Figure 4.3**). These outcomes clearly indicate that the network of higher-order areas devoted for planning grasping of tools for the right and left hand were nearly indistinguishable.



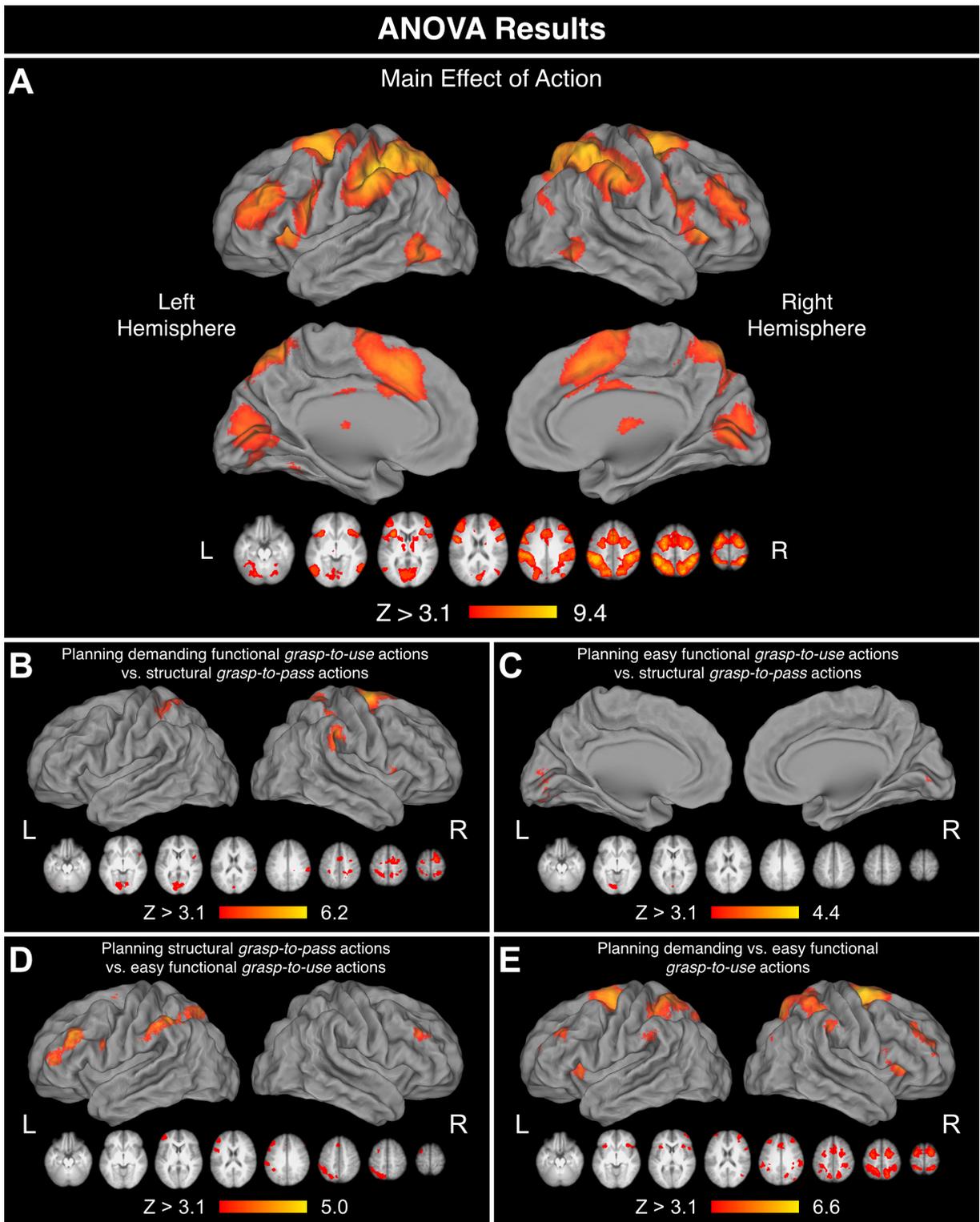
**Figure 4.3.** Brain areas showing significantly increased activity during the planning of tool-directed grasp pantomimes (as compared to the planning of control *reach-and-move* actions) with the left hand vs. the right hand.

#### 4.1.1.3. Repeated-measures ANOVA

A whole-brain repeated-measures 2 (Hand: right, left)  $\times$  2 (Action: demanding functional *grasp-to-use* action, easy functional *grasp-to-use* action, structural *grasp-to-pass* action, control *reach-and-move* action) ANOVA revealed a main effect of Hand, a main effect of Action, and no significant interaction between the two factors. As the goal of this analysis was to directly compare planning-related neural activity across hands for different action goals, the main effect of Hand is not discussed here.

As can be seen in **Figure 4.4A**, modulatory effect of the planned tool-directed action on brain activity was demonstrated in a widespread bilateral network including parieto-frontal and occipito-temporal areas. The results of post-hoc comparisons between the three grasp-related conditions of the main experiments were very similar to the effects obtained for the

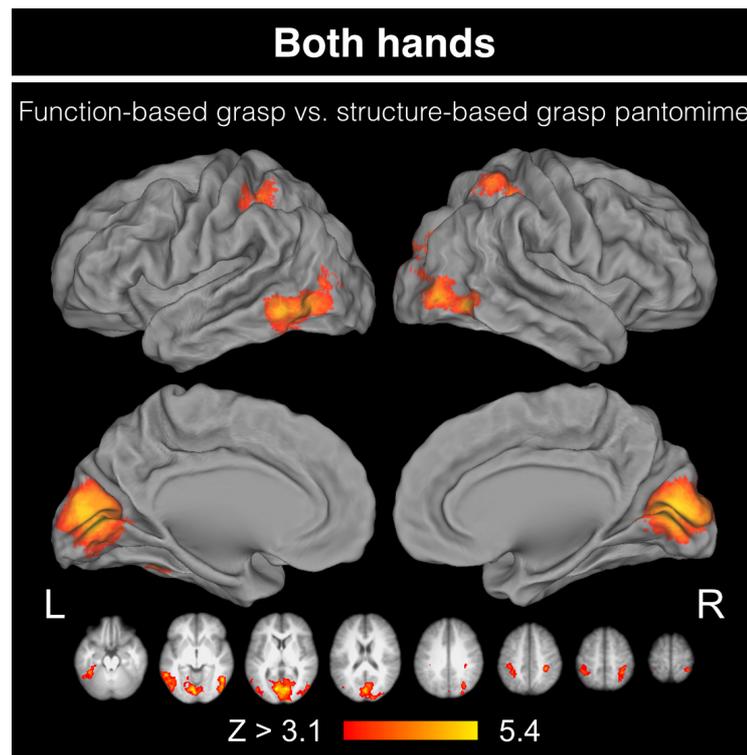
contrasts performed separately for each of the hands. Specifically, planning demanding functional *grasp-to-use* actions relative to planning structural *grasp-to-pass* actions invoked right-sided PMd and SMG/TPJ, as well as bilateral aSPL, SMA, and visual cortices (see **Figure 4.4B**). Planning easy functional *grasp-to-use* actions as compared to planning structural grasps was associated with significantly greater engagement of the visual cortices, predominantly in the left hemisphere (see **Figure 4.4C**). The reversed contrast of planning structural grasps vs. planning easy functional grasps revealed significantly increased activity in bilateral rMFG and pre-SMA, and left-hemispheric PMv, pre-PMd, aSMG/IPS, and cSPL. This contrast can be seen in **Figure 4.4D**. Finally, as presented in **Figure 4.4E**, planning demanding as compared to easy functional grasps involved bilateral rMFG, aIC, PMd, aSMG and SPL.



**Figure 4.4.** The results of whole-brain repeated-measures  $2$  (Hand: right, left)  $\times$   $2$  (Action: demanding functional *grasp-to-use* action, easy functional *grasp-to-use* action, structural *grasp-to-pass* action, control *reach-and-move* action) ANOVA. (A) Brain areas showing a main effect of Action. (B-E) The results of post-hoc comparisons for the main effect of Action. Brain areas showing significantly increased activity during the planning of: (B) demanding functional grasps as compared to structural grasps, (C) easy functional grasps as compared to structural grasps, (D) structural grasps as compared to easy functional grasps, and (E) demanding as compared to easy functional grasps.

#### 4.1.1.4. Functional Grasp Localizer results

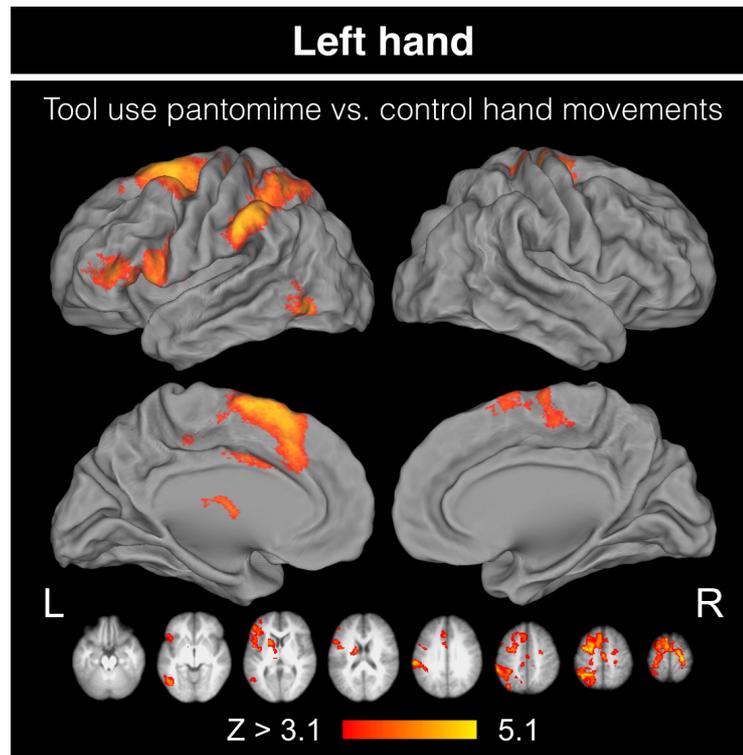
Pantomiming function-based (*grasp-to-use*) as compared to structure-based (*grasp-to-move*) actions irrespective of the tested hand was associated with significant signal modulations in bilateral LOTC, including cMTG and cITG, aSPL/aIPS, and visual cortices. Fusiform cortex involvement was observed exclusively in the left hemisphere. These results are presented in **Figure 4.5**.



**Figure 4.5.** Brain areas showing significantly increased activity during the pantomimed function-based grasps vs. structure-based grasps, irrespective of the hand used in the task.

#### 4.1.2. ROI analysis

Spherical ROIs for Experiment 2 were centered on maximally activated voxels from PRN-related clusters involved in pantomiming the use of familiar tools with the left hand in the Tool Use Localizer paradigm. The results of tool use pantomime vs. simple abstract hand movements contrast from TUL are presented in **Figure 4.6**, and the MNI coordinates of the centers of ROIs for Experiment 2 are given in **Table 4.1**, along with their Z values in the above-mentioned contrast. In the case of rMFG ROI, as no significant differences were found in this area when the tasks in question were performed with the left hand, the peak voxel obtained from the right-hand contrast was used to create the left-hand ROI.



**Figure 4.6.** Brain areas showing significantly increased activity during the pantomimed tool use as compared to simple repetitive hand movements. Both actions were performed with the left hand.

**Table 4.1.** Regions of interest - spherical ROIs of 5-mm radius – from Experiment 2. ROIs were based on maximally-activated voxels from clusters involved in tool use pantomime vs. simple repetitive hand movements performed in an independent localizer task with the non-dominant left hand. MNI coordinates of the peak voxels and their Z values are reported.

Left hemisphere region	MNI coordinates			Peak Z value
	x	y	z	
rostral Middle Frontal Gyrus (rMFG, from Experiment 1)	-44	38	24	–
ventral Premotor Cortex (PMv)	-46	2	24	4.79
dorsal Premotor Cortex (PMd)	-22	-14	68	4.16
Superior Parietal Lobule (SPL)	-20	-66	58	4.03
anterior Supramarginal Gyrus (aSMG)	-60	-26	34	4.81
Lateral Occipito-Temporal Cortex (LOTc)	-48	-66	-8	4.86

In the **rMFG ROI**, a 2 (Task)  $\times$  4 (Action) ANOVA revealed no main effect of Task [ $F_{(1,19)} = 0.004, p = 0.95$ ], but a significant main effect of Action [ $F_{(3, 57)} = 18.1, p < 0.001$ ]. Specifically, performing tasks involving structural *grasp-to-pass* actions was associated with significantly stronger activity than performing tasks involving demanding functional *grasp-to-use* actions (Bf- $p < 0.01$ ), easy functional *grasp-to-use* actions (Bf- $p < 0.001$ ), or control

*reach-and-move* actions (Bf- $p < 0.001$ ). Similarly to Experiment 1, though, these results should be interpreted carefully because there was also a significant Task by Action interaction [ $F_{(3,57)} = 4.8, p < 0.01$ ]. Responses associated with planning each kind of grasp exceeded those evoked by the control condition (demanding functional grasps vs. control actions: Bf- $p < 0.01$ ; easy functional grasps vs. control actions: Bf- $p < 0.05$ ; structural grasps vs. control actions: Bf- $p < 0.001$ ). Moreover, planning structural grasps engaged the region more than planning easy functional grasps (Bf- $p < 0.01$ ), while there was no significant difference between planning structural grasp and demanding functional grasps (Bf- $p = 1.00$ ). In contrast, in the execution phase, performing structural grasps evoked larger responses than performing demanding functional grasps (Bf- $p < 0.01$ ). The observed effects are shown in **Figure 4.7A**.

In the **PMv ROI**, there was a significant main effect of Task [ $F_{(1,19)} = 15.0, p < 0.01$ ], such that planning actions was associated with significantly weaker activity than their execution. A significant main effect of Action [ $F_{(1,9,35,4)} = 11.5, p < 0.001$ ] revealed that performing tasks involving structural grasps engaged this region more than performing tasks involving easy functional grasps or control actions (Bf- $p < 0.01$  in both cases), and tasks concerning demanding functional grasps evoked larger responses than tasks concerning control actions (Bf- $p < 0.05$ ). A significant Task by Action interaction effect was observed again [ $F_{(2,37,4)} = 4.2, p < 0.05$ ]. As shown in **Figure 4.7B**, responses associated with planning each kind of grasp exceeded those evoked by the control condition (Bf- $p < 0.001$  in all cases). No significant differences between actions were found in the execution phase (Bf- $p = 1.0$  in all cases).

In the **PMd ROI**, the analysis revealed a main effect of Task [ $F_{(1,19)} = 93.9, p < 0.001$ ], such that planning actions was associated with significantly weaker activity than their execution. A main effect of Action was also significant [ $F_{(2,38,9)} = 7.6, p < 0.01$ ]. Namely, performing any task involving demanding functional grasps engaged the PMd more than performing tasks involving easy functional grasps (Bf- $p < 0.001$ ) or control actions (Bf- $p < 0.05$ ). The Task by Action interaction was revealed as well [ $F_{(3,57)} = 9.1, p < 0.001$ ], where planning demanding functional grasps engaged the region more than planning easy functional grasps, structural grasps, and control actions (Bf- $p < 0.01$ , Bf- $p < 0.05$ , Bf- $p < 0.001$ , respectively). There was also a trend towards larger responses evoked by planning structural grasps than by planning control actions (Bf- $p = 0.07$ ). Similarly to Experiment 1, in the execution phase, performing control actions evoked significantly larger responses than performing easy functional grasps (Bf- $p < 0.05$ ). These results are displayed in **Figure 4.7C**.

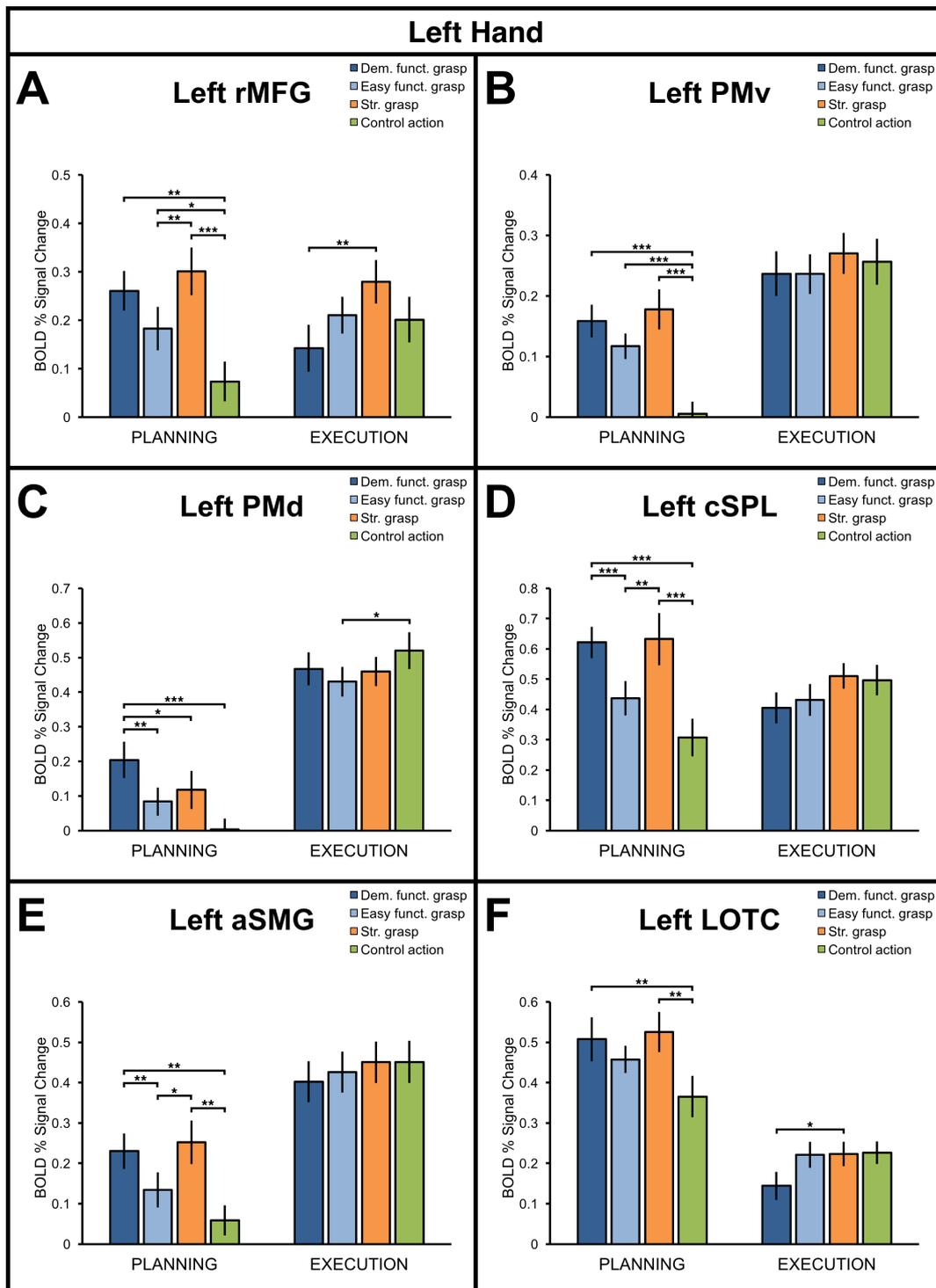
The pattern of activity found in the **cSPL ROI** for the non-dominant left hand closely resembled that observed in the same region for the dominant right hand. Namely, a main

effect of Task was not significant [ $F_{(1,19)} = 0.3, p = 0.59$ ]. There was a significant main effect of Action [ $F_{(2.3,42.8)} = 17.3, p < 0.001$ ], such that performing any task concerning demanding functional grasps or structural grasps resulted in higher activity than performing tasks concerning easy functional grasps (Bf- $p < 0.01$ , Bf- $p < 0.001$ , respectively) or control actions (Bf- $p < 0.05$ , Bf- $p < 0.001$ , respectively). The familiar Task by Action interaction effect was significant again [ $F_{(3,57)} = 12.3, p < 0.001$ ] and revealed that the effects of planning demanding functional grasps and planning structural grasps did not significantly differ from one another (Bf- $p = 1.00$ ), but they both engaged the cSPL more than planning easy functional grasps (Bf- $p < 0.001$ , Bf- $p < 0.01$ , respectively) and planning control actions (Bf- $p < 0.001$  in both cases). In the execution phase, there was a trend towards weaker engagement of the region by the execution of demanding functional grasps as compared to the execution of structural grasps (Bf- $p = 0.07$ ). The results are shown in **Figure 4.7D**.

In the **aSMG ROI**, a significant main effect of Task was observed [ $F_{(1,19)} = 16.1, p < 0.001$ ], such that planning actions was associated with significantly weaker activity than their execution. A significant main effect of Action [ $F_{(1.7,33.0)} = 9.0, p < 0.01$ ] revealed that performing tasks involving demanding functional grasps or structural grasps was associated with higher activity than performing tasks involving easy functional grasps (Bf- $p < 0.05$ , Bf- $p < 0.001$ , respectively), and tasks concerning structural grasps engaged this region more than tasks concerning control actions (Bf- $p < 0.01$ ). A significant Task by Action interaction [ $F_{(3,57)} = 6.2, p < 0.01$ ] showed that both planning demanding functional grasps and planning structural grasps employed this region more than planning easy functional grasps (Bf- $p < 0.01$ , Bf- $p < 0.05$ , respectively) or control actions (Bf- $p < 0.01$  in both cases). No significant differences between actions were found in the execution phase (Bf- $p > 0.29$  in all cases). The observed effects are shown in **Figure 4.7E**.

In the **LOTIC ROI**, there was a significant main effect of Task [ $F_{(1,19)} = 24.4, p < 0.001$ ], such that planning actions was associated with stronger activity than their execution, in contrast to the pattern observed for the left hand in PMv, PMd, and aSMG. A main effect of Action was also significant [ $F_{(2.3,45.5)} = 8.5, p < 0.001$ ] – performing tasks concerning structural grasps employed the region more than performing tasks concerning control actions (Bf- $p < 0.01$ ). A significant Task by Action interaction effect [ $F_{(3,57)} = 4.9, p < 0.01$ ] revealed that planning demanding functional grasps and planning structural grasps increased activity in the LOTIC more than planning control actions (Bf- $p < 0.01$  in both cases). In the execution phase, performing structural grasps engaged this region more than performing demanding functional grasps (Bf- $p < 0.05$ ), and performing easy functional grasps

tended to engage it more than performing demanding functional grasps ( $Bf-p = 0.08$ ). The results can be seen in **Figure 4.7F**.



**Figure 4.7. ROI analysis for Experiment 2.** Mean percent signal change within each ROI (A-F) is plotted relative to the resting baseline separately for two tasks (planning, execution) and the following actions: demanding functional *grasp-to-use* actions, easy functional *grasp-to-use* actions, structural *grasp-to-pass* actions, and control *reach-and-move* actions. Asterisks indicate differences with Bonferroni-corrected  $P$  values of at least 0.05 (\*), 0.01 (\*\*), or 0.001 (\*\*\*)

## 4.2. Discussion of Experiment 2

In summary, planning both functional *grasp-to-use* actions and structural *grasp-to-pass* actions as compared to planning control *reach-and-move* actions with the non-dominant left hand increased activity within a network of brain regions that was comparable to the one observed in Experiment 1. This result is consistent with the outcomes of numerous studies on transitive (tool use) actions performed with either hand (Bohlhalter et al., 2009; Jacobs et al., 2010; Króliczak & Frey, 2009; Mäki-Marttunen, Villarreal, & Leiguarda, 2014; Vingerhoets et al., 2012).

Similarly to Experiment 1, planning demanding functional as compared to structural grasps was associated with greater activity of predominantly dorso-dorsal stream areas – bilateral PMd (as revealed by the whole brain and ROI analyses) and contralateral aSPL – which again points to a greater biomechanical demands associated with planning grasps that required a major hand and wrist rotation. The additional engagement of SMA (not observed in Experiment 1) may suggest that planning demanding functional grasps with the left, less skilled hand required more extensive processing of the sensory consequences of movement (Makoshi, Króliczak, & van Donkelaar, 2011). Likewise PMd and SPL, this region has also been implicated in the preparation of reaching movements (Fabbri et al., 2014; Hoshi, 2004), and the integration of reach and grasp components of prehensile actions (Cavina-Pratesi et al., 2010).

Unlike in the case of the dominant hand, no brain areas were more engaged/less inhibited when planning easy functional grasps was compared with planning structural grasps, which suggests that in the case of non-dominant hand, even the simpler functional grasp was associated with substantial inhibition of the default mode network.

As in Experiment 1, both whole brain and ROI analyses revealed that rMFG and cSPL were invoked more by planning structural grasps than by planning functional grasps of similar kinematics. ROI analysis has demonstrated also the greater engagement of left-hemispheric ventro-dorsal stream area aSMG in the comparison in question. Unlike in Experiment 1, though, the activity in the PMv was too low to reach the significance threshold in the ROI analysis.

Relative to Experiment 1, planning demanding vs. easy functional grasps in Experiment 2 was associated with greater engagement of bilateral frontal, parietal, and medial cortices. As revealed by the ROI analysis, the strong trend observed in Experiment 1 for higher involvement of aSMG in planning demanding functional grasps reached here a significance threshold. These results suggest that compared to grasps with the same action

goal but lower biomechanical demands, planning functional grasps directed at tools presented in non-canonical orientations, albeit difficult with the dominant hand, is even more challenging when the non-dominant, less skilled hand is involved.

Differently from the case of the right hand, the results of LOTC ROI analysis for tasks performed with the left hand revealed no significant differences between the planning of any of the two functional grasps and the structural grasp. Instead, planning both demanding functional grasp and structural grasp – the most biomechanically and/or cognitively challenging actions in this study – engaged this area more than planning control actions, which again may reflect the less skilled/natural character of these actions performed with the non-dominant hand. This interpretation is in line with a recent study by Lausberg, Kazzner, Heekeren, and Wartenburger (2015), who demonstrated that left LOTC is specifically involved in simulated as compared to real actions, and its role may concern integrating the known *visuo-tactile image* of an object into the action plan. Thus, the more precise and/or specific finger configuration is required by the grasping task, the greater LOTC involvement observed.

Finally, consistently with the data for the dominant hand, the vast majority of within-task differences between the examined actions were detected in the planning phase and disappeared when participants made a progression from action planning to action execution. Once more, as revealed by the ROI analysis, the only area involved significantly more in planning actions than their execution was the left LOTC.

## Chapter 5. General discussion

The goal of this project was to probe the neural bases of preparing different goal-oriented interactions involving familiar tools. A series of two neuroimaging experiments was administered to a group of strongly right-handed participants. Their task was to plan and subsequently pantomime the execution of the following actions: (1) grasping a tool with an intention to use it in a function-appropriate way (functional grasp), (2) grasping a tool with an intention to pass it to a different person (structural grasp), and (3) reaching towards a tool and moving it with the back of the hand. The neural activity associated with these actions was examined separately for the dominant right hand (Experiment 1) and non-dominant left hand (Experiment 2). In what follows, I discuss the results of both experiments in the light of the three hypotheses put forward at the end of Chapter 1.

### 5.1. Hypothesis 1: PRN engagement in grasping tools

I predicted that relative to planning *reach-and-move* actions, planning both functional *grasp-to-use* actions and structural *grasp-to-pass* actions would involve the left-hemispheric network implicated in representing praxis skills in the human brain. This hypothesis was supported by the data concerning both the dominant right and the non-dominant left hand.

The fronto-parieto-temporal network in question has been shown to be involved in representing many higher order manual skills such as tool use actions (Choi et al., 2001; Hermsdörfer et al., 2007; Imazu et al., 2007; Johnson-Frey et al., 2005; Króliczak & Frey, 2009; Mäki-Marttunen et al., 2014; Moll et al., 2000; Vingerhoets et al., 2011), intransitive gestures (Bohlhalter et al., 2009; Fridman et al., 2006; Króliczak & Frey, 2009; Króliczak et al., 2016), visually-guided grasping with a hand or a tool (Jacobs et al., 2010; Króliczak et al., 2008; Marangon et al., 2011; Martin et al., 2011), grasping based exclusively on haptic information (Marangon, Kubiak, & Króliczak, 2016), or visual processing of skilled actions including tool use pantomimes (Kubiak & Króliczak, 2016). Noteworthy, based on the results of a functional connectivity study, Vingerhoets and Clauwaert (2015) has recently proposed that the production of hand postures for different action goals is mediated by a task-general neural network that involves all of the crucial nodes of PRN. According to the authors, depending on the goal of the current action, some nodes and/or their mutual connections would be differently engaged in the preparation and execution of goal-appropriate hand posture. The current results are in line with this proposition, but also extends it by suggesting

that the relative engagement of some nodes and/or the strength of their functional connections may be modulated by the hand involved in task preparation/execution. This suggestion, however, calls for further investigation.

## **5.2. Hypothesis 2: Ventro-dorsal divisions of PRN and goal-directed motor cognition**

My second hypothesis stated that a subset of areas within the praxis representation network – the areas of the ventro-dorsal stream – would be specifically involved in planning functional *grasp-to-use* actions as compared to structural *grasp-to-pass* actions. Intriguingly, this hypothesis was not supported by the current outcomes. When both types of grasps were directed towards tools presented in non-conventional orientations, the areas of the ventro-dorsal stream were engaged to a similar extent. Instead, in such conditions, areas linked to the dorso-dorsal stream demonstrated significantly greater involvement in planning functional than structural grasps.

The dorso-dorsal pathway of the fronto-parietal action circuit has been conceptualized as a neural substrate for *acting on objects* (Johnson & Grafton, 2003), a *Structure* (Buxbaum & Kalénine, 2010) or *Grasp* (Binkofski & Buxbaum, 2013) system specialized for grasping objects on the basis of their visually-perceived structural and spatial features, or a network subserving the moment-to-moment processing of objects' variable (i.e., derived from temporary object characteristics) affordances (Sakreida et al., 2016). In line with these proposals, the differences observed in aSPL, PMd, and sensorimotor regions for the contrast of planning demanding functional grasps vs. structural grasps point to the additional engagement of these areas associated with preparing actions that were biomechanically demanding and require a precise coordination of the wrist and finger movements (Davare et al., 2006; Fabbri et al., 2014; Grafton, Fagg, & Arbib, 1998; Króliczak & Frey, 2009; Macuga & Frey, 2014; Marangon et al., 2011). This interpretation is strengthened by the results of a direct comparison between demanding and easy functional grasps. Indeed, irrespective of the hand involved in task performance, both SPL and PMd were more invoked for the harder functional grips. Given that the responses were directed at the same target tools and motivated by the same action goal, this difference cannot be attributed to any higher-order tool-related processing (Przybylski & Króliczak, 2017).

Counter to Hypothesis 2 and in contrast to the previous reports highlighting the greater role of PRN in functional interactions with tools (e.g., Króliczak & Frey, 2009; Przybylski & Króliczak, 2017), the expected greater engagement of the ventro-dorsal stream areas in preparing tool-directed grasps was observed in the case of planning structural grasps as

compared to functional grasps of similar grasp kinematics. Specifically, planning structural grasps invoked substantially more the left rMFG, aSMG/aIPS, and cSPL, but also PMv, and, in the case of the right hand, also LOTC (as revealed by the ROI analysis). Importantly, these effects were mostly independent of the hand and suggest that the modulations of activity within some of the crucial PRN nodes are sensitive to more cognitively demanding aspects of task performance contingent on action goals (Boronat et al., 2005; Króliczak et al., 2008; Lingnau & Downing, 2015; Przybylski & Króliczak, 2017; Vingerhoets & Clauwaert, 2015).

The ventro-dorsal pathway of the fronto-parietal action circuit has been suggested to constitute a neural substrate for *acting with objects* (Johnson & Grafton, 2003), a *Function* (Buxbaum & Kalénine, 2010) or *Use* (Binkofski & Buxbaum, 2013) system computing skilled, functional object-related actions, or a network implicated in representing stable (i.e., related to invariant object features) affordances (Sakreida et al., 2016). Furthermore, areas of this pathway has been also linked to the retrieval of action semantics and inferring goals of the observed actions (Iacoboni, Molnar-Szakacs, Gallese, Buccino, & Mazziotta, 2005; Johnson Frey et al., 2003). The observed activation of the ventro-dorsal PRN areas in the current study extends these proposals by suggesting that not only functional, but also other actions performed in more complex cognitive settings or contexts, but still involving tools, may be represented within the ventro-dorsal stream. This could explain why there was no significant activation in higher-order areas devoted for tool-related skills when planning functional grasps was contrasted with planning structural grasps of similar kinematics, both separately for each hand, as well as in the whole-brain ANOVA. Furthermore, in light of this proposal, the greater engagement of brain areas linked to the ventro-dorsal PRN in preparing structural *grasp-to-pass* actions as compared to easy functional *grasp-to-use* actions may be explained by the less skilled nature of the structural grasps. Namely, as functional interactions with tools are more natural/stereotyped, the retrieval of their representations in response to pictures of tools is likely to be much easier than the preparation of actions necessary to pass an object to someone else (Tulving & Thomson, 1973; cf. Osiurak et al., 2013). Indeed, as indicated in Chapter 1, tool-related affordances may automatically potentiate a functional response, especially when it is the response required in half of the study trials (cf. Valyear et al., 2011). As a result, planning functional grasps in the current study might have been associated with weaker brain activity than planning structural grasps for which a greater effort was necessary (Króliczak & Frey, 2009; Króliczak et al., 2008). Furthermore, planning structural *grasp-to-pass* actions might have automatically invoked representations of the distant action context, such as images/thoughts of a potential receiver and/or his or her ability

to immediately use a handed tool. Preparing such a deliberate action would then be expected to engage the brain more, which indeed was the case in this study.

The proposed interpretation gains further support from the results of Functional Grasp Localizer performed by the participants of this study. A comparison between function-based grasps intended to use a tool vs. structure-based grasps intended to simply displace it to a different location revealed greater engagement of bilateral LOTC and aSPL/aIPS. Given that both actions were directed at the same target tools presented in the same orientations, this difference may be ascribed to the retrieval of the conceptual knowledge of functional actions associated with presented tools and/or the informed selection of the proper, function-appropriate hand posture (cf. Króliczak et al., 2016). The lack of significant differences in activity within LOTC in contrasts of functional *grasp-to-use* actions vs. structural *grasp-to-pass* actions for either the right or left hand, in either the whole brain or ROI analysis, suggests that conceptual and/or motor representations concerning tool-related actions were involved also in the preparation of grasps with an intention to pass an object to a different person. Note that in the case of the dominant right-hand, the activation of LOTC was even greater for planning structural grasps than for planning easy functional grasps, as revealed by the ROI analysis.

### **5.3. Hypothesis 3: Hand-independent left hemisphere dominance for action**

Finally, I predicted that the left-lateralized activity associated with planning functional *grasp-to-use* actions as compared to planning structural *grasp-to-pass* actions would be very similar independent of the tested hand. This hypothesis was directly related to Hypothesis 2, as I expected that the crucial differences between the study conditions, revealing the engagement of PRN in planning different manual interactions involving tools, would be observed in a comparison of planning functional grasps vs. structural grasps. However, this was not the case. The contrasts in question performed separately for the dominant right and the non-dominant left hand revealed hand-dependent, mostly contralateral engagement of brain areas belonging to bilateral dorso-dorsal stream (Binkofski & Buxbaum, 2013; Buxbaum & Kalénine, 2010; Johnson & Grafton, 2003; Sakreida et al., 2016). Instead, the most striking results of these study were observed in a comparison of planning structural grasps vs. functional grasps of similar kinematics. Indeed, both whole-brain analyses performed separately for each hand, as well as repeated-measures ANOVA revealed hand-independent leftward asymmetry of ventro-dorsal PRN areas involved in preparing *grasping-to-pass* actions. These results are consistent with hand-independent role of PRN in representing

skilled manual actions (Króliczak & Frey, 2009; Przybylski & Króliczak, 2017; Vingerhoets et al., 2012), as well as with the postulated specialization of the left hemisphere in the preparation and execution of visually-guided manual actions (Gonzalez, Ganel, & Goodale, 2006; Janssen, Meulenbroek, & Steenbergen, 2011; Schluter, Krams, Rushworth, & Passingham, 2001; Steenbergen, Meulenbroek, & Rosenbaum, 2004).

#### **5.4. Limitations and future directions**

Ecological validity of the study could be increased by the use of real objects instead of their photographs as stimuli (Brandi et al., 2014; Squires et al., 2015). Additionally, varying the order of Goal cue and Stimulus picture presentation would allow to investigate the influence of the presence of action context on affordance perception/action planning (Baumann, Fluet, & Scherberger, 2009).

As only right-handed participants were tested in the current study, the generalizability of its results to the left-handed population is limited. Both neuropsychological (Goldenberg, 2013) and neuroimaging (Vingerhoets et al., 2012) studies point to a less asymmetric (more bilateral) organization of cognitive and manual functions in the brains of sinistrals, as compared to dextrals. The reasons for this phenomenon are currently debated (Króliczak, 2013; Michałowski & Króliczak, 2015). Nevertheless, despite the fact that until recently left-handers remained a group that was underrepresented in scientific research (Willems, der Haegen, Fisher, & Francks, 2014), there is now growing evidence that a subset of areas linked to the praxis representation network is involved in complex manual actions independent of the handedness of the actor (Króliczak et al., 2016; Martin et al., 2011; Vingerhoets et al., 2012; Frey, Funnell, Gerry, & Gazzaniga, 2005).

A recently developed approach to neuroimaging data analysis – the multi-voxel pattern analysis (MVPA) – provides researchers with a tool to decode the information represented in the patterns of activity distributed across a population of voxels instead of looking for task-associated differences in the average response of a given brain region (Norman, Polyn, Detre, & Haxby, 2006). Hitherto, MVPA has been successfully used in distinguishing patterns of neural activity corresponding to different hand- or tool-mediated actions directed towards simple neutral objects (Gallivan, Chapman, Mclean, Flanagan, & Culham, 2013; Gallivan et al., 2015; Gallivan, McLean, Flanagan, et al., 2013; Gallivan, McLean, Valyear, et al., 2013; Gallivan, McLean, Valyear, Pettypiece, & Culham, 2011), reaching and grasping movements performed in different directions (Fabbri et al., 2014), planning actions driven by external cues or internal choices (Ariani et al., 2015), and

representations of action and function knowledge of tools (Chen et al., 2015). Therefore, it seems perfectly suited for extending the results of the current study by investigating a more fine-grained patterns of neural activity underling the planning of hand-tool interactions motivated by disparate goals.

Another interesting avenue for future research is to examine the relationship between the lateralization of activity associated with planning meaningful (i.e., not exclusively functional) tool-directed actions and the activity observed during language-related tasks. Based on previous studies demonstrating a link between the functional and/or structural organization of manual and cognitive skills, such as language, in the human brain (Biduła & Króliczak, 2015; Króliczak, Piper, & Frey, 2011; Vingerhoets, Alderweireldt, et al., 2013; Roby-Brami, Hermsdörfer, Roy, & Jacobs, 2012; Corballis, Badzakova-Trajkov, & Häberling, 2012; van Schie, Toni, & Bekkering, 2006), it can be predicted that a significant correlation between the activity related to each of the tasks would be found.

## Conclusions

The present study is one of the first functional magnetic resonance imaging studies to directly compare the neural underpinnings of planning different goal-oriented interactions involving common tools. In a series of two experiments the present study demonstrated that the critical nodes of the praxis representation network (PRN) implicated in the processing of purposeful, skilled hand movements were engaged significantly more in preparation for actions that were not use related, but, nevertheless, involve tools. This was the case irrespective of the hand used for task performance.

These findings contribute to the field of cognitive neuroscience of action by shedding a new light on how disparate intended action outcomes combined with task constraints influence the perception of object affordances, and to what extent they modulate the fMRI activity within the parieto-frontal action networks. Specifically, the results of the present study refine our understanding of the role of PRN in the control of goal-directed behavior and indicate that modulations of activity within the ventro-dorsal PRN areas are sensitive to more cognitively demanding aspects of task performance contingent on action goals.

Future research could extend upon the outcomes of the current study to examine whether manipulating the distant context of action may influence the role played by core function-related object features in the planning of disparate functional and non-functional actions involving tools. Furthermore, the present findings could potentially inform the methods of assessing praxis-related disorders in patients suffering from ideomotor apraxia. Together, such investigations might have an impact on theories of affordance processing and action organization in the human brain.

## Summary

The way we manipulate tools varies substantially depending on the intended outcome of action. Although the neural underpinnings of functional interactions with such objects are relatively well understood, little is still known about the neural representations underlying the planning and execution of actions that are not use related, but nevertheless involve tools.

The aim of this thesis was to investigate the contribution of the praxis representation network (PRN) – a set of left-hemispheric parietal, frontal, and temporal areas implicated in the control of skilled, purposeful manual actions such as using tools – to the preparation of actions directed at familiar tools and motivated by disparate, both functional and non-functional goals. It was hypothesized that PRN, and particularly its ventro-dorsal divisions, would be engaged more in planning actions related to objects' functions. A series of two functional magnetic resonance imaging experiments was administered to 20 strongly right-handed participants. Their task was to plan and subsequently pantomime the execution of the following actions: (1) grasping a tool with an intention to use it in a function-appropriate way, (2) grasping a tool with an intention to pass it to a different person, and (3) reaching towards a tool and moving it with the back of the hand. Neural activity associated with these actions was examined separately for the dominant right hand and non-dominant left hand.

The results showed that contrary to the predictions, the key nodes of PRN were more involved in planning grasping actions that did not involve tool use. This was the case irrespective of the hand used for task performance. These findings refine our understanding of the role of praxis representation network in the control of goal-directed behavior and indicate that modulations of activity within its ventro-dorsal divisions are sensitive to more cognitively demanding aspects of task performance. Consequently, this thesis contribute to the field of cognitive neuroscience of action and shed a new light on how disparate intended action outcomes combined with task constraints influence the perception of object affordances, and to what extent they modulate the fMRI activity within the parieto-frontal action networks and beyond them.

**Keywords:** action planning, affordances, grasping tools, motor cognition, tool use

## Streszczenie

Sposób, w jaki manipulujemy narzędziami różni się istotnie w zależności od zamierzonego efektu działania. Choć neuronalne podłoże funkcjonalnych interakcji z takimi przedmiotami zostało stosunkowo dobrze poznane, wciąż niewiele wiadomo na temat neuronalnych reprezentacji leżących u podstaw planowania oraz realizacji działań, które nie są związane z użyciem narzędzi, ale mimo to ich dotyczą.

Celem niniejszej pracy było zbadanie udziału sieci reprezentującej prakcję (*praxis representation network*, PRN) – zbioru lewopółkulowych obszarów ciemieniowych, czołowych oraz skroniowych związanych z kontrolą umiejętności, celowych działań manualnych, takich jak użycie narzędzi – w przygotowywaniu działań, które dotyczyły znanych narzędzi, ale motywowane były różnymi, zarówno funkcjonalnymi, jak i niefunkcjonalnymi celami. Postawiono hipotezę, że PRN, a szczególnie jej brzuszno-grzbietowa część, będzie bardziej zaangażowana w planowanie działań związanych z funkcjami przedmiotów. Dwudziestu silnie praworęcznych uczestników wzięło udział w serii dwóch eksperymentów z wykorzystaniem obrazowania funkcjonalnym rezonansem magnetycznym. Zadaniem osób badanych było zaplanowanie, a następnie wykonanie pantomimy następujących czynności: (1) chwycenie narzędzia z zamiarem użycia go zgodnie z jego funkcją, (2) chwycenie narzędzia z zamiarem podania go innej osobie, (3) sięgnięcie w kierunku narzędzia i odsunięcie go wierzchem dłoni. Aktywność neuronalna mózgu skojarzona z wykonywaniem tych zadań analizowana była osobno dla dominującej ręki prawej i niedominującej ręki lewej.

Wyniki analiz pokazały, że w przeciwieństwie do przewidywań, kluczowe węzły PRN były bardziej zaangażowane w planowanie działań, które nie dotyczyły użycia narzędzi. Było tak niezależnie od ręki, którą wykonywano zadanie. Powyższe ustalenia ulepszają nasze zrozumienie roli, jaką sieć reprezentująca prakcję pełni w kontrolowaniu celowych działań. Wskazują one także, że modulacje aktywności w obszarach brzuszno-grzbietowych PRN są wrażliwe na te z aspektów wykonania zadania, które są bardziej wymagające pod względem poznawczym. W rezultacie niniejsza praca wnosi wkład do dziedziny neuronauki poznawczej, rzucając nowe światło na to, w jaki sposób zamierzone efekty końcowe działań, w połączeniu z ograniczeniami narzuconymi przez zadanie, wpływają na percepcję afordancji przedmiotów oraz do jakiego stopnia modułują one aktywność fMRI w ciemieniowo-czołowych sieciach związanych z działaniami oraz poza nimi.

**Słowa kluczowe:** afordancje, chwytanie narzędzi, planowanie działania, poznanie motoryczne, używanie narzędzi

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## Appendix

**A list of tools used in Experiments 1 and 2:** clothes peg, comb, dropper, eraser, hammer, key, nail file, rake, screwdriver, spatula, razor, wrench.

**A list of tools used in Functional Grasp Localizer:** corkscrew, lighter, scissors, sprinkler, syringe, toothbrush.

**A list of tools used in the Tool Use Localizer:** ax, hammer, knife, masher, paintbrush, peeler, pliers, screwdriver, shovel, scissors, wrench.

**A list of animals used in the Tool Use Localizer:** bat, bear, dolphin, elephant, fish, horse, hummingbird, orca, parrot, pigeon, sea turtle, wolf.