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Perception meets action: fMRI and behavioural investigations of human tool use

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Graduate Program in Neuroscience
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PERCEPTION MEETS ACTION: fMRI AND BEHAVIOURAL INVESTIGATIONS OF HUMAN TOOL USE

(Spine title: fMRI and Behavioural Investigations of Human Tool Use)

by

Kenneth F. Valyear

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A thesis submitted in partial fulfilment
of the requirements for the degree of
Doctor of Philosophy

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
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Perception Meets Action: fMRI and Behavioural Investigations of Human Tool Use

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Abstract

Tool use is essential and culturally universal to human life, common to hunter-gatherer and modern advanced societies alike. Although the neuroscience of simpler visuomotor behaviours like reaching and grasping have been studied extensively, relatively little is known about the brain mechanisms underlying learned tool use.

With learned tool use, stored knowledge of object function and use supervene requirements for action programming based on physical object properties. Contemporary models of tool use based primarily on evidence from the study of brain damaged individuals implicate a set of specialized brain areas underlying the planning and control of learned actions with objects, distinct from areas devoted to more basic aspects of visuomotor control. The findings from the current thesis build on these existing theoretical models and provide new insights into the neural and behavioural mechanisms of learned tool use.

In Project 1, I used fMRI to visualize brain activity in response to viewing tool use grasping. Grasping actions typical of how tools are normally grasped during use were found to preferentially activate occipitotemporal areas, including areas specialized for visual object recognition. The findings revealed sensitivity within this network to learned contextual associations tied to stored knowledge of tool-specific actions. The effects were seen to arise implicitly, in the absence of concurrent effects in visuomotor areas of parietofrontal cortex. These findings were taken to reflect the tuning of higher-order visual areas of occipitotemporal cortex to learned statistical regularities of the visual world, including the way in which tools are typically seen to be grasped and used. These areas are likely to represent an important source of inputs to visuomotor areas as to learned conceptual knowledge of tool use.

In Project 2, behavioural priming and the kinematics of real tool use grasping was explored. Behavioural priming provides an index into the planning stages of actions. Participants grasped tools to either move them, grasp-to-move (GTM), or to demonstrate their common use, grasp-to-use (GTU), and grasping actions were preceded by a visual preview (prime) of either the same (congruent) or different (incongruent) tool as that which was then acted with. Behavioural priming was revealed as a reaction time advantage for congruent trial types, thought to reflect the triggering of learned use-based motor plans by the viewing of tools at prime events. The findings from two separate experiments revealed differential sensitivity to priming according to task and task setting. When GTU and GTM tasks were presented separately, priming was specific to the GTU task. In contrast, when GTU and GTM tasks were presented in the same block of trials, in a mixed task setting, priming was evident for both tasks. Together the findings indicate the importance of both task and task setting in shaping effects of action priming, likely driven by differences in the allocation of attentional resources. Differences in attention to particular object features, in this case tool identity, modulate affordances driven by those features which in turn determines priming. Beyond the physical properties of objects, knowledge and intention of use provide a mechanism for which affordances and the priming of actions may operate.

Project 3 comprised a neuroimaging variant of the behavioural priming paradigm used in Project 2, with tools and tool use actions specially tailored for the fMRI environment. Preceding tool use with a visual preview of the tool to be used gave rise to reliable neural priming, measured as reduced BOLD activity. Neural priming of tool use was taken to reflect increased metabolic efficiency in the retrieval and implementation of stored tool use plans. To demonstrate specificity of priming for familiar tool use, a control task was used whereby actions with tools were determined not by tool identity but by arbitrarily learned associations with handle colour. The findings revealed specificity for familiar tool-use priming in four distinct parietofrontal areas, including left inferior parietal cortex previously implicated in the storage of learned tool use plans. Specificity of priming for tool-action and not colour-action associations provides compelling evidence for tool-use-experience-dependent plasticity within parietofrontal areas.

Keywords: tool use, action priming, affordances, grasping, action planning, fMRI, visuomotor control, inferior parietal cortex, ventral and dorsal visual streams

Co-Authorship

All contents of the current thesis were carried out in collaboration with my advisor, Dr. Jody C. Culham. The research and writing were supervised by Dr. Culham, who contributed to every aspect of the work (e.g. experimental design, data analysis, interpretation, manuscript write-up). Project 2 (Chapter 3) was an additional collaboration with Craig Chapman, Jason Gallivan, and Robert Mark. Jason Gallivan and Craig Chapman assisted with the design of the experiment, data collection, analysis, interpretation, and provided feedback on the written manuscript. Robert Mark assisted with data collection and provided feedback on the written manuscript. Project 3 (Chapter 4) involved additional collaboration with Jason Gallivan and Adam Maclean, both of whom were involved with project design, data collection, and manuscript write-up. Adam Maclean also helped with programming stimuli for presentation in the MR unit and operated the scanner. The written material in this thesis is my own work, but, as my advisor, Dr. Culham provided assistance, editing and revising all aspects of the writing.

Acknowledgments

First and foremost, I would like to acknowledge my supervisor, Dr. Jody Culham. Jody has been such an incredible mentor (and friend) over the years. She has provided me with such tremendous support and encouragement, patience and understanding, and has helped me to push through difficult times when my confidence in myself had wavered. Her guidance and insights have been absolutely pivotal in my progression as a scientist and researcher. One of Jody's greatest talents is her ability to teach, to communicate difficult concepts in a way that is easily absorbed and understood, and I have benefited tremendously from this. It is through her teaching and intellectual brilliance that I have grown as a researcher and academic. I could not have asked for a better mentorship, and will forever be grateful for these opportunities and experiences.

Next, I would like to thank my friends and co-authors, Jason Gallivan, Craig Chapman, Adam McLean, and Robert Mark. I have been friends and colleagues with these guys for many years now, and they have each contributed a great deal to the progression of the work presented here. We have shared countless discussions and have developed great friendships that extend beyond our work in the lab. Working with these guys has been terrific, each very bright and talented young researchers with so much to offer. I envision great and lasting friendships between us, and can only hope to continue our collaborations in the future.

I would also like to extend my thanks to the Culham and Goodale labs on the whole, both past and present members. This environment has been essential in my growth as an academic. So many great minds, and with such a cooperative nature; it has been an honour and privilege to be part of this group. To name a few individuals in particular, I would like to thank Daniel Wood, Jon Cant, Gavin Buckingham, Lucia van Eimeren, Lore Thaler, Cristiana Cavina-Pratesi, Tzvi Ganel, Erik Chang, David Whitney, Herb Goltz, Jennifer Steeves, and Haitao Yang for all of their thoughtful feedback, discussions, and insights over the years.

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Other individuals that I would like to thank include Elizabeth Hampson, who also served on my Advisory Committee for the majority of my graduate career. She has always been so kind and helpful. Elizabeth also generously agreed to serve as an Examiner, where she gave fair and insightful feedback on my thesis. Other professors whom I worked with during my Comprehensive exams, Ken McRae, Rob Bartha, Mel Goodale, and Matt Heath, were terrific teachers, and I would like to say thanks for their patience, guidance, and support. A special thanks to Scott MacDougall-Shackleton. Scott got me into research in the first place, taking me on as an undergraduate and then as a part-time research assistant in his lab. I learned a great deal from Scott during those early years; he is a terrific guy, and I am sure Scott is the reason why I was later hired by Jody and Mel. He must have said something good about me, and for that I will always be thankful.

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My family has always given me unconditional love and support. Without them I would not have been able to accomplish these goals. I am thankful and proud to have such a loving and supportive family. I know just how privileged I am for this, and I owe them great thanks for hanging in there and for continuing to encourage and support me over these years.

Finally, I wish to thank my bright and beautiful girlfriend Christina Merkley. For the last year and a half Christina and I have lived together, and as a new young couple living together for the first time we have worked through and mastered many challenges; a big one being our success in navigating the stresses and pressures of completing my PhD with success. Many long hard days and nights at work, and it was Christina there beside me, urging me forward, reminding me of my goals and filling me up with a belief in myself when my confidence had suffered. She believed in me when I did not, and it was her love, support, and encouragement that kept me at it. She understood when I needed time and space, when the work was all-consuming, when everything else around me had faded, she understood and continued to love and support me when I needed it most. I cannot measure nor hope to reciprocate all that she has done for me. But rather, I must simply say thank you Christina, I could not have done this without you.

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List of Abbreviations

3D: three dimensional
7a: visual area 7a
AG: atypical grasping
AIP: anterior intraparietal area
aIPS: anterior intraparietal sulcus
aTP: anterior temporal poles
BA: Broadmann's area
BDNF: brain-derived neurotrophic factor
BOLD: blood oxygenation level dependent
BSC: BOLD signal change
CC: colour changed
cm: centimetres
CR: colour repeated
EBA: extrastriate body area
EEG: electroencephalography
EPI: echo-planar image
ERP: event-related potential
F2: dorsal premotor area
F5: ventral premotor area
FA: flip angle
FBA: fusiform body area
fMRI: functional magnetic resonance imaging
GABA: gamma-aminobutyric acid
GLM: general linear model
GTM: grasp-to-move
GTU: grasp-to-use
Hz: hertz
IM: ideomotor apraxia
IPL: inferior parietal lobule
IPS: intraparietal sulcus
IREDS: light-emitting infrared diodes
lbs: pounds
LCD: liquid crystal display
L-dPreC: Left dorsal precentral cortex
LED: light-emitting diode
L-IPL: left inferior parietal lobule
LIPv: ventral lateral intraparietal area
LO: lateral occipital object area
LOC: lateral occipital complex
L-vPreC: left ventral precentral cortex
M: mean
M1: primary motor area
MFG: mid-fusiform gyrus
MIP: medial intraparietal area

mm: millimetres
mPO: medial parieto-occipital cortex
mOPJ: medial occipito-parietal junction
mIPS: medial intraparietal sulcus
mRNA: messenger ribonucleic acid
ms: milliseconds
MST: medial superior temporal area
MT: middle temporal area
MT+: middle temporal motion complex (area MT and MT+)
NT-3: neurotrophin 3
OA: optic ataxia
PET: positron emission tomography
pMTG: posterior middle temporal gyrus
PPC: posterior parietal cortex
RF: receptive field
RM-ANOVA: repeated measures analysis of variance
ROI: region of interest
RS: repetition suppression
R-SPL: right superior parietal lobule
s: seconds
SD: semantic dementia
SEM: standard error of the mean
SPECT: single photon emission computed tomography
SPL: superior parietal lobule
STS: superior temporal sulcus
T1: anatomical magnetic resonance image
T2*: functional magnetic resonance image
TC: tool changed
TE: time to echo
TEO: macaque posterior inferior temporal area
TG: typical grasping
TI: inversion time
TMS: transcranial magnetic stimulation
TPJ: temporoparietal junction
TPOc: caudal temporal parietal occipital
TR: tool repeated
tRF: tactile receptive field
***trk*B**: brain-derived neurotrophic factor receptor
V1: primary visual area
V4: visual area four
V6: visual area 6, within parieto-occipital cortex
V6A: visual area, just dorsal and anterior to V6
VIPm: medial ventral intraparietal area
vRF: visual receptive field
vTO: ventral temporo-occipital object area
WSD: Tukey’s wholly significant difference

Chapter 1

1. General introduction

1.1. Why study the cortical basis of human tool use?

From an evolutionary perspective, the study of human tool use and the brain is an extremely fascinating topic. In a span of less than one million years, brain size nearly doubled between *Homo habilis* (600-700 cc) and *Homo erectus* (900-1100 cc), and continued to increase with the emergence of modern *Homo sapiens* (approximate brain size of 1350 cc) (Holloway, 1996; Wilson, 1998, p. 18). The fossil evidence indicates concurrent advancements in tool-using and -making, generally agreed upon to have played a driving force in brain expansion (K. R. Gibson, 1993; Marzke, 1996; Washburn, 1960; Wilson, 1998; Wynn, 1996). In Wilson's *The Hand*, a compelling argument is made for how anatomical modifications to the hand of early humans greatly increased the flexibility and potential for far more complex object manipulation, which in turn helped drive new neural representations (see also Napier, 1993). Wilson highlights deep connections between language, thought, and complex tool use. Continuing interest in the neuroscience of human tool use alongside comparative studies of tool use in nonhuman primates is likely to reveal new insights as to the fundamental nature and evolutionary origins of human cognition.

The study of tool use and the brain is also interesting as a model of functionally distinct but interacting cortical systems. Both contemporary (Buxbaum, 2001; Johnson-Frey, 2004; Rothi, Ochipa, & Heilman, 1997) and longstanding (Geschwind, 1965; Liepmann, 1980) models of human tool use indicate functionally distinct brain areas underlying distinct types of knowledge. The strongest evidence for dissociable representations stems from the study of patients with brain damage. A wide variety of distinct neuropsychological conditions lead to problems with tool use, and the kinds of problems that arise following brain damage differ greatly depending on which areas have been compromised. Separation between systems underlying conceptual versus procedural motor representations of tool use is common. However, a clear picture of the cortical basis of tool use based on neuropsychological evidence appears to be exceedingly out of reach. Incredible variation in the number of distinct manifestations of disorder that bear relevance to the study of tool use, somewhat ironically, stands as a significant roadblock to progress. No single neuropsychological model to date can account for all the various patient dissociations that have been reported. Human neuroimaging techniques like fMRI offer a valuable complement to patient research in this area. In contrast to patient work, which provides a window into the functions of a damaged network of brain areas, fMRI reveals the activity of widely distributed cortical networks. Findings from the current thesis provide clear illustration of how neuroimaging experiments can extend existing models of tool use derived from neuropsychology.

The study of tool use is also the study of relatively high-level action planning. For good reason, the vast majority of previous work has focused on simpler visuomotor behaviours like reaching and grasping. These studies reveal key principles, essential behavioural and neural mechanisms. We now know a great deal about the planning and control of grasping according to location, orientation, and physical properties of target objects. However, to date, grasping has been primarily addressed within the context of actions where the end goal is prehension (to simply grasp). In real life, grasping is almost always part of a greater action plan, with specific goals in mind; we rarely (if ever) grasp objects just for the sake of grasping. The field is now well poised to advance new questions, such as the driving influence of high-level goals and intentions on the programming of actions. Tool use is one clear example of this. High level action goals supervene requirements for action programming according to low level properties like object size, shape, orientation, and spatial location. Tool use also offers a unique opportunity to study how stored object knowledge is used to plan actions. These ideas represent a focal point of the current thesis – I set out to disentangle behavioural and neural mechanisms tied to learned aspects of tool use (identity, function, and use) from factors tied to physical object properties.

The current thesis is framed within the context of existing models of tool use based primarily on evidence compiled from neuropsychology. The concept of dissociable but interacting cortical systems represents a major overarching theme. I begin with a review of the two visual streams hypothesis and the distinction between systems underlying vision-for-perception versus vision-for-action (section 1.2). The model clearly predicts that tool use must involve the coordination of both visual streams. Specialization of inferior parietal areas for tool use is also implicated, developed further in convergence with newer more detailed accounts (section 1.4). A left-lateralized inferior parietal stream for learned tool use is distinguished from a bilaterally represented superior parietal stream devoted to online visuomotor control (Figure 1.3).

Findings from neural recording studies of grasping and tool use in monkeys (section 1.3) also played a distinct role in motivating the current projects. In a general sense, given the highly constrained nature of cellular evolution (Krubitzer, 2009), neural mechanisms of grasping and tool use in monkeys are likely to have at least partial correspondence in humans. Further, several distinct findings from monkey neurophysiology have had a direct impact on the development of specific hypotheses put forth in the current thesis. Namely, the response properties of two particular neuron types (section 1.3.1) indicate that parietofrontal areas important for grasping are activated by merely viewing objects (canonical neurons) and/or object-directed actions (mirror neurons) even in the absence of overt movement. Viewing tools (Projects 2 and 3) and tool use grasping actions (Project 3) were hypothesized to activate motor areas important for tool use. Also, neurophysiological studies of tool use in monkeys provide dramatic examples of experience-dependent plasticity (section 1.3.2). Such findings provide an important basis for assumptions made about cortical plasticity and learned tool use in humans. An overarching hypothesis of the current thesis is that tool use learning gives rise to changes in the brain that serve to represent paired associations between tools and actions, and that such representations are detectable at the systems level (i.e. at the level of gross populations of cortical neurons, visible at the resolution of standard neuroimaging methods).

1.2. The visual brain divided

Despite our conscious experience of the visual world as a unitary phenomenon, research in psychology and neuroscience has revealed the neural physiology of vision as a highly modular process. The beginnings of modular models of vision perhaps best owe to the work of Schneider (Schneider, 1969; although see also Trevarthen, 1968, cited in

Milner & Goodale, 1995), who with lesion methods in the hamster provided evidence for fundamentally different functional roles between the retinal pathways projecting to superior colliculus, important for maze navigation, versus those projecting to striate cortex, important for pattern discrimination. Also, by re-wiring neural pathways in the frog, Ingle (1973) showed that distinct visual channels give rise to the control of distinct motor behavior; retinal projections to the optic tectum were found to mediate visual control of prey catching, whereas projections to the pretectal nuclei were shown to mediate visual control of obstacle avoidance. This early work clearly demonstrates the partitioning of visual function along distinct channels; however, the first great steps in uncovering functional modularity of vision at the ***cortical*** level were made by Mishkin, Ungerleider and colleagues in their seminal work with macaque monkeys (Mishkin, 1972; Mishkin, Lewis, & Ungerleider, 1982; Mishkin & Pribram, 1954; Mishkin & Ungerleider, 1982; Mishkin, Ungerleider, & Macko, 1983; Ungerleider & Brody, 1977; Ungerleider & Mishkin, 1982; Ungerleider & Pribram, 1977). In an important initial study by Pohl (1973), lesions were made to either a ventral pathway projecting from occipital to inferior temporal cortex or a dorsal pathway projecting from occipital to posterior parietal cortex and then performance on two types of tasks was tested. One task required the discrimination of two objects based on distinct visual features (shape, colour, and texture), while the other task required discrimination between two possible targets based on their spatial proximity with respect to a landmark item. Lesions to the ventral pathway gave rise to deficits in the object discrimination task but not the spatial landmark task; whereas lesions to the dorsal pathway led to the reverse pattern, deficits in the landmark but not the object discrimination task. Following these and other related findings, Ungerleider and Mishkin (1982) proposed a distinction between 'object vision' as mediated by inferotemporal cortex and 'spatial vision' as mediated by posterior parietal cortex (see also Mishkin, 1972; Mishkin et al., 1983). In this view, both streams are important for conscious visual perception, but are tuned to different features of the visual array: the ventral 'what' pathway is tuned to intrinsic object features and mediates identification, whereas the dorsal 'where' pathway is tuned to spatial relations between objects and mediates localization. The model was found to nicely account for a number of findings from human neuropsychology (Balint, 1909; Hecaen & De Ajuriaguerra, 1954; Kimura, 1963; Ratcliff & Davies-Jones, 1972; Warrington, 1982; Warrington & James, 1967) monkey electrophysiology (Gross & Mishkin, 1977; Gross, Rocha-Miranda, & Bender, 1972; Hyvärinen & Poranen, 1974; Robinson, Goldberg, & Stanton, 1978), and subsequently carried well with neural computational methods of the time (Vaina, 1990).

The next major advancements were made by Goodale and Milner (1992; Goodale, Milner, Jakobson, & Carey, 1991; Milner & Goodale, 1995) who re-characterized the roles of the dorsal and ventral visual streams, in what is now known as the two visual streams hypothesis. According to this view, the ventral stream provides the rich and detailed conscious visual experience of the world around us, critical for the perception and recognition of objects (vision-for-perception), whereas the dorsal stream is devoted to the visual guidance and control of actions, responsible for the (unconscious) transformation of visual information to appropriate motor outputs (vision-for-action) (Figure 1.1). The authors formulate a thorough and convincing account, not only backed by a wealth of scientific evidence from a wide range of disciplines, but also in confluence with a number of sensible theoretical principles that map onto the proposed functions of either stream. I will return to this point, and provide some coverage of these basic principles in my discussion of tool use and the two visual streams hypothesis below. But first, consideration of a particular set of findings from the work of Goodale and colleagues derived from testing a single patient, DF, provide a nice illustration of the contrasts between dorsal and ventral stream functions (Goodale & Milner, 2004). Indeed, these discoveries with patient DF have come to represent a kind of centrepiece of the two streams model. DF suffered from carbon monoxide poisoning, and as a result has bilateral lesions to her lateral occipitotemporal cortex (ventral stream). Consistent with the two streams model and the proposed functions of the ventral stream, DF can no longer perceive the form or orientation of objects, and thus cannot recognize objects on the basis of vision alone. What is truly remarkable about DF is that she can nonetheless use vision to accurately guide her actions; for example, to grasp those same objects she fails to recognize. Indeed, the way DF shapes her hand when grasping demonstrates that she has access to visual information about the size of objects, opening and closing her hand on route to an object (in ‘flight’) just as neurologically healthy individuals do, with appropriate extent (‘scaling’) and timing according to object size and location. However, when asked to indicate the size of these same objects by simply opening her hand to an extent that reflects perceived object size, without actually executing a grasp, paradoxically, she performs badly. Similarly, DF chooses appropriate points on an object to place her fingers and thumb when grasping in accordance with object shape, but yet when asked to discriminate two of these same objects based on whether or not they are the same shape or different, her performance is again very poor; showing chance levels of accuracy, as if she was simply guessing. Likewise, DF is able to access information about the orientation of a visual stimulus, but only when that stimulus is the target of an action. In all of these examples, visual information about the physical properties of objects (size, shape, and orientation) is clearly accessible to DF’s motor system for the guidance of action, but at the same time she appears ‘perceptually blind’ to this same information. Presumably, it is DF’s largely intact dorsal stream that allows her to use vision for action in the absence of conscious visual recognition.

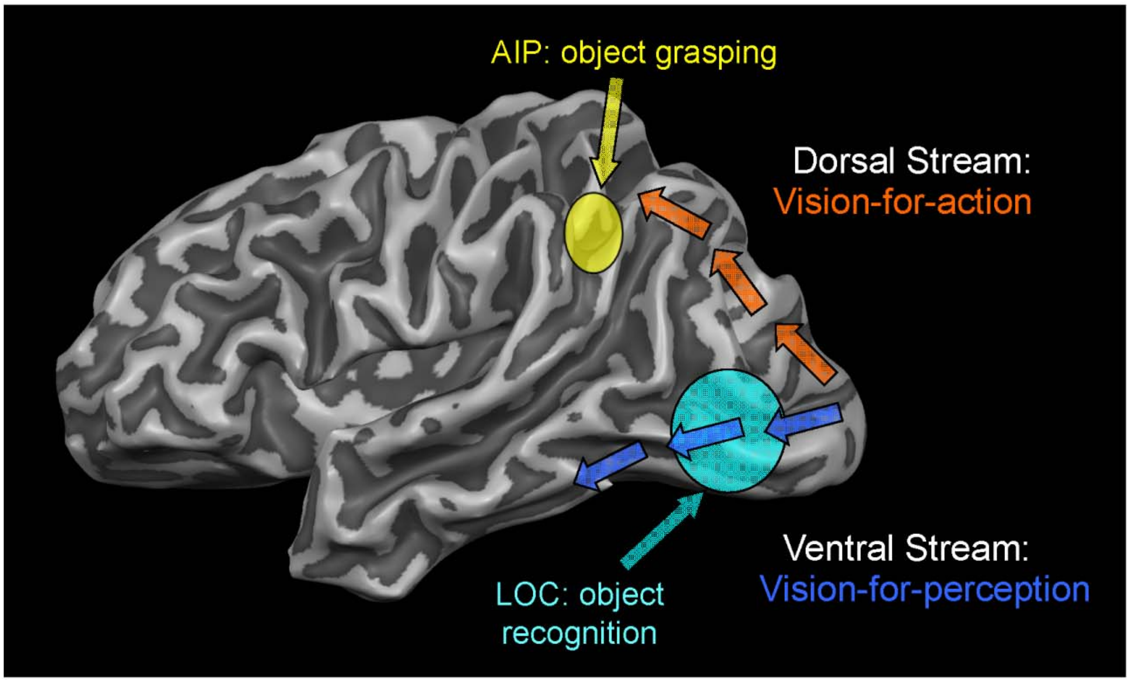

Figure 1.1. The two visual streams hypothesis (Goodale & Milner, 1992). The dorsal stream, shown with orange arrows, projects from occipital to posterior parietal cortex and is specialized for the control of actions. For example, a dorsal stream area at the anterior extent of the intraparietal sulcus, area AIP, shown in yellow, is critical for object grasping (Culham, 2003). The ventral stream, shown with blue arrows, projects from occipital to lateral and inferior temporal cortex and is specialized for visual perception. For example, a collection of areas within the ventral stream, known as the lateral occipital complex (LOC), shown in cyan, is critical for object recognition (Malach et al., 1995).

Milner and Heywood (1989) provide the first descriptions of DF's deeply impaired perceptual deficits, with a later description of her astonishingly good visuomotor abilities in the face of such impairments presented a few years later (Goodale et al., 1991). Since these fascinating discoveries, our group has studied a second patient, MC, with extensive damage to early visual and ventral stream areas, who shows similarly startling dissociations between impaired vision-for-perception and spared vision-for-action (Culham, Witt, Valyear, Dutton, & Goodale, 2008; Goodale et al., 2008). Likewise, Karnath and colleagues (2009) recently describe a patient with focal damage to the ventral but not dorsal pathway who, like patients DF and MC, shows preserved grasping and visuomotor control in the face of severe perceptual recognition deficits.

Importantly, with damage to the dorsal but not ventral stream, the opposite patterns of deficit and preserved function often emerge. Patients with optic ataxia as a result of damage to posterior parietal cortex (dorsal stream) show problems with online control of actions such as reaching and grasping, but yet are able to perceive and recognize objects perfectly well (Goodale et al., 1994; Milner & Goodale, 1995, pp. 92-101; Perenin & Vighetto, 1988). Visual form agnosia versus optic ataxia therefore constitutes a double dissociation between vision-for-perception versus vision-for-action, in strong support of the Goodale and Milner two visual streams account.

1.2.1. Visuomotor control and the dorsal stream

The dorsal visual stream originates in primary visual cortex and extends to posterior parietal cortex (PPC), which is densely interconnected with both dorsal and ventral premotor areas of frontal cortex. A number of studies have comprehensively mapped monkey parietofrontal connectivity (Andersen, Asanuma, Essick, & Siegel, 1990; Cavada & Goldman-Rakic, 1989; Goldman-Rakic, 1996; Lewis & Van Essen, 2000a; Seltzer & Pandya, 1980; Wise, Boussaoud, Johnson, & Caminiti, 1997), and cytoarchitecture (Lewis & Van Essen, 2000b); as well as more recent mapping efforts in humans (H. J. Choi et al., 2006; Eickhoff, Grefkes, Zilles, & Fink, 2007; Petrides & Pandya, 1999). With visual cortex situated just posterior and somatosensory cortex just anterior, PPC is well positioned to receive and integrate visual and somatosensory inputs. The intraparietal sulcus (IPS) divides the superior parietal lobule (SPL) from the inferior parietal lobule (IPL). Extensive research using neural recording methods in the macaque monkey have identified a complex arrangement of areas within PPC that show functional specialization for the control of specific effectors (body parts). Together with interconnected frontal areas, these circuits make up the cortical machinery critical for the planning and online control of actions. Since the arrival of neuroimaging, similar patterns of functional specificity have been identified in human PPC (Culham, Cavina-Pratesi, & Singhal, 2006; Culham & Valyear, 2006).

Figure 1.2A shows the key dorsal stream areas involved in the control of reaching and grasping as identified with human neuroimaging methods, and Figure 1.2D provides an illustration of putative functionally equivalent areas in the monkey as identified with neural recording methods. Also depicted are the locations of parietal activations specifically associated with tool use (Figure 1.2B) and action observations (Figure 1.2C), again, along with comparisons in the monkey brain (Figure 1.2E and F, respectively). For simplicity, several other functionally defined areas important for action programming and control have been omitted. The purpose of Figure 1.2 is to simply provide a few examples of functional similarities between dorsal stream pathways of man and monkey – in both species, PPC comprises a constellation of functional areas devoted to the control and representation of action. In section 1.3, neurophysiology of grasping and tool use in monkeys is reviewed, while in section 1.4, I revisit human PPC with a specific focus on the putative functional organization of areas critical for learned tool use.

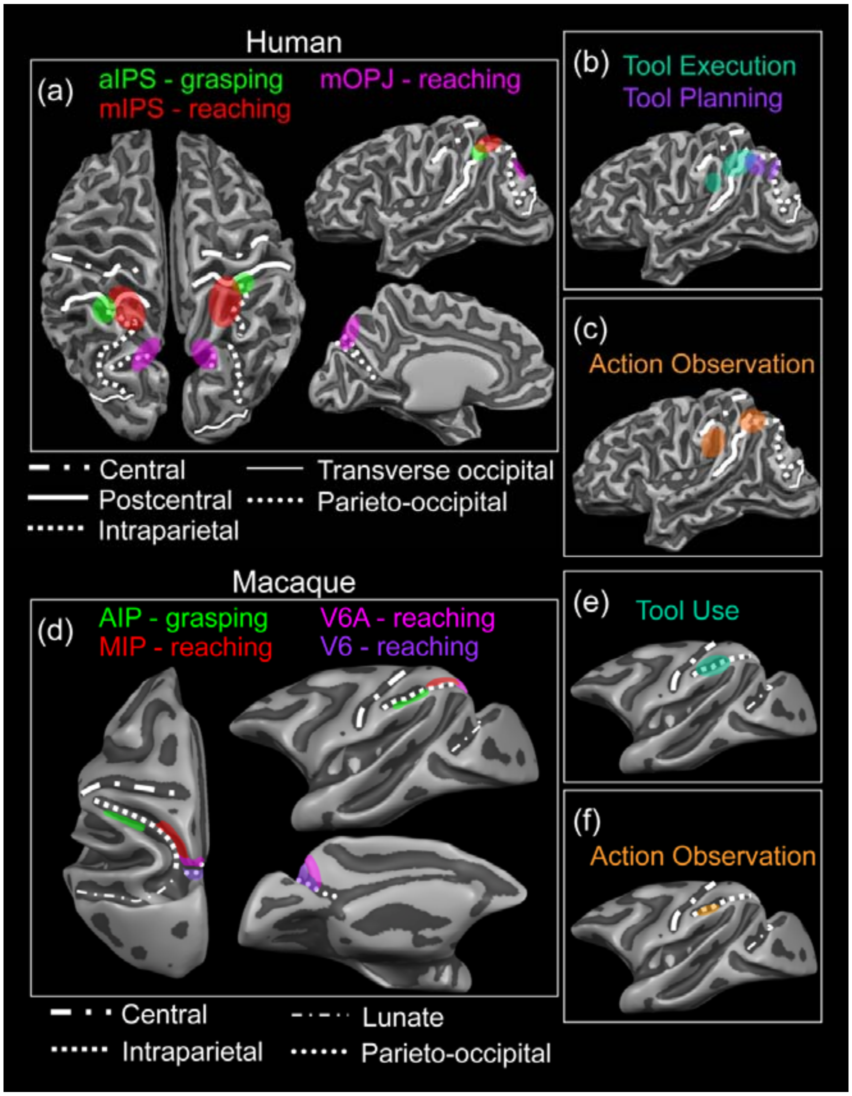

Figure 1.2. Schematic representation of action-related areas of parietal cortex shown on the cortical surface of a human brain (a, b, c) and a macaque monkey brain (d, e, f). The cortical surfaces were defined at the gray-white matter boundary and have been partially inflated to reveal regions within the sulci while preserving a sense of curvature. White lines indicate labelled sulci. Human neuroimaging has identified areas involved in: **(a)** reaching (mIPS/mOPJ) (Prado et al., 2005) and grasping (aIPS) (Culham et al., 2003), **(b)** planning and execution of tool use (Johnson-Frey, Newman-Norlund, & Grafton, 2005), and **(c)** action observation (Buccino et al., 2004). Neural recording methods in macaque monkeys have identified areas involved in: **(d)** reaching (MIP/V6A/V6) (Galletti et al., 2003; Rizzolatti et al., 1998) and grasping (AIP)(Rizzolatti et al., 1998), **(e)** tool use (Hihara et al., 2006), and **(f)** action observation (Fogassi et al., 2005). Areas are coded with similar colours to suggest possible functionally equivalent areas between species; however, such comparisons must always be undertaken with considerable caution (for an extended discussion of the issues, see Culham et al., 2006). Only parietal areas are shown. Reprinted with permissions from Culham and Valyear (2006).

1.2.1. Visual object recognition and the ventral stream

The ventral visual stream originates in primary visual cortex and extends to inferior and lateral temporal cortex. At its anterior most end, the ventral stream interfaces with lateral and medial structures of the temporal lobe known to be particularly critical for various aspects of memory formation, storage, and retrieval (Eichenbaum, Yonelinas, & Ranganath, 2007; Martin & Chao, 2001; Patterson, Nestor, & Rogers, 2007; Squire & Zola-Morgan, 1991). With visual cortex situated at its posterior end and temporal cortex at its anterior end, the ventral stream is well positioned to receive and integrate visual information with long-term memory representations.

We have already seen how patient DF, and others like her (e.g. patient MC), provide powerful insights into the functions of the ventral stream. DF suffers from a type of agnosia, known as visual form agnosia. The literature on visual agnosias is long and extensive (Farah, 1990; Grüsser & Landis, 1991), well beyond what I will discuss in this thesis. Instead, I intend to simply introduce a single rather broad distinction that stems from this literature, before I move on to provide short coverage of some recent highlights from neuroimaging on this topic.

Patients with ventral stream damage and object recognition deficits may differ fundamentally in what they can and cannot perceive. For some patients, like DF, the problems are with constructing coherent percepts, bringing together the various features of objects so to perceive them as meaningful wholes. For other patients, it seems not so much a failure to construct coherent percepts, but rather to ‘match’ such percepts with internal, memory-bound representations so as to recognize and retrieve their meaning (Hillis & Caramazza, 1995; Riddoch & Humphreys, 1987). The distinction maps onto what was originally referred to as ‘apperceptive’ versus ‘associative’ agnosia (Lissauer, 1890). A simple method to reveal such distinction is to ask patients to try and copy pictures of objects; an apperceptive agnosic will be unable to do so, while associative agnosics will perform reasonably well. Likewise, if you ask an associative agnosic patient to draw an object from memory, they will typically be unable to do so, simply because they often cannot *associate* object name and meaning to its visual appearance. Conversely, a patient with apperceptive agnosia may perform appreciably well at drawing from memory, indicating that for these patients recognition failure is not a matter of failed access to stored representations, but rather a failure to *perceive* objects as coherent meaningful images in the first place. Apperceptive agnosia is classically associated with damage to more posterior ventral stream regions while associative agnosia corresponds more closely with damage to anterior ventral stream areas. While a straightforward, stepwise processing scheme is now thought to be overly simplistic (Humphreys & Riddoch, 1987; Riddoch, Humphreys, Gannon, Blott, & Jones, 1999), the basic notion of a posterior-to-anterior continuum of processing complexity within the ventral stream remains useful, and, as I will discuss next, this simple scheme fits quite well with more recently proposed organizational principles evident from neuroimaging work. Given the general layout of the ventral stream, it would certainly seem sensible if more anterior areas abutting temporal lobe structures specialized for long term memory formation and retrieval played a closer, more intimate role in 'matching' visual percepts based on bottom-up processing with stored representations based on top-down knowledge. This line of thinking necessarily merges with theories on the organization of conceptual knowledge in the brain, for which a consensus on how object meaning is stored, represented, and retrieved has not yet been reached (for various models, see Barsalou, 2007; Cree & McRae, 2003; Damasio, 1989; Humphreys & Forde, 2001; Mahon & Caramazza, 2009; Martin & Chao, 2001; Patterson et al., 2007; Simmons & Barsalou, 2003; Tyler & Moss, 2001; Warrington & McCarthy, 1987; Warrington & Shallice, 1984).

Since modern neuroimaging methods have come on the scene, progress in mapping the functional organization of the ventral stream has moved forward rapidly. In a recent review, Grill-Spector and Malach (2004) highlight and provide convincing support for two main organizational principles that have emerged from this work: hierarchical processing and functional specialization. Hierarchical processing describes a continuum, from simple, feature-based representations, to more complex, holistic, multimodal representations within the ventral processing pathway, and fits rather well with the distinctions between apperceptive and associative agnosia noted above. The second principle, functional specialization, goes along in parallel with this hierarchical continuum, and places its emphasis on the separation of visual information types, like colour, motion, and form, along distinct processing channels. Again, where and how such separation of information types ultimately ‘binds’ together and interfaces with stored representations to instantiate deep conceptual knowledge of objects is not yet well established (see also Kourtzi & DiCarlo, 2006).

With respect to the functional characterization of particular areas in the ventral stream important for object recognition, neuroimaging has identified a collection of activation foci within lateral and inferior temporo-occipital cortex known as the lateral occipital complex (LOC). Two main divisions of the LOC separate its lateral aspects from its more inferior/anterior activity, within posterior fusiform cortex. The LOC is activated by intact objects (and shapes) versus scrambled-up or non-sense counterparts (jumbled images without coherent form), independent of the type of cue used to define object shape (e.g. Grill-Spector, Kushnir, Edelman, Itzchak, & Malach, 1998) and regardless of image format (Ishai, Ungerleider, Martin, & Haxby, 2000). Moreover, various studies have shown that parts of LOC, in particular anterior fusiform components, show size, position, and orientation invariance (Grill-Spector et al., 1999; James, Humphrey, Gati, Menon, & Goodale, 2002; Valyear, Culham, Sharif, Westwood, & Goodale, 2006; Vuilleumier, Henson, Driver, & Dolan, 2002), a useful and expected property for a brain region(s) underlying object recognition (i.e. since recognition should be achievable despite variations in object size, position, and observers’ viewpoint). Most important, several studies demonstrate that recognition performance closely aligns with activation patterns in LOC (for review, see Grill-Spector & Malach, 2004, pp. 658-659). Consistently, when James et al. (James, Culham, Humphrey, Milner, & Goodale, 2003) compared the locations of LOC activations from normal participants with the lesion patterns carefully defined in patient DF, close overlap was observed, reinforcing claims that LOC activity is critical to successful object recognition.

Finally, an area of continuing focus and contention among neuroimagers interested in ventral stream function is the issue of object categorization and the ventral stream (Grill-Spector & Malach, 2004; Martin, 2007; Reddy & Kanwisher, 2006). Several areas considered part of the ventral visual pathway have been shown to activate rather selectively for particular object categories, most notably faces, scenes, and human bodies. The main debate centres around whether or not such activations reflect areas truly specialized for processing a particular category of objects (modular coding), versus the idea that these activations instead represent nodes of a wider distributed network, the ***collective*** activations of which instantiate the coding of particular objects (distributed coding). In some excellent work by Malach and colleagues, activations in face and scene selective areas are shown to overlap with central versus peripheral processing preferences, respectively (Hasson, Harel, Levy, & Malach, 2003; Hasson, Levy, Behrmann, Hendler, & Malach, 2002; Levy, Hasson, Avidan, Hendler, & Malach, 2001). This has led to a more principled account of higher level object processing and category specificity in the ventral stream, one that makes steps towards unifying the concepts of hierarchical processing and functional specialization as a coordinated force driving the functional organization of visual areas (Grill-Spector & Malach, 2004; Malach, Levy, & Hasson, 2002).

1.2.1. Tool use and the two visual streams hypothesis

An attractive aspect of the two visual streams proposal is in how the principles defined for vision-for-perception and vision-for-action so sensibly differ. The frame of reference for action must be with respect to the body and must take into account real world metrics; an actor must compute the real size, shape, distance, and orientation of objects with respect to themselves, in ‘egocentric’ coordinates. In fact, the brain is able to transform visual information within and between multiple coordinate frames tied to particular body parts (Andersen & Buneo, 2002; Buneo & Andersen, 2006; Graziano & Gross, 1998). The frame of reference for perception does not require consideration of the absolute metrics of objects or relations between them, but instead, to be most adaptive perception must operate in relative metrics. Recognition of objects independent of viewing conditions, individuation of objects in a cluttered scene, and classification of newly seen objects based on stored knowledge can be achieved much more efficiently and reliably if the operations are performed in relative terms. The basic concept is well appreciated by considering how easily we make sense of images on TV; objects on the screen are perceived and understood in relation to one another, not with respect to real world dimensions (Milner & Goodale, 2006, pp. 239-240). A second operating principle that divides the proposed functions of the two streams is related to timescales. For action, it makes little sense to store the computational outcomes of previous actions to guide and control new ones, given that, in general, actors and objects in the world are in constant flux; for example, the parameters needed to accurately transport and shape the hand to grasp a given object will change as the actor and/or object moves. Thus, it makes more sense for the action system to compute parameters *de novo*; from the bottom-up each time a new action is carried out. In contrast, the perceptual system needs to construct and operate within long standing representations of the world in order to recognize objects, including people and places, despite various changes in appearances and viewing conditions. To recognize old objects as they change over time, and to categorize new ones, the perceptual system must ultimately compare what is seen with what is stored in memory. The systems underlying perception and action appear to operate on fundamentally different timescales and frames of reference (Goodale, 2001; Goodale & Haffenden, 1998).

With learned tool use, the separation between vision-for-perception and vision-for-action would seem to reach its limits. Familiar tools are bound to action plans that stretch beyond what is available on the ‘surface’, defined instead by previous experience, unlocked only with successful recognition. How the hand is shaped when grasping-to-use tools depends not only on their physical aspects (e.g. size, shape, and orientation), but also on stored knowledge of function and use. Once the actions of tools are known, identity, and thus visual object recognition, represents an efficient route to learned motor plans. The implications with respect to the two streams hypothesis are clear: familiar tool use is likely to involve explicit cooperation between ventral and dorsal streams. Further, the ventral stream is expected to act as a first step in retrieving and activating stored motor representations. After all, stored action plans represent the hallmark of skilful tool use. That is to say, for tool use, as with any other learned motor skill, procedural memory storage, retrieval, and implementation is essential to lasting improvements in motor performance. To summarize, the actions of learned tool use extend beyond physical object properties and the timeframe by which routine dorsal stream function is thought to operate, and instead appear to rely on stored object representations and successful recognition as mediated by the ventral stream.

In their original account of the two streams dichotomy, Milner and Goodale predicted that familiar tool use would require the cooperation of both streams, and that the ventral stream would lead the way (Milner & Goodale, 1995, pp. 202-204). In particular, in conjunction with recognizing tools, they suggested that the ventral stream would also take part in selection of where and how to grasp tools in accordance with intended use and known function. Notably, they were also clear to indicate that this process of action specification, solving the 'how to' part of the puzzle, would critically depend on ventral stream cooperation with specialized areas of inferior parietal cortex. Finally, the end products of this processing would reach the dorsal stream, where actual sensorimotor transformations critical to motor implementation and control are computed and carried forth. The basic scheme fits well with their broader account of how the two streams are likely to interact in general. With everyday actions, individual objects are parsed from others in busy crowed environments by the ventral stream, selected for potential action, while the dorsal stream then specifies particular motor outputs and governs online control (Goodale & Humphrey, 1998; Milner & Goodale, 2006, pp. 231-233).

What evidence is there for ventral stream involvement in familiar tool use? The strongest support has come from testing functional grasping in patient DF (Carey, Harvey, & Milner, 1996). When asked to grasp and use familiar tools, DF shaped and oriented her hand perfectly well with respect to the metrical properties of tools; however, she often failed to posture her hand in a way that reflected knowledge of function and use. The most obvious example of this functional orienting of the hand when grasping tools can be seen with handled tools, when the handle is faced away from the actor. In this situation, people will typically rotate their hand to end up in a final posture well suited for use (see Chapter 2, Figure 2.1A). While control participants were seen to follow this tendency, DF did not. The tendency is part of a broader 'rule' in motor control, identified by Rosenbaum and colleagues (Rosenbaum, van Heugten, & Caldwell, 1996; Rosenbaum, Vaughan, Barnes, & Jorgensen, 1992), whereby the kinematics of early aspects of multistep actions are selected in anticipation of comfortable end-states. Most clearly, people will reliably adopt relatively awkward grasping postures if this will enable more comfortable postures upon completion of end goals. The tendency to grasp handled tools in a way that is appropriate for use was specifically addressed in a study by Creem and Proffitt (2001), and their findings provided additional evidence for ventral stream involvement in tool use. They found that when participants were asked to grasp tools while simultaneously performing a task involving semantic processing, grasping actions appropriate for tool use were made less frequently than when participants either grasped without performing the concurrent semantic task or when they instead simultaneously performed a spatial imagery task. The results were taken to indicate that planning functional grasps to tools necessarily involves semantic systems, presumably including ventral stream areas. When the semantic task was being performed at the same time as grasping, grasping did not tend to incorporate functional knowledge, presumably because resources from semantic systems were not fully available. Insofar as semantic processing involves the ventral stream, the findings nicely converge with those of functional grasping in patient DF. Apparently ventral stream functioning is needed to grasp tools appropriately for use, precisely in line with the scheme initially proposed by Goodale and Milner reviewed above.

1.3. Parietal mechanisms of grasping and tool use in monkeys

1.3.1. Neurophysiology of grasping

With respect to neural recording methods, the first indication of an important role for PPC in the visual guidance and control of grasping came from a paper by Hyvarinen and Poranen (1974), followed by the pioneering work of Vernon Mountcastle and colleagues (1975). Recording from single neurons in monkey IPS/SPL, Brodmann’s areas (BA) 5 and 7, Mountcastle et al. (1975) described “hand manipulation” neurons which fired selectively when objects were grasped and manipulated; in particular, during the final stages of grasping, just before and as the hand made contact and during subsequent manipulation. These neurons were not activated during the transport phase of grasping, by passive peripheral stimulation, or when the monkey actively performed non-object-directed movements of “an aggressive or aversive nature” (Mountcastle et al., 1975, p. 881). Since these early discoveries, others have continued to use electrophysiological recording methods to further characterize the response properties of neurons within the IPS during object grasping and manipulation tasks. Sakata and colleagues made the next major breakthroughs, specifying area AIP at the anterior end of the IPS as the key parietal region critical for grasping, and elucidating some of its most important response properties (Murata, Gallese, Luppino, Kaseda, & Sakata, 2000; Sakata, Taira, Kusunoki, Murata, & Tanaka, 1997; Sakata, Taira, Murata, & Mine, 1995; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). They looked at the visual and motor responses of neurons separately, and showed that many AIP neurons were tuned to particular grasp configurations in accordance with object shape. Further, visual response selectivity often matched motor response selectivity, such that a neuron showing selectivity for a given object when viewing also showed selectivity for that same object when grasping. The significance of these findings were clear: this was exactly the kind of response signature that could in principle mediate the transformation of visual information regarding physical object properties to corresponding motor programs for grasping (Jeannerod, Arbib, Rizzolatti, & Sakata, 1995). More recent recording studies from Gardner and colleagues distinguish response properties of AIP neurons from somatosensory driven responses in the postcentral gyrus, and show that specific populations of neurons are tuned to specific temporal phases of object grasping and manipulation (Debowy, Ghosh, Ro, & Gardner, 2001; Gardner et al., 2007; Gardner, Debowy, Ro, Ghosh, & Babu, 2002; Gardner, Ro, Debowy, & Ghosh, 1999; Ro, Debowy, Ghosh, & Gardner, 2000). Notably, earlier work had also looked at grasping responses in somatosensory cortex (Iwamura & Tanaka, 1978; Iwamura, Tanaka, Hikosaka, & Sakamoto, 1995), but these authors did not probe or distinguish responses to grasping in IPS. Finally, the critical importance of AIP in the guidance and control of grasping was verified by Gallese et al. (1994) who showed that inactivation of AIP neurons by injection of GABA-receptor agonist (muscimol) results in profound deficits in hand preshaping when grasping. Monkeys performed awkward grasps, showing poor anticipatory shaping of the hand in accordance with object size and shape, and sometimes even failed to complete grasps altogether.

AIP sends outputs to, and has dense reciprocal connections with area F5 in ventral premotor cortex (Borra et al., 2008; Luppino, Murata, Govoni, & Matelli, 1999; Matelli & Luppino, 2001). The response properties of many neurons in F5 show strikingly similar characteristics of those defined in AIP. Rizzolatti et al. (1988) describes F5 as a ‘motor vocabulary’, with neurons specifying the kinematics of particular actions, but tuned to action goals, not necessarily to the motoric specifics of constituent movements. For example, two actions with similar movement kinematics, but performed in different contexts and with different goal-defined outcomes will not tend to activate the same F5 neurons (Rizzolatti & Luppino, 2001). Further, just like AIP, F5 contains neurons that show response selectivity for particular objects, with visual and motor response specificity tightly matched (Murata et al., 1997; Raos, Umilta, Murata, Fogassi, & Gallese, 2006; Rizzolatti et al., 1988; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). Objects that activate these neurons most strongly when viewed are typically of a shape that conforms to the neurons' preferred grasp configuration. These neurons were given the name 'canonical neurons', and alongside functionally equivalent coding in AIP, were said to instantiate the neural mechanisms needed to match and transform vision of objects to the motor specifications governing skilful grasping and manipulation (Luppino et al., 1999, p. 181). I will return to canonical neurons, as the response characteristics of these cells have important implications for Projects 2 and 3 of the current thesis. Reversible inactivation of area F5 with muscimol injections disrupts hand preshaping during grasping (Fogassi et al., 2001); hand shape no longer matched object size or shape, similar to the effects seen with inactivation of AIP (Gallese et al., 1994). More recent work has shown that multi-unit recordings from area F5, reflecting the pooled activity of many neurons, can predict upcoming kinematic features of reach and grasp actions with remarkable accuracy (E. Stark & Abeles, 2007). Notably, signals from multiunit recordings predicted actions much better than signals from either single neurons or local field potentials (which reflect also sub-threshold synaptic events), suggesting that coding for grasp type in F5 is achieved through population firing, represented in the coordinated responses of multiple neurons. Also, new work comparing response properties in F5 with primary motor area M1 has shown that object/grasp-specific coding is present in both regions, but in greater proportions and with earlier activations in F5 (Spinks, Kraskov, Brochier, Umilta, & Lemon, 2008; Umilta, Brochier, Spinks, & Lemon, 2007). These data are consistent with the notion that F5 neurons translate visual information about object features into corresponding motor plans, which are then received and refined in M1 for delivery to appropriate spinal machinery controlling hand and digit muscles (Umilta et al., 2007).

In summary, it has been proposed that macaque AIP-F5 circuitry constitutes the cortical mechanisms underlying “pragmatic vision”, responsible for the visuomotor transformations critical to the guidance and control of object grasping and manipulation (Fagg & Arbib, 1998; Jeannerod et al., 1995; Matelli & Luppino, 2001; Rizzolatti, Fogassi, & Gallese, 1997). It should be emphasized, however, that this system operates in parallel with other key neural circuitry; many other cortical areas are no doubt important for object grasping and manipulation. For example, mounting evidence indicates that dorsal premotor cortex (area F2) is also critical for the control of grasping (reviewed in Castiello & Begliomini, 2008; Grafton, 2010; Matelli & Luppino, 2001; e.g. Raos, Umilta, Gallese, & Fogassi, 2004; for connections with parietal areas, see Wise et al., 1997). Likewise, newer electrophysiological studies indicate that medial posterior parietal area V6A, previously thought of as more specifically related to reaching and arm control, shows response coding for grasping similar to that observed in area AIP (Fattori et al., 2009; Fattori et al., 2010). Indeed, widespread parietofrontal control is nicely exemplified by monkey neuroimaging studies of grasping, which indicate recruitment of multiple foci spanning much of posterior parietal and frontal cortices (Evangeliou, Raos, Galletti, & Savaki, 2009; Nishimura, Onoe, Morichika, Tsukada, & Isa, 2007).

Another type of neuron found in both areas AIP and F5 was shown to fire both when the monkey executes ***and*** observes an action (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti et al., 1996). These are known as mirror neurons. Mirror neurons share a common property with canonical neurons in that the execution of actions are not needed to make them fire, a property that relates directly to the methodology used in the current projects. Together, these neurons represent sensitivity to purely visual stimuli in areas F5 and AIP; dynamic actions in the case of mirror neurons and graspable objects in the case of canonical neurons. Moreover, like canonical neurons, for a good proportion of mirror neurons the selectivity of visual responses matches that of motor responses. Those actions that make these neurons fire most rigorously when observed are the same actions that make them fire most rigorously when executed (Gallese et al., 1996). This was proposed to provide a means by which observed actions can be understood, through a process of implicit motor simulation in the observer (Gallese & Goldman, 1998). Various versions of the motor resonance hypothesis have since emerged, and mirror neuron mechanisms have been proposed to underlie a wide range of functions in addition to action understanding (Rizzolatti & Craighero, 2004; Rizzolatti, Fogassi, & Gallese, 2001), including imitation (Buccino et al., 2004; Iacoboni et al., 1999), observational learning (Cross, Kraemer, Hamilton, Kelley, & Grafton, 2009; Frey & Gerry, 2006; Mattar & Gribble, 2005), theory of mind (Agnew, Bhakoo, & Puri, 2007; Iacoboni et al., 2005), empathy and social cognition (Gallese, 2006; Iacoboni & Dapretto, 2006; Leslie, Johnson-Frey, & Grafton, 2004), and even aesthetic experience (Calvo-Merino, Jola, Glaser, & Haggard, 2008; Freedberg & Gallese, 2007). Despite the number of plausible (and not so plausible) accounts, the true function and significance of mirror neurons is not yet well established (Decety & Grezes, 1999; Hauser & Wood, 2010; Hickok & Hauser, 2010; Jacob & Jeannerod, 2005).

1.3.2. Neurophysiology of tool use

New and fascinating discoveries regarding the neural basis of tool use in monkeys have recently been made and are continuing to surface thanks to the brilliant work of a group of neuroscientists in Japan, led by Atsushi Iriki. This work is making steps towards answering some of the most important questions surrounding evolution of the human brain (Iriki & Sakura, 2008). What brought about the great expanse of brain and mind? How and why do human cognitive capacities appear to so greatly outstretch those of our closest primate relatives?

Japanese macaque monkeys were trained to use a simple rake-like tool to retrieve food items that were otherwise out of reach (Ishibashi, Hihara, & Iriki, 2000). Macaque monkeys rarely use tools in the wild (Tomasello & Call, 1997), and at first, progress in training the monkeys to use the rake tool was slow, typically at a rate of more than a few months per monkey (Iriki & Sakura, 2008, pp. 2229-2230). However, as the training program was made optimal, monkeys learned to use the rake skilfully in about 14 days time, and according to a recent review (Iriki & Sakura, 2008), over 50 individuals have now been rake-trained, all of which have successfully acquired the skill.

The first exciting finding was made when Iriki et al. (1996) compared recordings obtained from single neurons within the anterior bank of the IPS before and after tool use training. The neurons of interest showed bimodal response properties, responding to both visual and tactile stimuli. Further, the visual receptive fields[1] (vRF) of these neurons were tied to the body, anchored to the tactile receptive fields (tRF) of particular body parts. For example, a neuron with a tRF located on the hand, would fire to visual stimuli in a radius of space immediately around the hand, and the vRF would ‘track’ with the hand as it moved in space. In other words, the vRFs of these bimodal neurons in anterior IPS were bound to specific body parts, independent of where the monkey’s gaze was fixed. The remarkable findings came when Iriki and colleagues noticed that after tool use training, the vRFs of many of these bimodal neurons changed to include the area of space around the tool. For example, a neuron with its vRF tied to the hand, after training showed sensitivity to visual stimuli near the space around the tool, as if the vRF properties of the neuron expanded to now encompass the space around the tool. Incredibly, such expanded vRFs depended on the monkey actively using the rake; after a period of rest (about 5 min), vRFs ‘regressed’ back to only include the area of space coded prior to training, even though the monkey still held the rake in hand when these recordings took place. These findings indicate that the cellular changes induced by tool use training are capable of dynamic moment-to-moment alterations depending on the active state, or goal-state of the monkey.

These initial findings were strengthened and extended when the group later looked at tool use learning induced changes in IPS neurons at the molecular level (Ishibashi et al., 2002a, 2002b). They had hypothesized that the vRF changes correspond with new synapses; in particular, new contacts to IPS neurons from other areas carrying visual information were predicted to correspond with tool use learning. In search for support of this hypothesis, they developed a novel method of testing expression levels of messenger RNA (mRNA) corresponding to the following neurotrophins: brain-derived neurotrophic factor (BDNF), neurotrophin 3 (NT-3), as well as BDNF receptor *trk*B. A variety of previous evidence indicates that these neurotrophins are important for various cellular events tied to the formation of new synapses, including neurite arborization, synaptic plasticity and transmission, and processes critical to learning and memory (see

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[1] The receptive field of a neuron is the part of space for which stimuli are effective in making the cell fire.

Ishibashi et al., 2002b, p. 4 for references). Consistent with their hypothesis, they found enriched mRNA expression for BDNF, NT-3, and *trk*B (and not for control genes) in the anterior bank of the IPS of monkeys that were sacrificed on day 12 of rake-training, a training period known to overlap with skill acquisition and learning (see also Ishibashi et al., 2000 for detailed time course of behavioural learning). In contrast, monkeys that were sacrificed on day 15 of training, a period beyond learning that coincides with already established skill, did not show such elevated levels of expression. In other words, increased expression of these markers of synaptic plasticity was specific to the learning phase of tool use, when skills with the rake were still being acquired and improved. Thus, alongside changes in neural response properties, namely dynamic modifications of vRFs, tool use learning was shown to correlate with upregulation of various neurotrophins in anterior IPS. The findings support the hypothesis that dynamic vRF modifications following tool use training in monkey IPS neurons comes about through the formation of new synapses. Notably, although not the main focus of the original paper by Iriki et al. (1996), tool use training not only showed changes in vRFs of bimodal neurons, but some neurons were also seen to 'take on' visual responses after training (see Ishibashi et al., 2002b, p. 3). Increased transcription of BDNF, *trk*B, and NT-3 may mediate cellular events underlying these changes. Ishibashi et al. (2002b) speculate that the dynamic moment-to-moment changes in vRFs seen when monkeys switch from active to passive tool use may correspond with 'silent' synapses, active only upon sufficient depolarization of membrane potentials brought about through active tool use. It was argued that plasticity at such short timescales is not likely to involve upregulation of BDNF at the level of gene transcription, which would explain why monkeys on day 15 did not show similar levels of heightened expression (although BDNF and NT-3 may still be important for these fast dynamic processes at the protein level).

The picture of tool use learning induced neural plasticity was made even more complete with the work of Hihara et al. (2006), who mapped the presence and organization of new connections within anterior IPS neurons following tool use training. First, the authors used a retrograde tracing technique to test for potential differences in afferent connectivity patterns within anterior IPS neurons of trained versus untrained monkeys. Labelled cells indicating sources of input to IPS neurons were uniquely identified within the temporoparietal junction (TPJ) and ventral prefrontal cortex of tool trained monkeys. No such labelling was observed in naïve untrained monkeys. TPJ neurons were located in the superior temporal sulcus (STS), in a region that appeared just caudal to motion area MSTda and TPOc and lateral to area 7a according to the cytoarchitectonic divisions defined by Lewis and Van Essen (2000b). Also, according to the connectivity maps of Lewis and Van Essen (2000a), this area normally projects to area VIPm and LIPv, located in the fundus and posterior bank of the IPS. Based on these comparisons, tool use learning led to the extension of connections from this region to more anterior IPS neurons. The TPJ populations are believed to correspond with higher level visual processing of motion and location, information that could be vital to the guidance of body part movements in space. The new inputs to IPS neurons from ventral prefrontal cortex were localized within the ventral sector of the principal sulcus (BA 46). The authors speculate that these new connections may support added levels of cognitive and contextual flexibility that may accompany newly acquired tool use behavior.

To gain a sense of the changes in synaptic connectivity patterns within anterior IPS after tool use training, and to complement their findings with retrograde tracing, the authors next injected an anterograde tracer within the TPJ region identified as a new source of visual information. This technique tracks forward the new connections from TPJ to IPS and provide details about the functional architecture of these connections within IPS. First, the density of labelled cells was much stronger in the IPS of trained versus untrained monkeys. Second, the distribution patterns of labelled fibres were also different. Whereas both trained and untrained groups showed inputs to deep layers in the fundus of the IPS (layers 4-6), inputs identified within the superficial layers (layers 2-3) and towards the crown of the postcentral gyrus were unique to trained animals. Lastly, single axon reconstructions specific to trained animals showed dense spreading of terminal fields and extensive branching throughout all layers of the IPS, and electron microscopy confirmed the presence of active excitatory synapses within the superficial layers of trained monkeys only. Altogether the findings indicate that tool use learning gives rise to incredibly elaborate changes in the underlying cellular architecture of anterior IPS, with new long-range connections originating from TPJ and ventral prefrontal cortex.

Additional studies by Iriki and colleagues have pushed the boundaries of their initial findings to new and surprising extents. With training monkeys were able to learn to use images of their hand/tool shown on a video monitor to guide their actions to retrieve otherwise inaccessible food rewards (Iriki, Tanaka, Obayashi, & Iwamura, 2001). Visual RFs of IPS neurons were shown to map onto the video screen, to track with the hand and expand to the tool, and, most remarkably, when the image of the hand/tool on the screen was position-translated and/or changed in size, the vRFs of IPS neurons followed suit. The neurons were tied to the visual characteristics of the screen image, when these images changed, so too did the vRFs of neurons. Such a mapping illustrates a profound level of abstraction; cells tied to the hand and arm were essentially ‘detached’ from real space and physical properties of hand and arm. The authors then slowly erased the image of the hand and tool on the monitor screen, until eventually a single spot corresponding to the functional end of the tool was sufficient to track with vRFs. Importantly, with all of these findings, correlated motion of real hand/tool and screen image/representation was necessary for vRFs to transfer and track. The findings indicate unprecedented flexibility in the kinds of associative cues monkeys can use to guide their actions and in the extent to which such external cues may come to represent specific parts of the body.

Upon concluding, the predominant theory put forth by Iriki et al. to account for tool-training-induced changes in the RF properties of IPS refers to the concept of body schema (Head & Holmes, 1911). The bimodal neurons at the anterior extent of the IPS are viewed as critical to encoding the body and near body space, and tool use learning is seen as leading to dynamic incorporation of the tool into the body schema (see also Umilta et al., 2008). Neural RF expansion translates into expansion of body representation, as if the properties of the tool were now represented as part of the body. According to Iriki and colleagues, this capacity underscores a more abstract capacity to represent the self as an independent entity (Iriki, 2006; Iriki & Sakura, 2008). They go on to argue that once reached, such capacities open the door to new cognitive progressions, and evolution of brain and mind is sped forward (see also, Hihara et al., 2006, p. 2645). The onset and continuing complexity of tool use behaviours in early hominids may have served to catalyze the great expanse of cortex that followed. It is argued that capacity to objectify the self, latent in wild monkeys untapped through the unique pressures of their tool use paradigm represents vital cognitive precursors necessary for subsequent neural expansion and specialization, key steps forward in the evolutionary history of the human brain and mind.

Do the findings just reviewed suggest that the complexity of tool use behavior in humans evolved through the expansion of pre-existing parietal mechanisms related to more basic visuomotor control? While there is evidence of similar expansion-of-space-encoding effects in humans after the use of tools that extend the reach (Berti & Frassinetti, 2000; Maravita & Iriki, 2004; Maravita, Spence, Kennett, & Driver, 2002), tool use in humans far exceeds that of other primates (Frey, 2007; Johnson-Frey, 2003b; McGrew, 1993), and expanded space is not sufficient to explain the transformations of more complex tool use (Arbib, Bonaiuto, Jacobs, & Frey, 2009). It appears as though while neural mechanisms revealed with tool use studies in monkeys undoubtedly lay the foundation for mechanisms present in humans, the remarkable extent and capacity of human tool use must rely at least in part on newly evolved brain areas (Frey, 2007; Peeters et al., 2009).

1.4. Parietal cortex divided

In a number of recent review papers, several different authors have put forth a similar message: the functions of PPC in action extend beyond the visuomotor transformation and sensorimotor control (Buxbaum & Kalenine, 2010; Creem-Regehr, 2008; Culham & Valyear, 2006; Daprati & Sirigu, 2006; Frey, 2007; Jeannerod & Jacob, 2005; Rizzolatti & Matelli, 2003). In general, these newly emphasized functions of PPC are considered higher level cognitive-motor functions, which include tool use knowledge and action understanding. In the following I will cover some of the key ideas that have recently surfaced regarding the functional organization of areas specialized for tool use.

1.4.1. Parallel parietal streams to action: Grasping versus using

The central theme of these more recent discussions of parietal function in action is that the PPC is divided, with separate channels devoted to online control of actions versus the planning and use of tools (amongst other dissociations). As shown schematically in Figure 1.3, a lateral stream projecting to inferior parietal areas (lateral-IPL stream), is distinguished from a medial stream projecting to superior parietal areas (medial-SPL stream) (Buxbaum & Kalenine, 2010; Johnson & Grafton, 2003; Rizzolatti & Matelli, 2003).

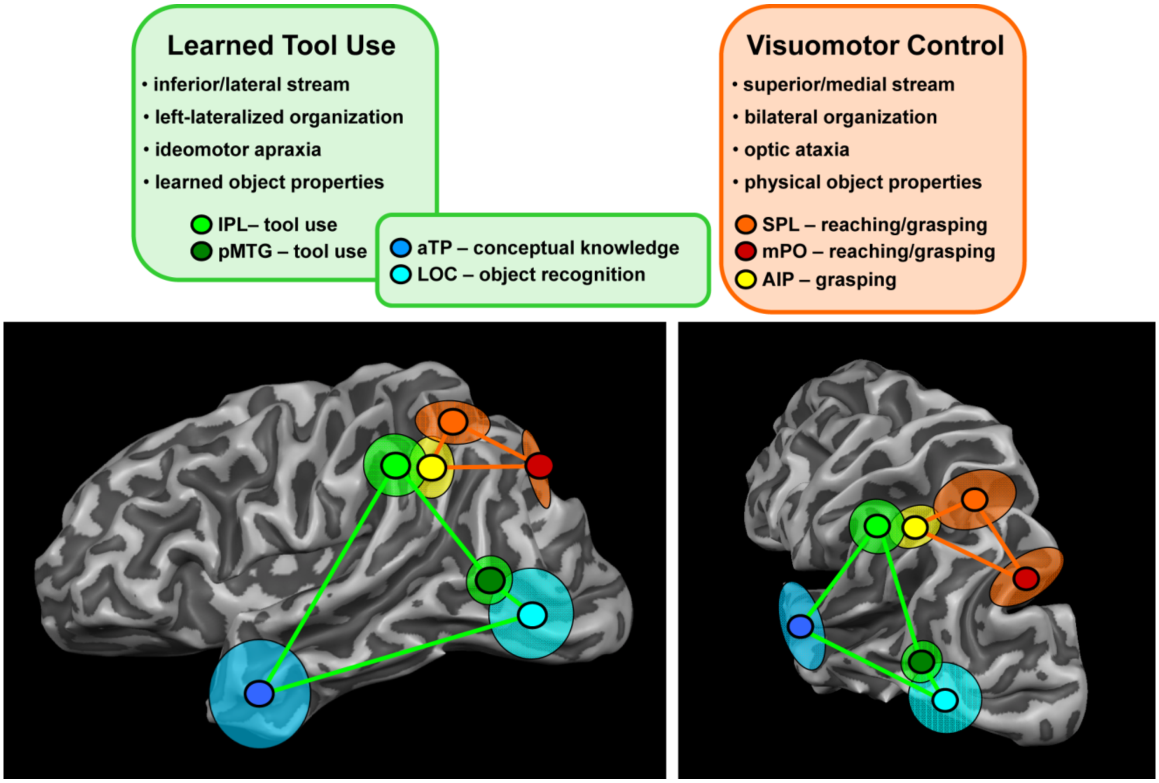

Figure 1.3. Parallel parietal routes to action. A schematic of the two proposed routes to action, shown on a partially inflated cortex. The left hemisphere is shown from a lateral view (left), and dorsal lateral view (right). The lateral parietal stream specialized for learned tool use is shown in green, with two main areas specified, inferior parietal lobule (IPL) and posterior middle temporal gyrus (pMTG). Also, ventral stream areas comprising the lateral occipital complex (LOC) important for object recognition and the anterior temporal poles important for stored conceptual/semantic knowledge of objects are included as putative additional components of the lateral parietal stream. The medial parietal stream specialized for online motor control is shown in orange. The superior parietal lobule (SPL) and medial parieto-occipital (mPO) cortex are important nodes within this stream, shown to be critically involved in reaching and grasping. Grasping-defined anterior intraparietal area AIP is shown on the side of the medial stream; however, AIP may represent a common end-point for both streams.

The functions of the medial-SPL stream correspond with the classic dorsal stream as described by Milner and Goodale (1995). The main purpose of this stream is the online control of actions. The mechanisms of the medial stream operate in ‘real time’, within egocentric, effector-specific coordinates, tuned to veridical object metrics directly accessible from information available on the retina. Superior parietal cortex represents the main processing module of this stream, with key connections stemming from areas along the medial surface of parieto-occipital cortex (Gamberini et al., 2009). Conversely, the lateral-IPL stream is specialized for learned tool use, more closely aligned with mechanisms devoted to high level action planning, accessible to conceptual knowledge of objects and actions. Inferior parietal cortex represents the main processing module of this stream, with specialization for tool use thought to be primarily left lateralized. The lateral-IPL stream is hypothesized to involve key connections with ventral stream areas, including areas of the lateral occipital complex (LOC) specialized for object recognition. More inferior ventral stream areas, within fusiform cortex associated with category-selective object vision (Martin, 2007), as well as semantic knowledge stores within anterolateral temporal cortex (anterior temporal poles, aTP) (Patterson et al., 2007) may also be critical to the conveyance of high level conceptual object information within this stream. In contrast with the medial-SPL stream, the lateral-IPL stream must operate in both past and present. Somehow stored knowledge of tools and their associated actions must interface with real time effector-based mechanisms necessary for the guidance and control of actions. How this is accomplished is not yet known, but current theories of tool use suggest that the solutions are unravelled within inferior parietal cortex, within the lateral parietal stream to action.

Evidence for the theory of two parallel parietal streams to action starts with the recognition of distinct connectivity patterns to inferior versus superior parietal areas in the macaque. Areas within the IPL have connections with areas in the superior temporal sulcus (STS), not present in the pathways to SPL (Rizzolatti & Matelli, 2003). This is important in the context of tool use because STS neurons are endowed with high-level visual form and motion properties and are heavily interconnected with inferior temporal areas of the ventral processing stream. Indeed, both IPL and inferotemporal cortex have dense connections with areas in STS (Harries & Perrett, 1991; Morel & Bullier, 1990;

Young, 1992). Communication between IPL areas and the ventral stream may also be bridged through the dense reciprocal connectivity these regions both exhibit with prefrontal cortex (Goldman-Rakic, 1996; Petrides & Pandya, 1984) which is also interconnected with medial temporal lobe structures (Blatt, Pandya, & Rosene, 2003; Lavenex, Suzuki, & Amaral, 2002; Morris, Pandya, & Petrides, 1999). Finally, the IPL itself has direct connections with medial temporal lobe structures (e.g. parahippocampal cortex) (Clower, West, Lynch, & Strick, 2001; Munoz & Insausti, 2005; Rockland & Van Hoesen, 1999; Suzuki & Amaral, 1994). Cells in the STS are important for high level multimodal integration of visual form and motion (Barraclough, Xiao, Baker, Oram, & Perrett, 2005; Oram & Perrett, 1996; Oram, Perrett, & Hietanen, 1993), object (Baker, Keysers, Jellema, Wicker, & Perrett, 2001; Hietanen & Perrett, 1996) and face processing (Harries & Perrett, 1991; Perrett et al., 1991; Perrett et al., 1985), and demonstrate remarkable selectivity when observing others' actions (Barraclough, Keith, Xiao, Oram, & Perrett, 2009; Perrett et al., 1989; Perrett, Mistlin, Harries, & Chitty, 1990). For example, some cells not only discharge selectively when observing particular actions (e.g. grasping), but also show sensitivity to the gaze direction of actors. Such response specificity may implicate a special role for STS areas in encoding intentionality of others' actions (Jellema, Maassen, & Perrett, 2004; Jellema & Perrett, 2006). Further, I have already reviewed the evidence from tool use training in monkeys: new connections were found to sprout from STS neurons to reach anterior IPS following expertise with tool use, in parallel with changes in the molecular and physiological properties of the intraparietal neural circuitry. Presumably these new connections carry forward visual information important for tool use behavior. Perhaps it is of some significance that STS neurons have been shown to not only differentiate between motion of the self versus others, but also show selectivity for responses to self movements when an object is in hand (Hietanen & Perrett, 1993, 1996). Such differentiation could indeed be useful for coding self-controlled actions with objects. STS areas receive heavy inputs from motion specialized areas MT and MST, both of which show comparatively little connectivity with medial posterior parietal areas V6/V6A; which, as noted above, are key processing nodes along the medial-SPL stream to action (referred to as the 'dorsal-dorsal' pathway by Rizzolatti & Matelli, 2003). Thus, in the monkey, IPL has privileged access to high level visual motion, object, and action encoding within temporal cortex; information that may be particularly critical for tool use. Indeed, liken to what Iriki and colleagues have implied (Hihara et al., 2006, p. 2645; Iriki & Sakura, 2008), this route may represent a key evolutionary stepping stone in the progressive specialization of human tool use behavior. To this end, it is notable that the IPL in particular underwent significant expansion in the course of human evolution (Bruner, Manzi, & Arsuaga, 2003; Orban, Van Essen, & Vanduffel, 2004); even with full brain volume controlled, human IPL is disproportionately larger than both monkey and chimpanzee IPL (Eidelberg & Galaburda, 1984, as cited in Johnson-Frey, 2003, p.206).

That learned tool use and online visuomotor control separates in human parietal cortex is actually, in general, a very old idea. The origins of the disorder known as ideomotor apraxia (IM) trace back to the early 1900s and the work of Hugo Liepmann (see Goldenberg, 2003 for a historical account of Liepmann's work; Liepmann, 1977, 1980). Liepmann was the first to explain IM as a selective impairment in performing learned skilled actions, not explained by any elementary motor or sensory deficit, or related to general problems with cognition, comprehension, or attention. Although these patients can recognize tools and typically understand what it is they are supposed to do with them, they have great problems when it comes to actually carrying out proper movements. Specifically, these patients make gross spatiotemporal errors when attempting to perform tool use actions (Poizner et al., 1998). Most common, errors are more profound when asked to pantomime tool use actions; many patients show improvements with actual tool use (Goldenberg & Hagmann, 1998; Hermsdorfer, Hentze, & Goldenberg, 2006). Liepmann established that ideomotor apraxia predominantly follows left inferior parietal damage, a finding that has largely stood the test of time (Goldenberg, 2009; Goldenberg & Spatt, 2009; Haaland, Harrington, & Knight, 2000). Liepmann also maintained that apraxia and aphasia, although commonly overlapping, are in fact distinct, reliant on distinct neural systems, a precedent also confirmed in more recent times (Alexander, Baker, Naeser, Kaplan, & Palumbo, 1992). Critical to the current discussion, apraxia is also distinct from optic ataxia (OA). I made mention to OA above in the context of the two visual streams. I noted then that OA follows damage to the dorsal stream and results in problems with reaching and grasping. The disorder was first described by Bálint (1909), who examined a patient that showed problems reaching to visible targets with his right hand following bilateral damage to PPC. Bálint correctly deduced that the deficits with OA are visuomotor in nature, not explained by general impairment of basic sensory or motor functions. Although still most commonly associated with deficits in arm control and reaching to targets in space, when tested, patients with OA typically also show problems with grasping (Goodale et al., 1994; Jakobson, Archibald, Carey, & Goodale, 1991; Jeannerod, 1986). According to Perenin and Vighetto (1988), the IPS is most commonly damaged in patients with OA, more often encompassing aspects of the SPL rather than the IPL (see also Ratcliff & Davies-Jones, 1972; Rondot, 1989). With newer lesion subtraction methods Karnath and Perenin (2005) highlight a total of three distinct foci of maximal lesion overlap in OA patients: two foci near the junction of occipital and parietal cortex, extending medially in the precuneus and superior occipital gyrus, and a third focus in the SPL. Thus, while IM and problems with tool use are associated with damage to left IPL and the lateral-IPL stream to action, OA and problems with reaching and grasping are associated with damage to bilateral SPL and the medial-SPL stream to action (Figure 1.3)(Goldenberg, 2009).

The new, more surprising part of this story is that depending on a person's goals and intentions, grasping itself may depend on distinct parietal systems. The evidence begins with a single patient, LL, who showed signs of posterior parietal pathology (PET and SPECT imaging both revealed evidence of bilateral occipito-parietal hypometabolism) and had problems pantomiming and using familiar tools (Sirigu et al., 1995). The patient complained of troubles performing daily activities with objects, like brushing her teeth, locking a door, and using a fork and knife to eat. When tested formally in the lab with a set of 20 common objects, four independent raters judged LL's performance in the use of objects as severely impaired. Beyond this initial evaluation based on more global scoring of actions, the judges were asked to rate both the correctness of hand posture and reach trajectory separately, based on a set of well defined expectations. For example, in the case of a soup spoon, for hand posture, the stem of the spoon was expected to be held "between the thumb, index and middle fingers, with the palm of the hand turned slightly upward and towards the subject's body" (p. 44). Such specifications nicely illustrate the concept of functional grasping of tools as distinct hand shaping for grasping-to-use (see Chapter 3). For reach trajectory, the spoon “had to be moved in a back and forth manner between the table and the subject’s mouth” (p. 44). Thus, reach trajectory was evaluated on the basis of more global movements of body parts, their spatial localization, directionality and timing. To my knowledge, this was the first study to distinguish and closely evaluate the constituent components of grasping and reaching in a tool use task in an IM patient. The results showed that while LL was profoundly impaired at shaping her hand correctly for object use, her reach trajectories (and the coordinated movements of both arms when needed) were unimpaired. Further, the authors then asked LL to grasp the same set of 20 tools and looked closely at both the trajectory and smoothness of her grasping movements, as well as the distance between her index finger and thumb as a measure of the anticipatory scaling of her grasp in flight. With all tools, LL showed smooth and well directed grasping, her wrist orientation in flight was matched with that of the tools’ orientation, and her grasp aperture was highly correlated with the size of the grasped portion of tools. Altogether, the findings were clear: LL was able to shape her grasp according to physical object properties when grasping-to-move, but when asked to grasp-to-use those same objects her hand shaping was severely perturbed.

Since this study, Sirigu and colleagues (2003) went on to test grasping-to-use and grasping-to-move common tools in a group of five IM patients with damage to left IPL. In the grasping-to-move task, participants had to simply grasp and lift tools, whereas with grasping-to-use they also had to demonstrate conventional use. To characterize the detailed kinematics of grasping according to task, they used a specialized glove with multiple sensors that read out real time information about finger joint angles (CyberGlove; Virtual Technologies). Following the work of Santello et al. (1998), principle component analysis was used to identify specific kinematic features of grasping. These analyses use the data itself to identify statistical structures (i.e. components) that can account for the greatest amount of variance. In healthy subjects, grasping-to-move was characterized by two main components, whereas grasping-to-use included an additional component, thought to underlie the finer motor adjustments necessary for tool use. Analysis of grasping in IM patients lacked this third ‘use-specific’ component but grasping-to-move was similar to controls. Thus, as with patient LL, these findings indicate selective impairments in the kinematics of grasping based on function and intention of use. In contrast, grasping-to-move tools based on physical object metrics was preserved in IM patients with left IPL damage. More recently, Randerath et al. (2009) also tested IM patients when grasping-to-move versus grasping-to-use. Again, impairments were found for grasping-to-use only, and performance with subsequent tool use was predicted by performance with functional grasping; failure to grasp tools functionally was always followed by impaired tool use (i.e. apraxia). Consistent with this general theme, Buxbaum and others (Buxbaum, Sirigu, Schwartz, & Klatzky, 2003) showed that IM patients typically demonstrate appreciably better knowledge of hand postures based on physical structure versus function.

So far, the evidence presented has shown that grasping based on knowledge of tool function and use can dissociate from grasping based on structure, but what about the reverse pattern? Is it possible to have impairment in grasping-to-structure but not grasping-to-function? Jeannerod and colleagues (1994) described a patient, AT, who had bilateral damage to parieto-occipital cortex, disrupting the medial-SPL stream to action. The patient showed impaired grasping, inappropriately scaling his grasp to the size of objects. However, when tested with size and shape matched objects familiar to the patient (e.g. lipstick), grasp scaling was considerably improved. Evidently, the familiarity of objects allowed the patient to better program his grasping in flight. The authors attributed these improvements as compensation stemming from the patient's intact "semantic" visual system (i.e. ventral stream). Indeed, the patient did not have damage to the ventral stream and could visually identify objects perfectly well. The findings were taken to suggest that impairments in grasping due to disruption of the dorsal pathway may be compensated to some extent based on object-centred inputs from the ventral stream when the targets of action are familiar. However, such a hypothesis is incomplete without consideration of the findings from patient LL (and others like her, just reviewed). Object recognition and the ventral stream are spared in patient LL, yet she nonetheless shows selective impairments in shaping her hand for grasping based on learned object function and intention of use. Thus, an account of ventral stream involvement in familiar tool use can only be complete if the left IPL is considered; indeed, I believe a key aspect of IPL specialization for familiar tool use is its unique propensity to receive and integrate stored object knowledge stemming from ventral stream sources. Taken together, the findings reviewed suggest independent parietal routes to grasping, a medial route tuned to the metrical scaling of hand posture based largely on bottom-up sensory information, and a lateral route needed for eliciting functional hand postures dependent on top-down object knowledge (Daprati & Sirigu, 2006; Johnson-Frey, 2003a; Johnson & Grafton, 2003).

1.4.2. Evidence from neuroimaging of grasping and tool use

In principle, human neuroimaging techniques like fMRI should provide a rather straightforward means for testing theories of divided parietal function for tool use versus grasping. In practice, however, the way is not so easy. First and foremost, the study of real actions with fMRI is inherently very challenging. In any fMRI study, subject head motion is likely the number one cause of poor data quality; even very small movements of the head, especially if in time with the experimental paradigm, can lead to spurious activations and render results unreliable. Hand and arm movements can easily transfer to head motion, leading to signal artifacts that coincide with actions and contaminate responses of interest (i.e. neural driven responses tied to action performance). Also, even if the head is kept completely still during action performance, movements of the arm itself (indeed, any mass) in the magnetic field can also lead to MR signal perturbations (Barry et al., 2010). A second set of challenges relate to the limitations imposed by space. The bore size of typical MR units is very small (typically ~ 60 cm), limiting the range of arm and hand movements that can be performed; and in the case of tool use, space issues also put physical constraints on the size of tools that can be tested. Also, the subject configuration for most MR units is to lie supine in the scanner, making direct vision of real objects impossible without the use of mirrors. Even if subjects could tilt their heads so that viewing of objects and the manual workspace might be possible, standard whole-head radio frequency coils used in most MR setups do not easily allow for such tilted head configurations.

Fortunately, these technical hurdles can be overcome, and our lab has developed the strategies, resources, and equipment to do so. First, to solve issues of mass-movement-related signal artifacts we use slow event-related methods such that potential signal perturbations due to arm/hand movements occur in real time, whereas neural-related, blood oxygenation level dependent (BOLD) changes occur with a temporal lag. Thus, by spacing actions well apart in time, we can resolve neural-related signal changes from movement-related artifacts. Second, with specialized radio frequency coils and custom built stimulus presentation equipment we are able to scan participants in a head-tilted configuration to allow for direct viewing of objects while they perform real actions. Finally, a combination of careful head 'packing', simple biofeedback methods, recruitment of participants who are well informed and experienced with fMRI, and the use of small amplitude movements to limit transfer of arm motion to the head have proven successful in solving problems with action-induced head motion.

Unfortunately, challenges with comparisons of grasping and tool use with fMRI go beyond solving such technical hurdles. Case-in-point, consider an experiment aimed to test theories of divided parietal streams for grasping and tool use by comparing grasp-to-move actions directly against grasp-to-use actions. While the predications of such an experiment are clear based on the patient work reviewed above, interpreting the results of such a subtraction is not without its problems. The two types of actions, grasping and tool use, differ so greatly in kinematics (e.g. complexity, duration, and extent), greater activations for grasping-to-use may relate to such differences in general, rather than anything specific to tool use per se.

The problem stated above underscores a major weakness common to all tool use imaging studies to date. Of the few studies that have used real objects, tool use has been compared with conditions involving no object manipulation (i.e. pantomime tool use) (Hermsdorfer, Terlinden, Muhlau, Goldenberg, & Wohlschlager, 2007; Imazu, Sugio, Tanaka, & Inui, 2007), no overt action (i.e. imagined tool use) (Higuchi, Imamizu, & Kawato, 2007), or, quite specifically, the use of chopsticks to pick up objects versus grasping with the hand (Inoue et al., 2001). Thus, 'tool use activations' may relate to differences in motor complexities, durations, spatial extents, or somatosensory feedback, or, in many instances, all of the above. More common, studies do not involve object manipulation at all, but instead look at tool use pantomimed actions as a proxy for real tool use (e.g. S. H. Choi et al., 2001; Johnson-Frey et al., 2005; Rumiati et al., 2004). Here again, control actions are not carefully equated for kinematic complexity. In Project

3 (Chapter 4) of the current thesis, I present a novel tool use paradigm that solves this incessant problem of controlling for kinematic complexity. I use a visual priming paradigm to probe the neural substrates of learned tool use, while at the same time comparing trial types that involve the same tool use actions and thus the same motor outputs. My findings (and this new improved approach) serve to push the field forward, and provide a more selective account of the neural substrates of learned tool use than was previously available.

In a recent review, Lewis (2006) performed a meta-analysis compiling the reports from 35 imaging studies across 64 distinct paradigms involving tools. The types of tasks have ranged from more perceptual/conceptual (answering questions, reading words, viewing pictures) to more motor-related (imagined tool use, pantomiming tool use), to actual tool manipulation (with real tools used; discussed above). Lewis distinguished between a conceptual versus production tool use network based on the number of paradigms showing activation overlap and the type of task used (conceptual versus production). The main areas of the conceptual network comprised left inferior frontal gyrus, left posterior middle temporal gyrus, and bilateral fusiform cortex, while the main areas of the production network comprised PPC (both IPL and SPL), dorsal lateral premotor cortex, ventral premotor cortex, and posterior middle temporal cortex. Areas of the production network were bilaterally represented, but with clear left hemisphere prevalence in strength and extent of activity. While this separation is useful, the same data may also be taken quite differently. That is, with these same data one might instead highlight that activation patterns across a number studies show surprisingly high proportions of overlap for both conceptual and action tasks. Indeed, as Scott Frey has emphasized in his reviews of the neuroimaging literature on tools, both dorsal and ventral stream areas are often activated for both motor and conceptual tasks (Frey, 2007; Johnson-Frey, 2004). Dorsal stream activations for conceptual tasks have been taken as support for distributed accounts of conceptual knowledge stores (Barsalou, 2007). In this view, it is worth noting that several independent groups have shown that left IPL is activated more strongly during explicit retrieval of manipulation versus functional knowledge of tools (Boronat et al., 2005; Canessa et al., 2008; Kellenbach, Brett, & Patterson, 2003). Conversely, ventral stream activations in tool use production tasks have been taken as support for the cooperative role of both dorsal and ventral streams underlying familiar tool use (Frey, 2007), in line with the basic model shown in Figure 1.3. However, this interpretation may be confounded. Defining contrasts often involve object versus non-object conditions, and thus ventral stream activity may be attributed to visual object activity (or imagery). Also, most of these studies employ tool use pantomime which may specifically recruit ventral stream resources independent of real tool use, as do other memory-guided actions (Cohen, Cross, Tunik, Grafton, & Culham, 2009; Singhal, Kaufman, Valyear, & Culham, 2005) (however, see also Kroliczak, Cavina-Pratesi, Goodman, & Culham, 2007). In fact, pantomime in the absence of real 3D objects also obscures interpretation of parietal activations; added conceptual elements may 'push around' patterns of activity, giving rise to findings not otherwise representative of real tool use. In summary, additional work is clearly needed to: i) verify the role of ventral stream areas in real tool use planning and implementation, and ii) identify potential differences between real and pantomime tool use.

Before concluding, a few additional imaging findings demand specific attention (despite some of the caveats just discussed). First, Johnson-Frey et al. (2005) showed that posterior parietal activity for tool use pantomime was strongly left-lateralized regardless of which hand was used (see also Bohlhalter et al., 2009; Kroliczak & Frey, 2009). This contrasts with activation for grasping, which shows bilateral activations in AIP for either hand, although typically stronger activity in the hemisphere contralateral to the hand used for grasping (Begliomini, Nelini, Caria, Grodd, & Castiello, 2008; Culham et al., 2006; A. Stark & Zohary, 2008). The pattern is consistent with the proposed specialized role of the left lateral-IPL stream for learned tool use and its separation from the medial-SPL stream devoted to online control of more basic actions. With a clever "go"-"no-go" design, Johnson-Frey and colleagues (2005) were also able to tease apart activation for tool use pantomime planning versus execution. They showed a posterior-to-anterior continuum of planning-to-execution-related activity in inferior parietal cortex, remarkably consistent with the findings of another imaging study that independently surfaced at the same time (Fridman et al., 2006). Finally, Vingerhoets et al. (2009) used a motor imagery task to compare the following conditions: imagined pointing-to, imagined grasping-to-move, imagined grasping-to-use, and imagined grasping-and-using tools.

They also varied these conditions across familiar tools, unfamiliar tools, and simple shapes. In short, they report a collection of activation foci within the left IPS that are: i) more active for use versus move tasks, and/or ii) show sensitivity to tool familiarity. Again, these findings are consistent with the general idea that left inferior parietal cortex is specialized for learned tool use, and suggest that spatially distinct IPS populations may contribute to distinct aspects of tool use knowledge.

1.4.3. Viewing tools: A theory of use-based affordances

The first neuroimaging study to discover that PPC was selectively activated by simply viewing pictures of familiar tools was made by Chao and Martin (2000). Their findings were to make a considerable impact on the field, reaching the interests of many subsequent authors, as evident from the paper's impressive current count of 337 citations (Web of Science, August 2010). Viewing (and silently naming) familiar tools was compared with viewing animals, a contrast that overlaps directly with a rich history of neuropsychological evidence whereby patients with selective perceptual/semantic impairments for man-made vs. natural object categories (and vice versa) have been frequently noted (Humphreys & Forde, 2001; Warrington & Shallice, 1984). From this perspective the contrast of tools versus animals was a sensible comparison to explore. However, from the perspective of interpreting parietal activations for tools, the comparison was problematic. Did the activations reflect the fact that tools are graspable (versus animals), or, as the authors suggested, did this parietal activity represent stored manipulation knowledge of tool function and use? After all, their tool-related activity appeared close to where our lab has identified grasp-selective activity, and canonical neurons in monkey area AIP respond to the graspable properties of viewed objects (see section1.2.1). To resolve this uncertainty, we put forward our own version of this experiment (Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007). We tested responses to viewing the following categories of familiar objects: tools, graspable objects, and non-graspable objects. Graspable objects were clearly manipulable, but were considered non-tools, having much weaker and less clearly defined actions associations compared with the objects we selected as "tools". If parietal activity for tools reflects object graspability, then both categories were expected to show similar activation levels. Instead, if parietal activity is sensitive to the strength and extent of action associations, then tools should activate these areas more strongly. With three independent approaches, we found convergent evidence for the latter account. First, we replicated the findings from Chao and Martin (2000), and then showed that activity in the parietal tool area is indeed selective for tools versus other graspable objects, and no differences were evident between graspable and non-graspable objects (Figure 1.4). Next, we found distinct intraparietal activations for tools > graspable objects and for graspable objects > non-graspable objects (Figure 1.5). Finally, in a subset of the same subjects we aligned data from previous studies of real object grasping and showed that parietal activations for viewing tools were distinct from those selective for grasping (Figure 1.6).

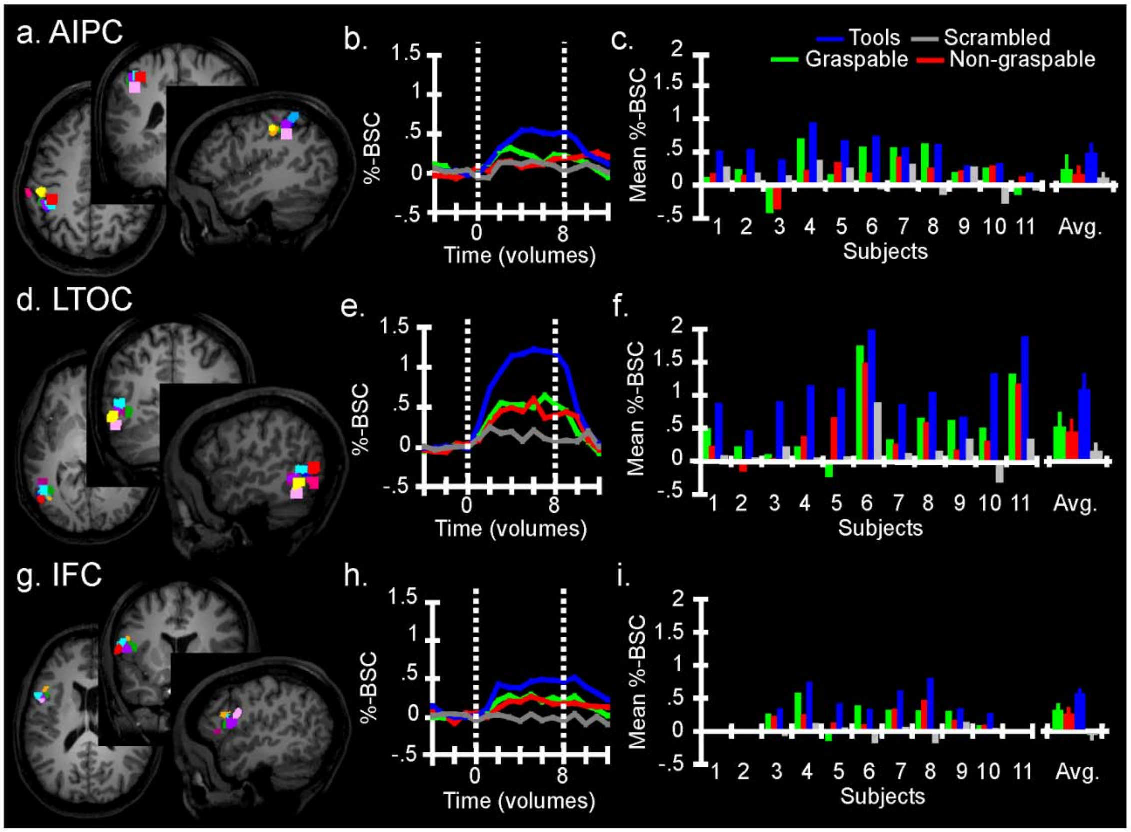

Figure 1.4. Results of ROI analysis from Valyear et al. (2007). Areas were identified within each individual by contrasting the naming of tools with the naming of animals based on localizer scans. Each subject's ROI is superimposed on the anatomy of a single individual, shown in a unique colour. Notice how closely the foci cluster together which indicates a good amount of functional-anatomical consistency across individuals. **(a)** Anterior intraparietal tool areas (AIPC) localized within the left anterior intraparietal sulcus of all eleven subjects. **(b)** The event-related averaged time course illustrating the pattern of activity during experimental scans, averaged across each individual's AIPC ROI. **(c)** The mean percent signal change from area AIPC for each experimental condition, shown for each subject and as the group average. **(d)** Lateral temporo-occipital tool areas (LTOC) localized within the left lateral occipital sulcus/posterior middle temporal gyrus of all eleven subjects. **(e)** Group event-related averaged time course, for LTOC ROI. **(f)** Mean percent signal change, per subject and as group average. **(g)** Inferior frontal tool areas (IFC) localized within the left inferior frontal gyrus of eight individuals. **(h)** Group event-related averaged time course, for IFC ROI. **(i)** Mean percent signal change, per subject and as group average.

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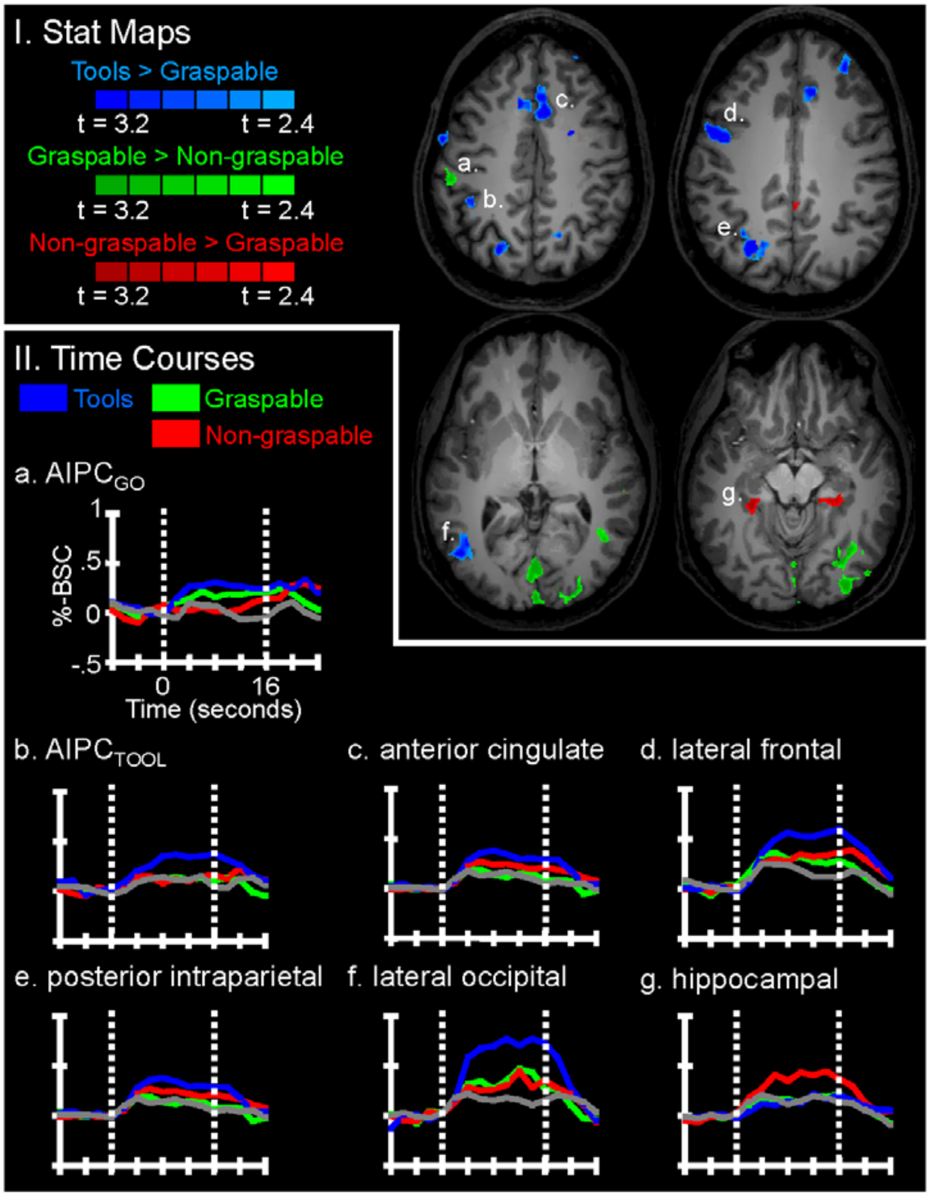

Figure 1.5. Results of voxel-wise analysis from Valyear et al. (2007). Section I (top) shows the activation maps corresponding to each of our comparisons of interest: the blue coloured activation indicates those areas showing significantly higher activity during the naming of tools relative to graspable objects; the green coloured activation indicates those areas showing significantly higher activity during the naming of graspable relative to non-graspable objects; the red coloured activation indicates those areas showing significantly higher activity during the naming of non-graspable relative to graspable objects (i.e. the opposite of green). Section II (bottom) shows the averaged time course activity extracted from each area aligned to the onset of each epoch. For both sections : **a.** left anterior intraparietal cortex (AIPC$_{GO}$); **b**. left anterior intraparietal cortex (AIPC$_{TOOL}$); **c.** bilateral anterior cingulated cortex; **d.** left lateral frontal cortex; **e.** left posterior intraparietal cortex; **f.** left lateral occipital cortex; **g.** bilateral parahippocampal cortex.

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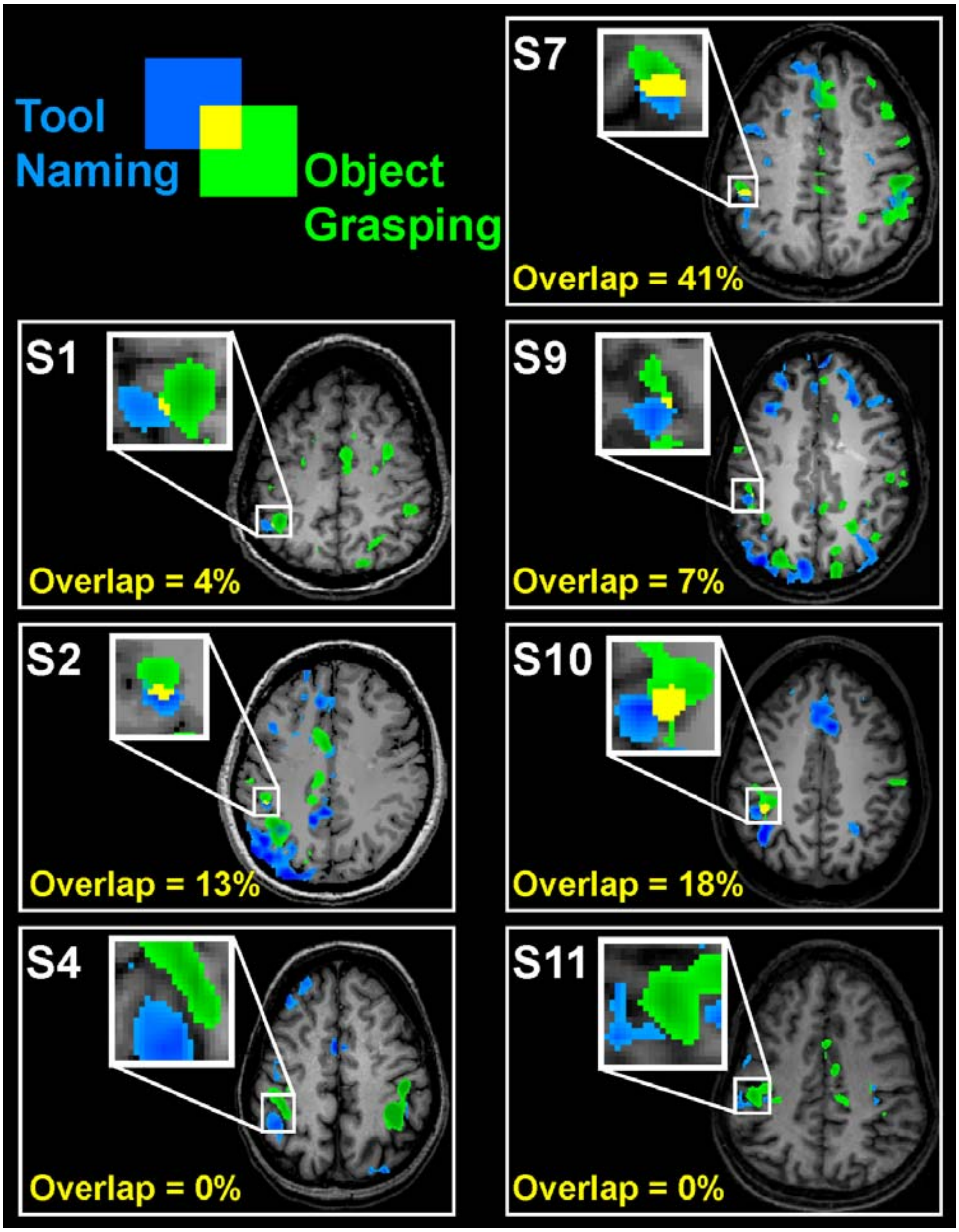

Figure 1.6. Comparisons of tool naming with object grasping from Valyear et al. (2007). Two activations maps are shown for each individual, with grasping activity (grasping versus reaching) shown in green, tool naming activity (tools versus animals) shown in blue, and the extent of overlap highlighted in yellow. The principle anatomical area of interest, the left anterior intraparietal sulcus near the junction of the postcentral sulcus, is marked and shown in closer detail to the left of each individual. The percent overlap between the two independently defined ROIs is indicated, computed as the number of overlapping voxels divided by the mean of the total voxels from each ROI combined. Notice how in each individual the activity associated with tool naming is reliably posterior to that associated with object grasping. Notice also that the anterior parietal activation for tools is largely left lateralized whereas the activation for grasping is evident bilaterally in most subjects.

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The findings indicate that parietal responses to viewing tools do not reflect processing of affordances for grasping, nor do they overlap with activations for real grasping. Notice that this distinction fits well with the theory of divided parietal streams for grasping and tool use just discussed; although, notably, our observations revealed separation in posterior-to-anterior aspects of IPS, rather than distinctions between lateral and medial PPC. More importantly, these findings led me to develop a theory of what I call use-based affordances, which I have since continued to formulate and test in the projects of the current PhD thesis. The ideas are quite simple. As a psychological concept, I take the term affordances to mean the properties of objects ***perceived*** as important for action, as a natural and intrinsic part of visual processing, in line with the original ideas of Gibson (1979). As a physiological concept, I take affordances to mean the corresponding activation of motor-related representations. Thus, for me affordances mean both the visually processing of object properties relevant for action ***and*** the concurrent activation of motor-related cortical areas. From this, the theory of use-based affordances is simply a distinction between two types of affordance effects based on the properties of objects for which these effects originate. On the one hand, affordances can be driven by the structural properties of objects, like size, shape, and orientation, and corresponding motor (e.g. parietal) activations relate to action plans that map onto these object features. These effects are independent of object familiarity, driven solely by the structural properties of objects, just as Gibson (1979) had originally described. A physiological correlate of these affordance types, which I call structure-based affordances, corresponds with canonical neuron responses in monkey AIP (and F5), and overlaps with grasp-selective parietal circuitry. In contrast, use-based affordances are driven by learned object properties corresponding with known function and way of use. Such affordances are not directly accessible to vision without access to prior knowledge, built up from previous sensorimotor experience, defined by specific motor interactions beyond what are called for by structural object properties. Such affordances directly correspond with familiar tools. As Jeannerod and Jacob (2005) so elegantly describe:

> Tools, as well as musical instruments or sport materials, are objects which cannot be characterized merely by their geometrical properties like size, shape or orientation. They have additional properties that cannot be detected unless one knows what the object is for and how to use it; yet, once they are known (by

> observation, training or verbal instructions), they do supervene upon the pure geometrical properties that are part of the non-conceptual content of more basic visuomotor representations (p. 306).

The distinction between structure-based and use-based affordances explained our neuroimaging findings (Valyear et al., 2007); viewing tools activates left posterior parietal areas important for tool use by way of use-based affordances. But, these interpretations were merely suggestive – activations were not directly tied to the use of tools. Projects 2 and 3 of the current thesis involved real actions with tools and aimed to provide further, more direct support for this theory.

1.5. Current projects

A central objective of my thesis was to gain new insights as to the processes by which stored knowledge and tool use are linked, both cortically, at the level of underlying brain systems, and behaviourally, at the level of action planning and kinematics.

Project 1 (Chapter 2) used fMRI to map brain activity in response to viewing tool grasping that was either consistent or inconsistent with how tools are typically grasped for use. Tool use is expected to involve changes in parietal representations, thought to underlie skilled performance. Such changes are thought to encode motor procedures typical of tool use. Movies of grasping typical of use were expected to activate parietal areas important for tool use skills more strongly by virtue of closer correspondence with underlying motor representations. As noted earlier, these predictions were motivated in part by the properties of mirror neurons in monkeys. Mirror neurons are important for real grasping, and are also activated by the observation of grasping. Preferential activity for typical tool use grasping was taken to indicate sensitivity to the learned aspects of tool use.

Project 2 (Chapter 3) compared behavioural priming and the kinematics of grasping tools between two tasks: grasping to move tools, grasp-to-move (GTM), versus grasping to demonstrate the conventional use of tools, grasp-to-use (GTU). Behavioural priming experiments have been used extensively in cognitive psychology. In general, priming refers to the facilitation of a current task event (often called the ‘probe’ event) due to some prior event (often called the ‘prime’ event). In Project 2, prime events involved viewing tools while probe events involved actions, either the GTU or GTM task. Critically, prime-probe pairs were either the same or different tools. Following our previous work and the hypothesis of use-based affordances for tools (section 1.4.3), the visual cuing of tool identity was expected to activate learned tool use plans. When prime-probe events involved the same tools, priming for the GTU task was predicted, measured as faster reaction times to initiate actions relative to when prime-probe events involved different tools. To help limit the possibility that priming might be carried by structural object properties important for grasping in general, we used tools with the same handle. This also provided the opportunity to characterize the detailed kinematics of functional grasping; differences in grasping across tools would reflect differences in the way tools are used, not differences in structural affordances of handles. Priming was taken as evidence of facilitation of programming due to the activation of learned tool use plans by the visual appearance of tools.

Project 3 (Chapter 4) used a priming paradigm similar to that of Project 2, but tailored for testing with fMRI. Following the hypothesis of use-based affordances (section 1.4.3), prime events involving the visual presentation of a given tool were expected to activate corresponding motor plans for use. If after a short delay the same tool is shown again and used, motor programs supporting its use will have already been activated (primed) and overlapping neural processes will translate to reduced BOLD signal. Neural priming is predicted for areas involved in the recruitment and implementation of stored tool use plans. Specificity of priming for tool use was tested by comparison with newly learned arbitrary colour-action pairings. If priming reflects differences in correctly versus incorrectly cued actions, then both tool and colour defined actions should lead to priming. However, if learned tool use is represented in specific brain areas, then specificity of priming for tool-action and not colour-action pairings is expected.

1.6. References

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Chapter 2

2. Observing learned object-specific functional grasps preferentially activates the ventral stream[2]

2.1. Introduction

According to one influential view of the human cortical visual system, a dorsal stream, projecting from occipital to posterior parietal cortex, uses visual information to guide actions while a ventral stream, projecting from occipital to inferior temporal cortex, uses visual information to construct detailed perceptual representations, including those critical for the visual recognition of objects (Goodale & Milner, 1992). In general, the advent of human neuroimaging has led to additional support for this account, describing several ventral stream areas as specialized for visual recognition (for review, see Grill-Spector & Malach, 2004) and various dorsal stream areas as specialized for the visual control of actions (for reviews, see Culham, Cavina-Pratesi, & Singhal, 2006; Culham & Valyear, 2006). However, as research progresses, the precise functionality of the two streams continues to be refined (e.g. Jeannerod & Jacob, 2005; Rizzolatti & Matelli, 2003). For example, various lines of evidence suggest several additional roles for the dorsal stream, beyond visuomotor transformations and the guidance of actions. In this study we take a closer look at two such processes, action observation and tool use, and consider the potential relationships between them. Specifically, we tested whether or not parietal tool use areas would respond to observing others grasping tools and, moreover, if such responses would differ depending on the functionality of the grasp (i.e. depending on whether or not the grasp was consistent with the use of the tool).

With tool use and manual praxis skills, accurate visuomotor control is obviously a key component, and areas within the posterior parietal cortex have long been thought of as critical (e.g. Haaland, Harrington, & Knight, 2000; for review, see Rothi & Heilman, 1997). However, several aspects of these types of actions greatly differ from the types of

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dorsal stream processing principles that have typically been emphasized. For example, Goodale and Milner (1992) showed that visually guided actions such as object grasping can be carried out independently and in the absence of conscious object perception and recognition (as mediated by the ventral stream). However, in the case of complex learned actions such as tool use, object recognition and access to stored semantic knowledge is likely to play an important role (Creem & Proffitt, 2001; Frey, 2007; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000; Hodges, Spatt, & Patterson, 1999; Milner & Goodale, 1995). Similarly, Milner and Goodale (1995) stressed that the visuomotor transformations performed by the dorsal stream are not likely to call upon stored representations of previous actions, but instead should be computed from the bottom-up, in real-time. Here again though, tool use is very much thought to rely on stored representations of actions (for review, see Rothi & Heilman, 1997). Thus, for Goodale and Milner, tool use is a special kind of visuomotor behavior, one that calls for explicit cooperation between dorsal and ventral pathways.

The role of the parietal cortex in observing the actions of others is a relatively recent discovery. In both humans and monkeys, parietal and frontal responses to observed actions appear to overlap with those areas critical for the control of actions (for review, see Rizzolatti & Craighero, 2004). Indeed, activity during both action execution and observation is considered a defining characteristic of mirror neurons in the monkey. Importantly, many of these parietal and frontal mirror neurons show tight congruence between the types of actions they encode motorically and those they encode visually. In studies involving action observations in humans, others have shown that the specificity of areas active when observing particular actions appears to closely match the specificity of areas active when performing those same actions (e.g. Filimon, Nelson, Hagler, & Sereno, 2007; Shmuelof & Zohary, 2005, 2006), and, similarly, responses to perceived actions appear to depend on the particular motor repertoire of the observer (for review, see Shmuelof & Zohary, 2007). For example, in some exciting imaging work by Calvo-Merino and colleagues (2005; 2006), greater activity within several parietal and frontal areas was reported when participants viewed actions that they themselves where able to perform than when they viewed actions they could not perform. Whether or not such activity truly reflects mirror-like mechanisms, similar to those noted in the macaque, is an issue of current contention that has not yet been resolved (Chong, Cunnington, Williams, Kanwisher, & Mattingley, 2008; Dinstein, Thomas, Behrmann, & Heeger, 2008; Turella, Pierno, Tubaldi, & Castiello, 2009).

Perhaps the most compelling evidence for the importance of parietal cortex in perceiving and recognizing actions comes from case studies of patients with parietal damage. Here, others have noted that deficits with action imitation often co-occur with problems in recognizing actions, and this particular pattern is most strongly associated with left inferior parietal lesions (Buxbaum, Kyle, & Menon, 2005; Heilman, Rothi, & Valenstein, 1982; Wang & Goodglass, 1992). Indeed, based on their close analyses of these types of patients, Buxbaum and colleagues (2005) suggest that the same parietal representations may be critical for both the production and recognition of complex actions, consistent with a "direct matching hypothesis" underlying action recognition (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996; for review, see Rizzolatti, Fogassi, & Gallese, 2001). From a theoretical perspective, an active role in perceiving and understanding actions may be particularly useful for areas involved in praxis, for example, when learning new skills through observation, as is often the case with human tool use learning.

We were interested in whether or not parietal responses to observing others' actions would depend on how well the observed actions matched those normally associated with tool use. To address this question, we scanned individuals while they viewed short movies of familiar tools being grasped in ways that were either consistent or inconsistent with how tools are typically grasped during use. By using tool grasping, as opposed to whole arm movements with a tool in hand, we were able to keep very tight control over our two critical stimulus conditions (see Figure 2.1). That is, our 'typical grasping' (TG) and 'atypical grasping' (AG) movies simply varied with respect to how a target tool was grasped in conjunction with how it was oriented. This design allowed us to manipulate the strength to which these actions were associated with typical tool use, while at the same time keeping other factors between conditions, like the constituent arm and hand movements themselves, very similar. In previous work, Creem and Proffitt (2001) showed that when individuals were asked to grasp familiar tools they typically rotated their wrist and hand in accordance with how the handle of the tool was oriented, as with our TG condition. This finding is one instance of a more general “end state comfort effect” whereby subjects will adopt an initially uncomfortable posture that enables a comfortable posture at the conclusion of an action (Rosenbaum & Jorgensen, 1992; Rosenbaum et al., 1990; Rosenbaum, van Heugten, & Caldwell, 1996). As already noted, previous imaging work involving action observations have shown that parietal areas respond more strongly to actions that closely match internal representations (e.g. Calvo-Merino et al., 2006). Thus, we predicted that parietal areas involved with tool use would respond more strongly to our TG actions, since these were the types of grasping actions normally associated with using tools (as opposed to AG actions). To help us identify parietal areas associated with tool use, independently from our main experiment, we used a separate localizer paradigm based on previous imaging work (see Methods, “Localizer 1”). We also thought that many other areas could be differentially active for our movie conditions, including the possibility of detecting areas that prefer viewing AG as compared with TG. For example, in some ways our AG movies may seem more surprising or unusual to subjects, which might be expected to influence the activity of areas involved with understanding the intentional aspects of others actions (e.g. temporo-parietal junction, Saxe & Kanwisher, 2003). Indeed, others have shown that unexpected or unusual events can lead to increased activity in many areas (Buccino et al., 2007; Liepelt, Von Cramon, & Brass, 2008; Murray, Kersten, Olshausen, Schrater, & Woods, 2002; Murray, Schrater, & Kersten, 2004; Summerfield, Trittschuh, Monti, Mesulam, & Egner, 2008). Thus, we also performed a whole-volume voxel-wise analyses, directly comparing activation between conditions.

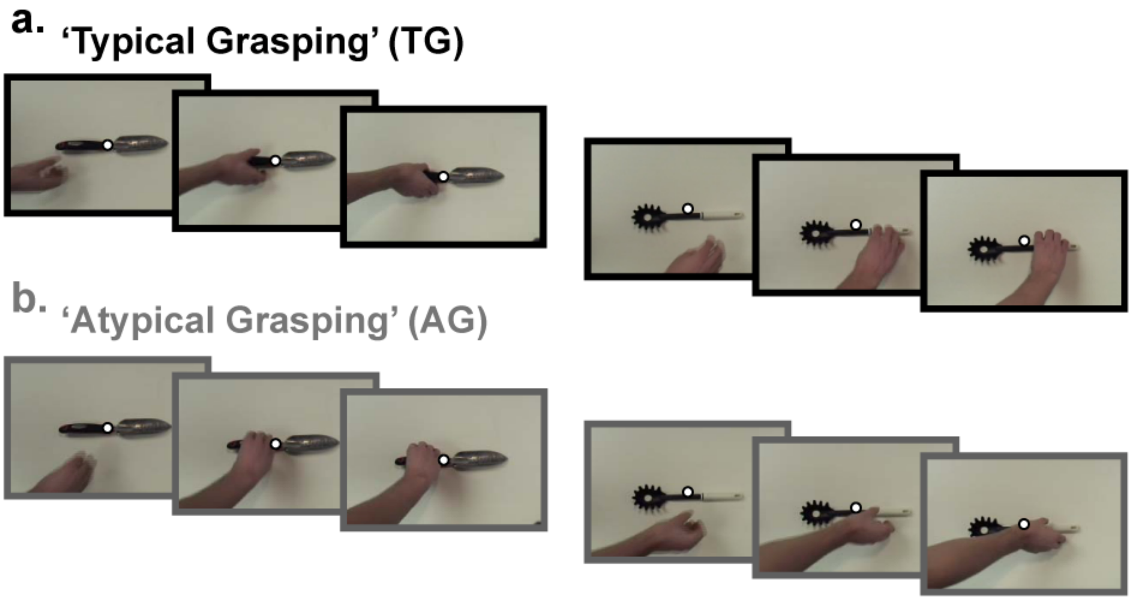

Figure 2.1. Experimental paradigm. a) Examples of our typical grasping (TG) movies. Shown are three individual frames from two different movie clips. In each case, regardless of handle orientation, the grasp is consistent with how tools are typically grasped for the purpose of using. **b)** Examples of our atypical grasping (AG) movies. Regardless of handle orientation, the grasp is inconsistent with how tools are typically grasped for the purpose of using. Both TG and AG conditions comprised the same proportion of tool identities, tool orientations, and hand trajectories.

Rather than finding a preference for viewing TG actions within parietal cortex, this pattern of activity was observed within several ventral stream areas. Our discussion focuses on interpreting the significance of these ventral stream activations, as well as addressing the findings within parietal cortex, in particular, within the context of action understanding and tool use.

2.2 Methods

2.2.1. MRI participants

Nine neurologically intact individuals participated in the study (five female; age range of 22 – 41 years) and each provided informed consent in accordance with the guidelines approved by the University of Western Ontario Health Sciences Review Ethics Board. All individuals were right-handed, with normal or corrected-to-normal visual acuity, and all were naïve to the purpose of the study.

2.2.2. Experimental paradigm

Movie clips were recorded and shown at 30 frames per second, were 2 s in duration, and each frame subtended 15° of the subject's visual field. There were three types of movie clips, TG, AG, and Reach movies, which were organized into separate 16 s epochs, with 6 clips per epoch and an inter-clip-interval of ~ 333 ms. Regardless of the movie type, each epoch comprised three movie clips in which the handle of the tool faced away from the actor and three movie clips in which the handle of the tool faced toward the actor. In TG, when the handle faced away from the actor the hand was rotated about the wrist at the point of prehension such that the tool was grasped in a functionally appropriate manner, whereas when the handle faced toward the actor the tool was grasped without such a rotation (but still in a functionally appropriate manner; see Figure 2.1a). In AG the reverse was true, such that when the handle faced away there was no rotation of the hand but when the handle faced toward the actor there was. This combination brings about grasping actions that do not easily allow for the actor to use the tool without further postural adjustments (see Figure 2.1b). The Reach movies simply involved the touching of the target tool (at the handle) with the actor's knuckles. Note also that, in the interest of keeping hand and arm trajectories similar across conditions, regardless of handle orientation, half of our Reach movies also involved a rotation of the hand at the point of contact. Also, we performed a left-right ‘horizontal flip’ on our movie clips, such that half of our blocks showed actions with the right hand approaching from the left side of space (Figure 2.1) while the other half showed actions with the left hand approaching from the right side of space, balanced across conditions. Our three movie conditions were interleaved with either 16 s fixation epochs or with epochs comprised of scrambled-up versions of the movies. In the scrambled epochs, like with the other movie conditions, six distinct movie clips of 2 s duration were shown with an inter-clip-interval of ~ 333 ms. Scrambled movie clips were created by deconstructing each clip into its constituent frames (using Adobe Premiere), dividing each frame into a grid of 48 x 48 cells and then randomly reordering the cells of the grid (with subsequent frames of a given clip scrambled and reordered in the same manner, using a custom Matlab code), and then finally reconstructing the movie clip from the newly scrambled frames (again, using Adobe Premiere).

Each run lasted 6 min and 40 s and comprised 25 separate epochs (6 fixation, 7 scrambled, and 4 epochs per movie type). Throughout each run subjects performed a 1-back task whereby responses were made, via a right-handed button press, whenever two successive video clips were identical. Each epoch could contain either 0 or 1 repeated clip, balanced across conditions (2 repeats per movie type, 3 repeats for scrambled). Subjects were told that their main goal should be to perceive each of the movies intently, that the repeated clips would occur quite infrequently, and that the task of detecting these repeats would be used as an index of their attention to the movies. A solid red circle, superimposed on the centre of each frame, served as a fixation point throughout.

Altogether, our collection of tools included 33 different identities (see Appendix A) and 4 different exemplars for each identity (e.g. 4 distinct umbrellas) for a total of 132 distinct objects, and for each object, any given hand posture might be associated with it. Each run was organized such that within the first half, all 33 distinct tool identities were shown (divided up among the first six intact movie epochs) and within the last half a different exemplar of the 33 identities were shown (divided up among the six remaining intact movie epochs). The following run showed the third and fourth exemplar versions, again distributed separately across the first and second halves of the run. The third run used the same tools as in the first run and the fourth run used the same tools as in the second run, however, in each case, the hand actions associated with each of the tools differed from those shown previously. That is, careful organization of clips ensured that when tool identities, and identity exemplars, were repeated they were not coupled with the specific hand actions for which they were previously associated. Thus, the time between repetition of tool identities (and exemplars) was maximized and the type of hand actions associated with each repetition was varied and unpredictable. Both of these measures were taken so to minimize the potential for complicated repetition effects to accrue upon the repetition of identities and/or exemplars. The order of runs was counterbalanced across individuals.

Note also, to gain some appreciation of how familiar our subjects were with the appropriate use of our different tools, we asked them to estimate levels of hands-on-experience using the following five-point scale: 1 = never used or seen in use, 2 = never used myself, but seen in use, 3 = used this tool maybe once or twice in my life, 4 = use this tool approximately once a year, 5 = weekly or daily use. This scale was taken directly from a recent imaging study by Vingerhoets (2008) that was specifically designed to address issues of tool familiarity. We received responses from 7/9 of our subjects, and the mean 'familiarity-of-use' score across all of our tools was found to be 4.4, with a standard deviation of 0.5, indicating that our tools were highly familiar to our subjects. Most importantly, given that each particular tool was distributed evenly across our three movie types, any observed activation differences across movie types could not be attributed to differences in tool familiarity.

2.2.3. Localizer 1: Bodies, objects, tools

Each of these runs included colour photos of familiar tools (87 different identities), headless bodies (87 different identities; 44 were females), non-tool objects (87 different identities, including vehicles, furniture and appliances, food items, plants, clothing items, and other objects from miscellaneous categories), and scrambled-up versions of these stimuli. All stimuli were selected from the Hemera Photo-Objects image database (Hemera Technologies Inc., Gatineau, QC). For the scrambled stimuli, we divided each of our photo images into a grid of 48 x 48 cells and then randomly reordered the cells of the grid. A small black circle was superimposed in the centre of each image to serve as a fixation point. Each image subtended 15° of the subject's visual field. Stimuli were organized into separate 16 s epochs, with 18 photos per epoch, presented at a rate of 400 ms per photo with a 400 ms inter-stimulus-interval. Each run lasted 6 min and 40 s and was comprised of six stimulus epochs per condition and seven (baseline) scrambled epochs. Stimulus epochs were organized into sets of three, separated by scrambled epochs, balanced for epoch history within a single run. All subjects received four of these localizer runs, photos were repeated across runs, and the stimulus and epoch orders were pseudo-randomized and balanced across runs. Subjects performed a 1-back task throughout, whereby responses were made, via a right-handed button press, whenever two successive photos were identical. Each stimulus epoch included either three or four repeated photos, balanced across conditions (with a total of 21 repeats per condition per run). Scrambled-up photos were not repeated and subjects were simply asked to passively view the stimuli during scrambled epochs.

2.2.4. Localizer 2: Motion sensitivity

Each of these runs included alternating 12 s epochs of stationary (baseline) and moving stimuli. Each subject (except one, due to time constraints) received two identical runs, with 7 stationary and 6 moving epochs per run, resulting in a single run length of 3 min and 28s. The stimulus was an annulus checkerboard pattern, which moved in and out during motion epochs and remained static during stationary epochs. Throughout each run subjects were simply asked to passively view the stimuli.

2.2.5. Imaging parameters

All imaging was performed at the Robarts Research Institute (London, Ontario, Canada) on a 4 Tesla, whole-body MRI system (Varian, Palo Alto, CA; Siemens, Erlangen, Germany) using a transmit-receive hybrid birdcage radiofrequency head coil. Each imaging session took approximately one hour and forty-five minutes to complete and included ten functional runs and a single high-resolution anatomical scan. Functional volumes were collected using a T2*-weighted, navigator echo corrected, segmented spiral acquisition (echo time, TE = 15 ms; flip angle, FA = 40°; time to repetition = 1000 ms with two segments/plane for a volume acquisition time of 2 s) to image the blood-oxygenation-level dependent (BOLD) signal over time (Ogawa et al., 1992). Each volume comprised 17 contiguous, 6 mm, axial-oblique slices, spanning from the most superior point of the cortex down through the ventral fusiform cortex, including approximately ⅔ of the cerebellum. The field of view was 22.0 cm x 22.0 cm, with an in-plane resolution of 64 x 64 pixels, resulting in a voxel size of approximately 3.4 mm x 3.4 mm x 6.0 mm. Anatomical volumes were collected in the same orientation and in-plane field-of-view as the functional scans using a T1-weighted 3D magnetization-prepared spiral acquisition (inversion time, TI = 1300 ms; TE = 3.0 ms; time to repetition = 50 ms; FA = 20°, matrix size of 256 x 256 x 96). The resultant voxel size was 0.9 mm x 0.9 mm x 2.0 mm.

2.2.6. Data preprocessing and analysis

Imaging data were preprocessed and analyzed using Brain Voyager QX version 1.7.9 (Brain Innovation, Maastricht, The Netherlands). Each functional run was assessed for subject head motion by viewing cineloop animation and by examining Brain Voyager motion detection parameter plots after running 3D motion correction algorithms on the untransformed two-dimensional data. No abrupt movements were detected in the animations and no deviations larger than 1 mm (translations) or 1 ° (rotations) were observed in the motion correction output. Functional data were then preprocessed with linear trend removal and underwent high-pass temporal frequency filtering to remove frequencies below three cycles per run. Functional volumes were aligned to anatomical volumes, which were then transformed into standard stereotaxic space (Talairach & Tournoux, 1988).

All imaging data were analyzed using contrasts within a general linear model (GLM) for each type of run (localizer and experimental runs). Each GLM included predictor functions for each of the conditions (except the baseline), generated by rectangular wave functions (high during the condition and low during all other conditions) convolved with the default Brain Voyager QX “two-gamma” function designed to estimate hemodynamic response properties. For the experimental runs, the baseline was defined as the scrambled movie epochs, and a predictor of no interest was included to account for the fixation epochs. Prior to GLM analysis, each run was z-transformed, effectively giving each run a mean signal of zero and converting beta weights into units of standard deviations.

2.2.7. Region-of-interest (ROI) selections and analyses

For each individual, data from the localizer scans were used to identify several distinct areas based on previous imaging work. A similar selection procedure was used to define all ROIs in all individuals, whereby the most significantly active voxel(s), or peak, was first identified based on a particular contrast (see Results), statistical thresholds were then set to a determined minimum, and a volume of interest up to $(10\ \text{mm})^3 = 1000\ \text{mm}^3$ around the peak was selected. The determined minimum threshold value varied depending on the nature of the contrast used to define the region and on the robustness of the resultant activity within each individual. For example, for both tool-selective areas, which were identified using a more stringent conjunction analysis (see Results), the minimum determinant threshold was set to a $p < .005$ (uncorrected) for each individual. Note that we define a conjunction contrast as a Boolean AND, such that for any one voxel to be flagged as significant it must show a significant difference in each of the component contrasts.

For each subject's ROI, we extracted the average time course activity, aligned to the onset of each epoch, from experimental runs. It is worth emphasizing that this activity is completely independent from the activity used to identify and select the regions based on either of the localizers. Within a given subject's ROI, the mean percent BOLD signal change (mean %BSC) associated with each condition was computed as the average of the activation at the peak of the response (i.e., volumes 5-7, corresponding to 10-14 s after the start of each epoch). In order to compare activations across conditions, the mean %BSC values were then entered into a one-way repeated measures analysis of variance, with subject as a random factor. Where significant differences were found, in order to test for differences between pairs of conditions, all possible post-hoc comparisons were performed by computing an F-statistic. Tukey's wholly significant difference (WSD) was then used to correct the critical significance value so to control for the problem of multiple comparisons.

2.2.8 Voxel-wise analyses

A whole-brain voxel-wise analysis was performed for the entire group of subjects using an averaged GLM fitted for random effects analyses, with separate predictor functions for each condition (except the scrambled baseline) for each subject. Three contrasts of interest were performed (see Results). Activation maps were set to reliable statistical thresholds ($p < .005$, minimum cluster size of 163 mm^3), using Monte Carlo simulations (performed with AlphaSim software, courtesy of Douglas Ward, Medical College of Wisconsin) to verify that the resultant clusters were unlikely to have arisen due to chance (corrected, $p < .05$), given the problem of multiple comparisons.

2.3 Results

2.3.1. Behavioural results

Two subjects' behavioural responses were not acquired due to technical problems. Repeated measures analysis of variance revealed no significant differences in response reaction times across conditions, $F(3,18) = 1.47$, $p = .26$, however, there were differences in the accuracy of correct responses, $F(3,18) = 11.39$, $p < .001$. Individual pair-wise comparisons revealed that these differences reflect a greater failed-detection rate for the scrambled condition (missed repeats = 22.62%, *SEM* = 5.67), as compared with all other conditions ($p < .001$); TG missed repeats = 3.57%, *SEM* = 3.57, AG missed repeats = 7.14%, *SEM* = 4.61, Reach missed repeats = 7.14%, *SEM* = 3.72. Differences between TG, AG, and Reach were not significant, $F(3,18) = 1.0$, $p = .73$.

2.3.2. ROI results

Our first localizer paradigm (see Methods for details) showed pictures of tools, other familiar objects, headless bodies, and scrambled stimuli. Tool-selective areas were identified by contrasting the viewing of tools versus objects, tools versus bodies, and tools versus scrambled images. In each individual, this conjunction contrast reliably revealed two areas of robust activity, one localized to the left posterior middle temporal gyrus (pMTG; see Figure 2.2a), and the other localized within the left anterior intraparietal sulcus, often on the medial bank of the sulcus, near the junction of the postcentral sulcus (aIPS; see Figure 2.2d). The locations of these foci are highly consistent with previous imaging studies involving tools, including tool viewing and naming (Chao, Haxby, & Martin, 1999; Chao & Martin, 2000; Martin, Wiggs, Ungerleider, & Haxby, 1996; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007), pantomime tool use (e.g. Fridman et al., 2006; Johnson-Frey, Newman-Norlund, & Grafton, 2005), imagined tool use (Creem-Regehr & Lee, 2005; Moll et al., 2000), and various other tool-related paradigms (for reviews, see Frey, 2007; Johnson-Frey, 2004; Lewis, 2006). Our primary interest was in evaluating how these tool-selective areas would respond during the observation of our different types of tool-directed actions. In particular, we predicted that if these areas were tuned to the functional aspects of learned object-specific actions then they would respond more robustly during the observation of TG as compared with AG. Of these two areas, we predicted that the parietal tool area would be the most likely candidate to show such response selectivity. Note, however, whether or not the tool-selective pMTG should be considered part of the dorsal or the ventral stream, or neither, remains uncertain. Indeed, as we will later discuss, the left pMTG is active in many different types of tool-related paradigms, and may have a particularly special role in processing the motion aspects of tool use. Thus, although we had clear predictions with regards to the parietal tool area, we were uncertain about how the pMTG would respond. Our findings are shown in Figure 2.2c and f. Contrary to our predictions, although the tool-selective aIPS showed higher responses to both types of grasping movies relative to the reaching movies (TG > Reach, $p < .01$; AG > Reach, $p < .001$), this area did not distinguish between our two different types of grasping actions ($p = .55$). In contrast, the tool-selective pMTG was more responsive to our TG movies as compared with our AG movies (TG > AG, $p < .001$), and the activity associated with viewing AG and Reach movies did not differ ($p = .71$).

It should also be noted that in the majority of subjects (8/9) an additional focus of activity within the intraparietal sulcus, posterior to our aIPS area, was detected using the conjunction contrast (which can be seen in Figure 2.2d and e). Tool selectivity within the more posterior regions of the intraparietal sulcus is also consistent with previous imaging work (e.g. Valyear et al., 2007). However, analysis of the time course activity within this area during the viewing of our experimental movies revealed no significant differences ($F(2, 14) = 0.01$, $p = .91$).

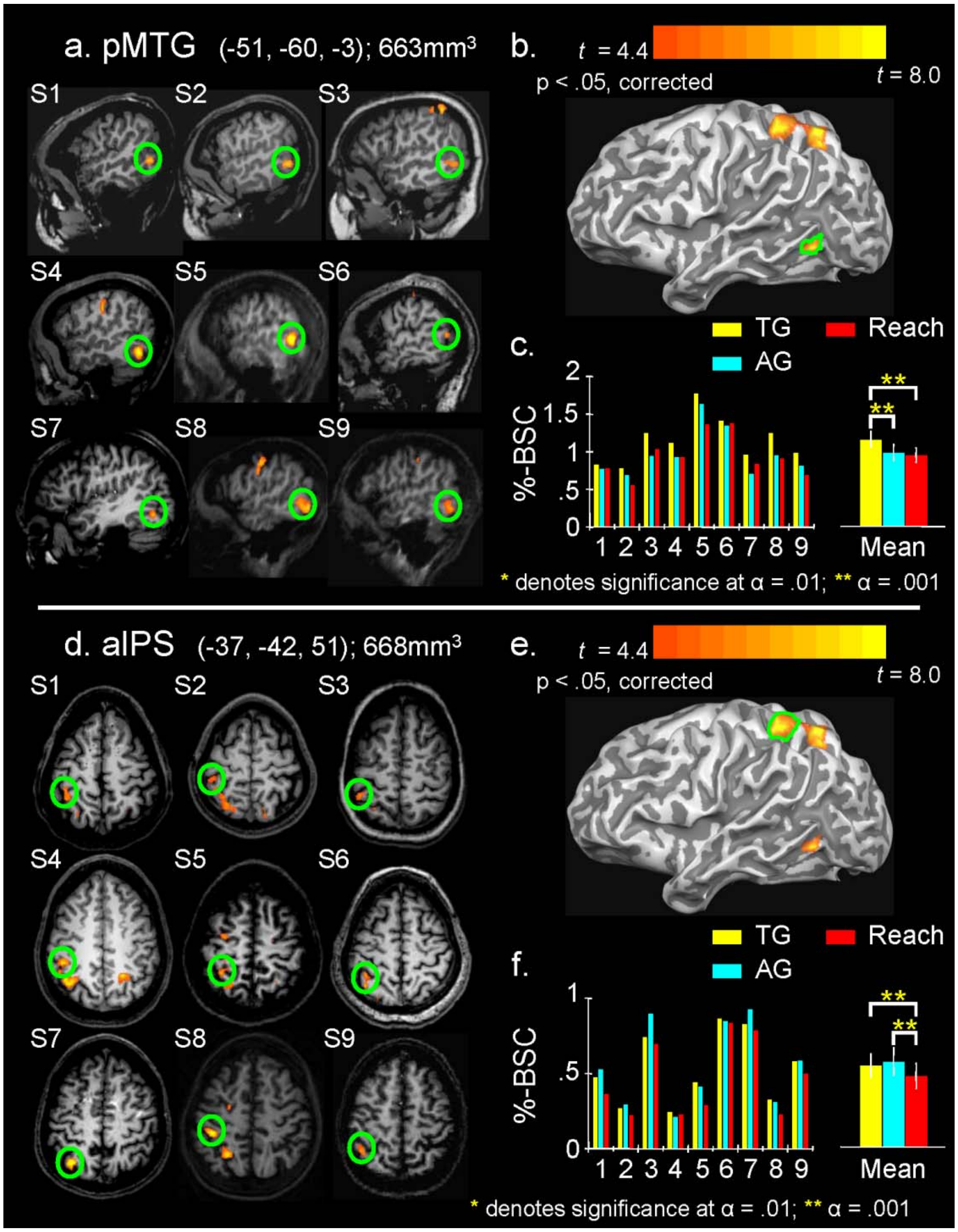

Figure 2.2. ROI results for tool-selective areas. a) Tool-selective activity within the posterior middle temporal gyrus (pMTG) is shown for each individual subject (S1-S9). **b)** Group averaged activity, based on random effects analysis, corrected for multiple comparisons, is shown on the partially inflated cortical surface of a single individual (S1), with the pMTG activity outlined in green. **c)** Mean percent BOLD signal change (%-BSC) values for the three experimental conditions are shown for each individual's pMTG. The group mean %-BSC is also plotted, with any significant differences between conditions denoted (see legend). **d)** Tool-selective activity within the anterior intraparietal sulcus (aIPS) is shown for each individual subject (S1-S9). **e)** Group averaged activity for aIPS is depicted, as in b). **f)** Mean %-BSC in aIPS is shown for each subject and the group, as in c). TG = typical grasping movies; AG = atypical grasping movies; Reach = reaching movies.

This localizer paradigm also allowed us to identify several other previously characterized visual areas, including body-selective areas, the extrastriate and fusiform body areas (EBA and FBA)(Downing, Chan, Peelen, Dodds, & Kanwisher, 2006; Downing, Jiang, Shuman, & Kanwisher, 2001; Peelen & Downing, 2005), and other higher-level object-related areas, the lateral occipital object areas (LO) and ventral temporo-occipital object areas (vTO) (e.g. Grill-Spector, Kushnir, Edelman, Itzchak, & Malach, 1998). Body-selective areas were identified using a conjunction contrast (bodies > tools, bodies > objects, and bodies > scrambled) and object-sensitive areas were identified using a simple contrast of objects versus scrambled. These results are summarized in Figure 2.3a and b. Most interestingly, the left vTO and area LO bilaterally showed a significant degree of selectivity for the TG movies as compared with both the AG and Reach movies (left LO: TG > AG, $p < .01$; TG > Reach, $p < .01$; right LO: TG > AG, $p < .0001$; TG > Reach, $p < .0001$; left vTO: TG > AG, $p < .001$; TG > Reach, $p < .01$) which did not differ from one another (left LO: $p = .95$; right LO: $p = .99$; left vTO: $p = .65$).

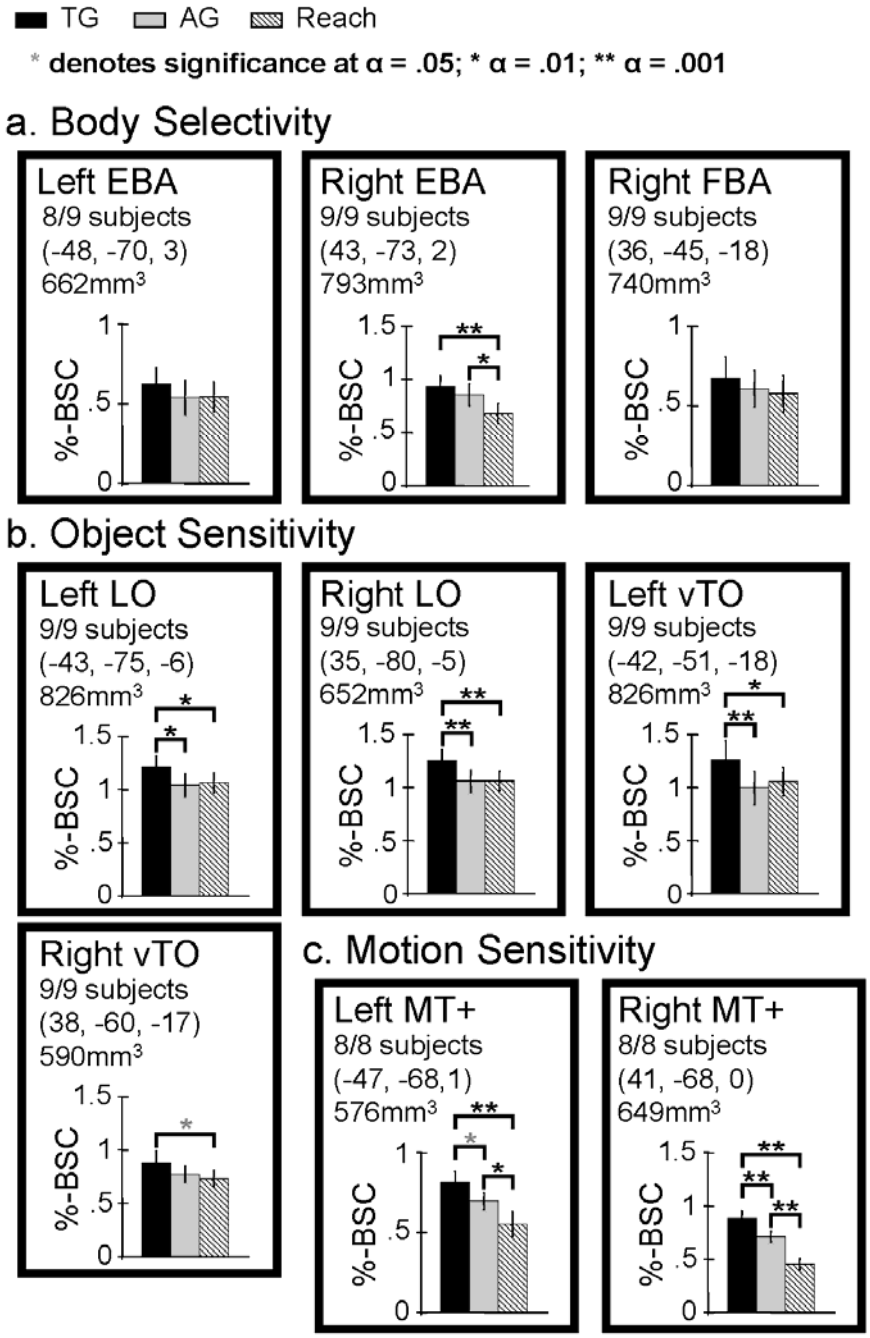

Figure 2.3. ROI results for body-, object- and motion-selective areas. a) Body-selective areas, the bilateral extrastriate body area (EBA) and the right fusiform body area (FBA). **b)** Object sensitive areas, the bilateral lateral occipital object area (LO) and ventral temporo-occipital object area (vTO). **c)** Motion sensitive areas, the bilateral motion complex MT+. For each of these areas, the group mean %-BSC values for each experimental condition are plotted, with any significant differences between conditions denoted (see legend). TG = typical grasping movies; AG = atypical grasping movies; Reach = reaching movies.

In addition to these localizer runs, all subjects except for one (due to time constraints) received two very short runs involving alternating blocks of moving and stationary patterns. This second localizer paradigm was used to identify the well studied human motion complex MT+ (Tootell et al., 1995). In all eight subjects area MT+ was identified bilaterally (Figure 2.3c), and the location of these foci were highly consistent with previous imaging studies (Dumoulin et al., 2000; Watson et al., 1993). Both the left and right MT+ showed a continuum of preferential activity in response to our action movies, showing the greatest amount of activity for TG actions, an intermediate level of activity for AG actions, and the least amount of activity for the Reach actions (left MT+: TG > AG, $p < .05$; TG > Reach, $p < .0001$; AG > Reach, $p < .01$; right MT+: TG > AG, $p < .001$; TG > Reach, $p < .000001$; AG > Reach, $p < .0001$).

Worth noting, a very consistent spatial relationship between nearby areas LO, EBA, MT+, and the tool-related pMTG was observed within and across individuals. This configuration is shown in Figure 2.4.

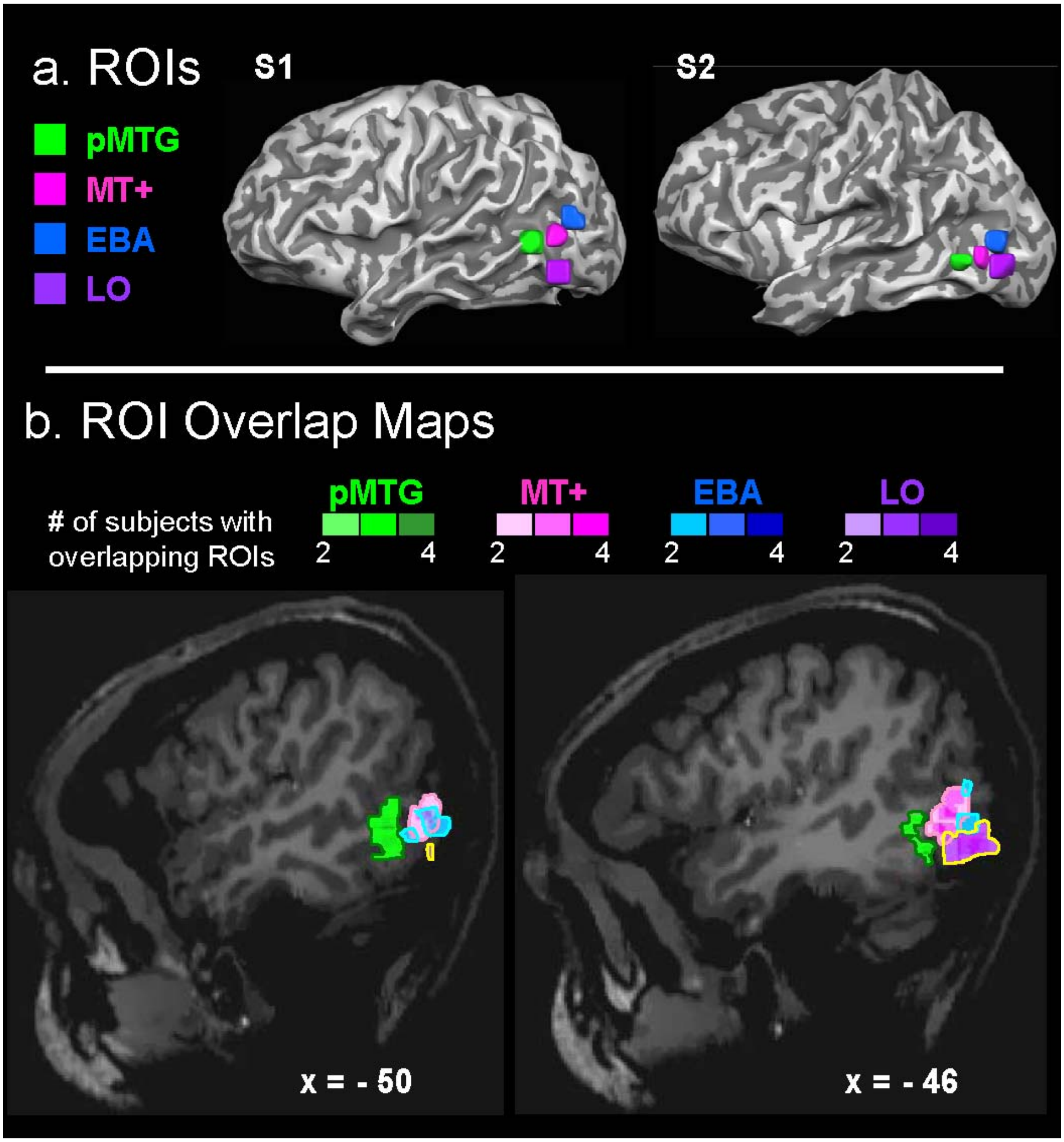

Figure 2.4. Spatial configuration of lateral occipito-temporal ROIs. a) The left hemisphere tool-selective pMTG (green), motion sensitive complex MT+ (pink), body-selective EBA (blue), and object area LO (purple) of subjects S1 and S2 are shown as 3D volumes superimposed on each individuals' partially inflated cortical hemisphere (sulci = dark gray, gyri = light gray). **b)** Statistical maps representing the number of subjects (>2) with overlapping ROIs. That is, the colour coding for a given voxel reflects the number of subjects for which that voxel was included as part of their selected ROI. For additional clarity, we have traced the boundaries of each area, and, in particular, to help disambiguate area LO from MT+, we have coloured the boundary of LO yellow. Most important to note, in both the group and individual the spatial relationships between and amongst the ROIs are highly consistent.

2.3.3. Voxel-wise results

Based on all experimental data collapsed across all individuals, fitted for random effects analyses, a direct contrast between TG and AG conditions revealed several, often contiguous, activation foci (Figure 2.5). These activations were localized to the posterior occipital and lateral temporo-occipital cortices; no significant clusters were observed within the parietal or frontal cortex, even at more liberal thresholds. This pattern of activity is highly consistent with our ROI findings. Indeed, many of the foci appear to correspond well with areas LO and MT+ (bilaterally) and the tool-selective pMTG (see Figure 5), all of which also showed a preferential response for the TG actions as revealed via our ROI analysis. However, increasing the thresholds so to isolate the individual hot spots also revealed a few areas that did not correspond as readily with our ROI results. In particular, three separable foci were noted in the posterior occipital cortex, one near the right calcarine sulcus and the other two appeared symmetrical, situated much more ventrally. In addition, one small area within the left putamen was found to be significantly more active for viewing our AG as compared with our TG movies (Table 2.1).

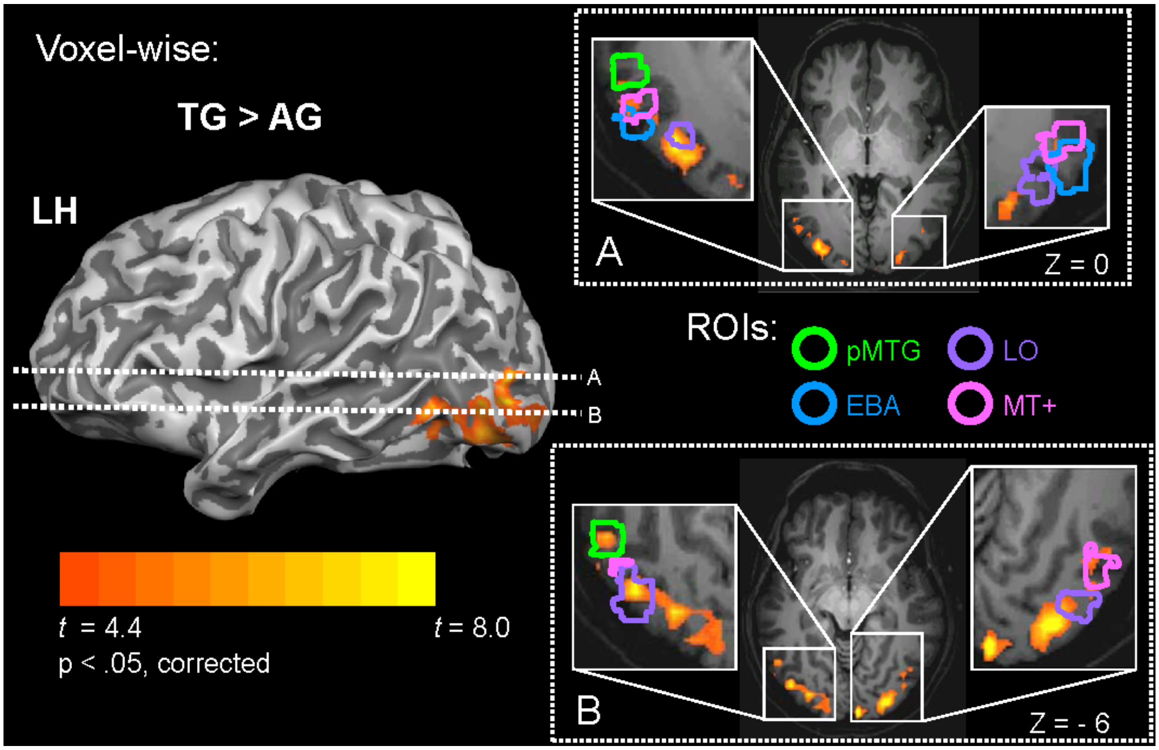

Figure 2.5. Group voxel-wise results showing areas preferentially active for TG (> AG). Activation is based on a random effects analysis, corrected for multiple comparisons, and shown on the cortical representation of a single individual (S1). Slices **A** and **B** show the same group activity superimposed on the anatomical image of S1. Activity was localized to the ventral stream, with no significant activations observed within parietal-frontal dorsal stream areas, even at more liberal thresholds. In order to facilitate comparisons with the ROI-based results, the group ROI overlap map boundaries (see Figure 2.4b) of areas pMTG, MT+, EBA, and LO are traced over the activity.

Table 2.1. Voxel-wise Group Results

TG > AG	**Talairach Coordinates**			**Volume mm^3**
Regions:	**x**	**y**	**z**	
left anterior lateral occipito-temporal cortex	-52	-64	-3	418
left posterior occipito-temporal cortex	-30	-82	-6	3864
right anterior lateral occipito-temporal cortex	41	-70	-4	376
right posterior occipito-temporal cortex	26	-87	-6	1486
right posterior medial occipital cortex	11	-87	-10	1021
AG > TG				
Regions:				
left putamen	-23	6	-7	166

Areas are based on the group averaged activity within experimental runs, using random effects GLM, with activation maps cluster size corrected for the problem of multiple comparisons ($p < .05$). Contrasts used to define each area, mean centre of mass Talairach coordinates, and the volumes for each area are indicated.

Most importantly, with respect to our a-priori objectives, the results from both our ROI and voxel-wise approaches failed to detect any differential activity within parietal or frontal areas in response to our different types of grasping movies.

2.4. Behavioural follow-up study

Since much of our imaging findings were unexpected, we decided to run the following behavioural experiment in order to help guide our interpretations of the data. In particular, this follow-up study was designed to help account for the pattern of activity observed within several ventral stream areas previously implicated as crucial for object recognition (e.g. area LO; see Figures 2.3b and 2.5). We reasoned that since our TG and AG movies evoked differential activity within these areas, object recognition processing within the context of either TG or AG actions may reflect these differences. Specifically, since our TG actions evoked stronger responses within these areas, we predicted that object recognition would be facilitated in this condition relative to AG.

2.4.1. Methods

We used an object naming paradigm and examined accuracy scores and voice-onset reaction times as measures of object recognition processing. Thirty-one subjects (17 female; age range of 19-43 years), different from those who participated in the imaging study, took part in this experiment. The task simply involved naming pictures of tools, presented singularly on a computer screen. Each picture was shown for 2s and subjects advanced each subsequent trial themselves, using a button press. Critically, in some of the pictures the tool was being grasped with a TG posture while in others the tool was grasped with an AG posture. As a control condition, which we referred to as Neutral, we had tools presented in isolation, with no hand involved. Most of the pictures (86%) were taken as single frames from our AG and TG movies used in the imaging experiment. That is, due to confounds such as differences in the amount of object being occluded at the point of grasping across some of the TG and AG movies, not all of the tool movies used in the imaging experiment could be used as stimuli for this naming experiment. The remaining tool pictures were taken from movies we had collected previously but had not used in the imaging experiment. For the TG and AG pictures, we used only the situation where the handle of the tool faced the actor, not unlike the last frames shown with the garden trowel in Figure 2.1a and b (see Figure 2.6). For the Neutral condition we simply took the first frame from either of our TG or AG movies, where no hand was yet present. Each subject received 6 different orders, and order by trial type was balanced across subjects. There were 22 trials for each condition per order, leading to a total of 132 trials per condition per subject. Mean voice-onset reaction times and accuracy scores per condition per subject were then entered into a one-way repeated measures analysis of variance, with subject as a random factor. Where significant differences were found, in order to test for differences between pairs of conditions, all possible post-hoc comparisons were performed by computing an F-statistic. Tukey's wholly significant difference (WSD) was then used to correct the critical significance value so to control for the problem of multiple comparisons.

2.4.2. Results

Repeated measures analysis of variance revealed significant differences in voice-onset reaction times across conditions, $F(2,60) = 4.47$, $p < .05$. The mean reaction times for each condition were as follows: TG = 838.7 ms, AG = 847.0 ms, Neutral = 839.3 ms. Individual pair-wise comparisons showed that naming pictures with an AG posture took significantly longer than naming both TG, $F(1,60) = 7.25$, $p < .05$, and our Neutral pictures, $F(1,60) = 6.09$, $p < .05$. In contrast, naming latencies for TG and Neutral conditions did not differ, $F(1,60) = 0.05$, $p = .99$. Plotted in Figure 2.6 are the differences in naming latencies between TG and AG versus Neutral, with error bars indicating the 95% confidence intervals, which reflect the variance in these difference scores across individuals. Clearly there is a small but reliable cost to naming AG pictures relative to Neutral, but no statistical difference between naming TG and Neutral pictures. There were no significant differences in naming accuracy across any of the three conditions; all conditions scored at ceiling, 99% correct, $F(2,60) = 2.38$, $p = .10$.

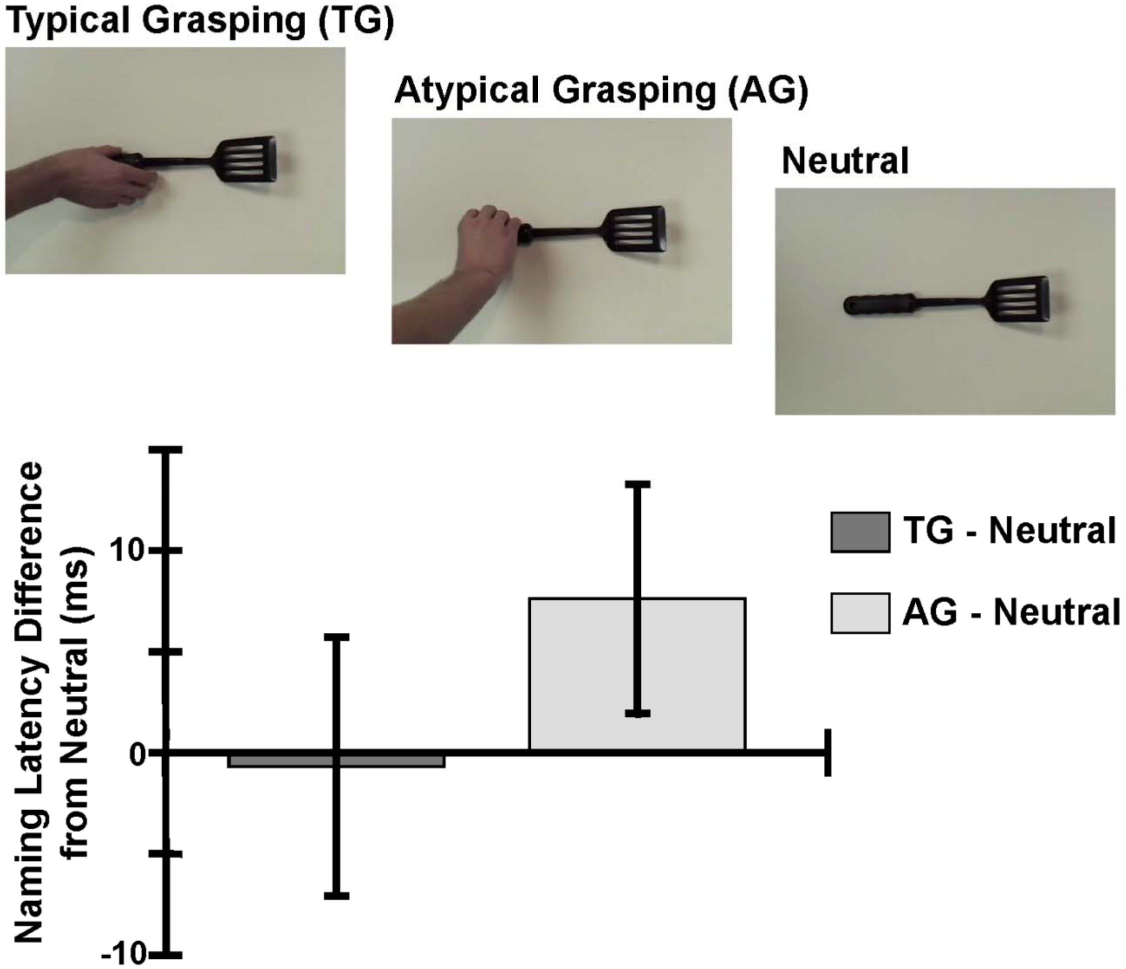

Figure 2.6. Naming latencies for behavioural follow-up study. Shown are example pictures from each condition (top) and the corresponding mean voice-onset reaction times for naming TG and AG relative to Neutral (below). For AG there is a significant increase in naming latencies compared with Neutral, whereas for TG there is a slight but unreliable decrease in naming latencies compared with Neutral. Error bars indicate 95% confidence intervals, which reflect the variability of the differences between TG and AG relative to Neutral across individuals. TG = typical grasping pictures; AG = atypical grasping pictures; Neutral = pictures with no hand grasping.

2.5. Discussion

We predicted that parietal areas involved in tool use and praxis would respond preferentially to our TG movies. Inconsistent with these predictions, both typical and atypical types of tool grasping actions were found to activate parietal areas in much the same way. Most intriguing, however, several areas more closely associated with the ventral stream were activated more strongly while observing TG as compared with AG. We view these findings as evidence for sensitivity within the ventral stream to learned semantic and/or contextual associations; in particular, those associations tied to stored knowledge of object-specific actions. In this way, our findings have important implications for understanding the cortical mechanisms underlying human tool use, and, more specifically, how semantic knowledge of tools and tool-related actions is likely to be represented in the brain.

Both of our approaches, ROI and voxel-wise strategies, converged upon much the same findings: viewing TG as compared with AG led to greater activation in the posterior and ventral temporo-occipital cortex (Figure 2.5). As our ROI findings indicate, these areas include the left hemisphere tool-selective pMTG, left vTO area, bilateral area LO, and bilateral MT+ (Figures 2.2a, 2.3b, and c). Areas LO and vTO are shape selective visual areas of the ventral stream, considered part of the lateral occipital complex (LOC), thought to be critical for perceiving and recognizing objects (e.g. Bar et al., 2001; e.g. Grill-Spector, Kushnir, Hendler, & Malach, 2000; for review, see Grill-Spector & Malach, 2004; e.g. James, Culham, Humphrey, Milner, & Goodale, 2003; e.g. James, Humphrey, Gati, Menon, & Goodale, 2000). Previous work has suggested a special role for the left mid-fusiform gyrus (MFG), near our left vTO area, in processing familiar tools (Beauchamp, Lee, Haxby, & Martin, 2002, 2003; Chao et al., 1999; Chao, Weisberg, & Martin, 2002). In particular, the left MFG is supposed to be important for processing the form and structure of tools (for review, see Beauchamp & Martin, 2007). Together with the activity seen in other parts of the LOC, as well as the left tool-selective pMTG (discussed in more detail below), we view these findings as evidence for sensitivity to the contextual aspects of our movies. Indeed, a ramping up of activity might arise within this network whenever object-directed actions are perceived within a familiar or stereotypical context; in our case the viewing of tools grasped in familiar ways resonates with these areas more strongly than the viewing of tools grasped in not so familiar ways. For example, perhaps seeing a garden shovel being grasped properly tends to more robustly activate other semantic associates, like plants and dirt, and this may have led to stronger and more extensive activations within the posterior and ventral temporo-occipital cortex, as we have observed.

The results from our follow-up behavioural naming study corroborate our imaging findings. We found significantly shorter naming latencies when subjects named tools that were being grasped with a TG posture as compared with an AG posture. If knowledge about the functional properties of tools were accessible to ventral stream areas critical for object recognition, then TG might lead to increased activations within these areas, as our imaging data support. This increased activity may then be expected to facilitate object identification and naming, as our behavioural data support. As one anonymous reviewer pointed out, our naming results are strikingly similar to the scene superiority effects described by Biederman and colleagues (Biederman, 1981; Biederman, Mezzanotte, & Rabinowitz, 1982), in which objects are more easily identified when presented in the context of a typical setting. For example, Biederman et al. (1982) found that detecting the presence of an object was more difficult if presented in an unusual scene (e.g. a fire hydrant in a kitchen) or in an unusual position (e.g. a fire hydrant on top of a car). It is easy to see how our findings can be considered consistent with these results; in our case, hand postures were either unusual, as with AG, which was found to be costly for object recognition, or usual, as with TG, which had no effect on object recognition (see Figure 2.6). In other words, depending on the posture of the hand, our objects were either presented in a typical or atypical context, and, like with the findings of Biederman et al., context influenced object identification (and, in the case of our movies, the patterns of activity within ventral stream areas known to mediate higher-level object processing).

Before proceeding, however, we would like to address the fact that our findings were not limited to the higher-level object areas of the ventral stream, but rather also included motion specialized area MT+, tool-selective pMTG, and, rather surprisingly, more posterior occipital areas. With respect to the activation observed in more posterior occipital cortex, in particular, we should consider the possibility that instead of higher-level semantic or contextual influences, our findings might simply reflect low-level differences between our TG and AG movies. Two such accounts seem possible. First, compared with TG, AG may have led to more occlusion of the functional aspects of our tools (see Figure 2.1). However, AG was also likely to involve more tool occlusion than with our Reach condition, such that if our effects were simply driven by differences in occlusion levels, differences between AG and Reach would have also been expected. Moreover, given that for all clips there was plenty of time for tools to be recognized before any occlusion took place (approximately 1000 ms), we do not feel that differences in occlusion levels would have had any substantial impact on our findings. Second, although the hand actions within our TG and AG movies were similar, upon close inspection TG appears to involve more fine-tuned postural adjustments of the wrist, fingers, and thumb, in particular at the point of grasp and as the object is being lifted. Again, however, any area sensitive to such differences would also be expected to show higher activity for AG versus Reach, since the grasping actions clearly have more postural movements and/or motion transients. Also, both TG and AG involve lifting and thus motion of the tool, whereas Reach movies do not. In fact, it is difficult to imagine any argument for low-level differences between TG and AG that would not also predict differences between AG and Reach. In other words, any low-level account of differential activations between TG and AG would also predict differences between AG and Reach. Of the areas we identified, only the pattern in area MT+ was consistent with such predictions (Figure 2.3c). Thus, it is possible that the activation pattern observed in MT+ simply reflects sensitivity to lower-level stimulus differences across movie types. However, as we will return to below, there is another possible account of the activation we observed in MT+ worth considering. For now, we would like to emphasize that the patterns of activity we have observed elsewhere, including early ventral occipital cortex, are inconsistent with any plausible low-level explanations.

Instead, we view the activity seen in more posterior areas of occipital cortex as coupled with that seen in higher-level visual areas, like LO and vTO. That is, we believe our findings reflect sensitivity to learned contextual and/or semantic associations within a widespread, albeit primarily ventral stream, network of the visual system. Notice that feedback projections are an integral part of the primate visual system (Felleman & Van Essen, 1991), and mounting evidence suggests that feedback from higher to lower level visual areas plays an important if not essential role in perceptual processing (for reviews, see Blake & Logothetis, 2002; Bullier, 2001; Lamme & Roelfsema, 2000; Murray, Boyaci, & Kersten, 2006; Murray et al., 2004; Pascual-Leone & Walsh, 2001). Perhaps the activity we observed in higher-order visual areas, like LO and left vTO (and/or the tool-selective pMTG), is driving the effects observed in more posterior areas, via recurrent connections. Moreover, Biederman and colleagues were explicit to emphasize that their findings, discussed above, did not fit well with a strictly bottom-up view of perceptual processing. Instead, their results indicate that object semantics are accessible very early on, and can influence perception and object recognition rather immediately. Similar findings have been described with letters and words, in which letters are more accurately identified within the context of real words versus non-words, or in isolation (e.g. Reicher, 1969). To account for such findings, McClelland and Rumelhart (McClelland & Rumelhart, 1981; Rumelhart & McClelland, 1982) put forth a computational model describing parallel excitatory and inhibitory interactions between multiple levels of processing. When letters are shown within the context of a word, low (e.g. visual feature) and high-level (e.g. word knowledge) representations interact with one another to strengthen the overall excitatory activity of the network, leading to a perceptual advantage. It is exciting to consider that just such a mechanism may relate to our imaging findings, and, more directly, may in fact underlie the naming effects we have observed. Along a similar vein, one of the core principles of many prominent theories on the organization of semantic knowledge is the importance of multidirectional interactions between higher-level representations and more bottom-up, modality-specific, systems (for reviews, see Barsalou, 2007; Humphreys & Forde, 2001; Simmons & Barsalou, 2003). Indeed, we believe our imaging results reflect this kind of organization, whereby conceptual knowledge about the functional properties of objects is anchored within areas of the ventral stream specialized for object recognition.

Importantly, differences in general attentional mechanisms, like sensitivity to task demands, cannot adequately account for our findings. First, there is no evidence to suggest that subjects would have paid more attention, or that the 1-back task was more demanding for TG; in fact, if anything, AG would seem more likely to capture the greater interest, since these actions are less familiar, and less predictable. Second, if attentional processes were driving our effects, then one would predict highest activation for our scrambled movies, for which our 1-back task was appreciably more difficult. Lastly, areas previously implicated as sensitive to attention and task demands (e.g. superior parietal areas) (for review, see Kanwisher & Wojciulik, 2000), were not preferentially active for TG, as would be expected if differential allocation of general attentional resources were driving our effects. There are a few other possibilities, however, that may or may not involve differential attentional mechanisms. For example, TG movies may hold more implied motion than our AG movies, by virtue of the fact that these movies may more readily predict future movements. Such an account may be particularly attractive for area MT+, considering that many previous studies have shown this area to be sensitive to implied motion (Fawcett, Hillebrand, & Singh, 2007; Kourtzi & Kanwisher, 2000; Lorteije et al., 2006; Peuskens, Vanrie, Verfaillie, & Orban, 2005; Senior et al., 2000). We should emphasize, however, that this interpretation may also account for the activity seen in other areas, besides MT+. Most importantly, such sensitivity to anticipated motion patterns must be based on stored knowledge about object-specific actions. Finally, we wish to acknowledge that preferential responses to TG need not reflect the activation of explicit semantic representations, but instead may relate to implicit experiential or procedural knowledge of tool use actions. That is, we cannot rule out the potential role of pragmatic processing related to tools and/or the actions for which they typically afford. We do, however, find it difficult to accept a purely pragmatic-based account of our findings, mainly because many previous data indicate a strong parietal/frontal involvement when it comes to the pragmatic aspects of actions (e.g. Boronat et al., 2005; Kellenbach, Brett, & Patterson, 2003).

Why do we not find preferential activity for our TG movies within parietal/frontal areas? There is certainly plenty of evidence showing that these areas play a crucial role in underlying praxis and object-specific action knowledge (Haaland et al., 2000; Johnson-Frey, 2004; Rothi & Heilman, 1997). There is also plenty of neuroimaging evidence showing that these areas can become active in the absence of any overt movement (e.g. with imagined tool use). Are parietal/frontal areas simply insensitive to the familiarity, or typicality, of observed tool use actions? Consistent with our findings, Frey and colleagues (2003), using a very similar imaging paradigm to ours but with static pictures, also found that frontal areas were insensitive to the functionality of observed grasps (note, however, that these authors constrained their analyses to only frontal areas). However, this conclusion seems particularly surprising for inferior parietal areas, given that others (e.g. Buxbaum et al., 2005; Heilman et al., 1982) have argued that the recognition of tool use actions critically depends on the integrity of such areas. Instead, we believe the pattern of activation we observed in parietal cortex was strongly influenced by the particular types of actions we chose to use. Specifically, if we had shown movies of tools being used, rather than simply being grasped, differential modulation within parietal and/or frontal cortex may have been observed. In other words, perhaps parietal tool areas specifically encode actions ***with*** tools, and not simply ***toward*** them. Indeed, most studies interested in the parieto-frontal representations critical for knowing how to use tools, not surprisingly, have looked only at those actions associated with having the tool in hand. For example, to test for damage to these representations patients are often asked to pantomime how they would use objects, not how they would grasp-to-use them. Worth mention, however, when tested, deficits specific for grasping-to-use objects have been noted in some apraxic patients with parietal damage, suggesting that there are parietal areas specialized for mediating object-specific functional grasps (for review, see Daprati & Sirigu, 2006; Sirigu et al., 1995). Still, these areas may be important for functional grasping in the sense that they provide a special interface, critical for receiving and integrating input from other areas. In this way, our results suggest that prior to the actual use of objects the ventral stream provides important information to specific parietal areas about how to most efficiently engage an object based on semantic knowledge about its identity, function, and how it is to be moved and used (Creem & Proffitt, 2001; Milner & Goodale, 1995).

There is certainly growing consensus about the left pMTG and its importance in knowing about object-specific actions and familiar tools. This area is active during the generation of words associated with object-specific actions (Martin, Haxby, Lalonde, Wiggs, & Ungerleider, 1995), when viewing and naming tools relative to other objects (e.g. Martin et al., 1996; Valyear et al., 2007), during the retrieval of semantic information about object function and manipulability (Boronat et al., 2005; Kellenbach et al., 2003), during pantomime object use (e.g. Fridman et al., 2006; e.g. Johnson-Frey et al., 2005), and is even preferentially responsive to the sounds of familiar tools in action (Beauchamp, Argall, Bodurka, Duyn, & Martin, 2004; Beauchamp, Lee, Argall, & Martin, 2004; Lewis, Brefczynski, Phinney, Janik, & DeYoe, 2005). Also, exciting new findings indicate that tool-selectivity in this area comes about as individuals learn about the function and manipulability of novel objects (Weisberg, van Turennout, & Martin, 2007). Human pMTG has not yet been classified as either a dorsal or ventral stream area; like MT+, it may have crosstalk with both of the classic visual streams. Notably, pMTG is in a good position to receive various types of input (e.g. visual and auditory, Beauchamp, Argall et al., 2004; Beauchamp, Lee et al., 2004) and to mediate interactions between dorsal and ventral pathways. As shown in Figure 2.4, the tool-selective pMTG sits just anterior, lateral, and slightly ventral to the well studied human motion complex MT+. This relationship is consistent with previous descriptions by Beauchamp and colleagues (Beauchamp et al., 2002, 2003), who also showed that the pMTG is more active for tools in motion than for bodies in motion, whereas MT+ shows comparable activity for both. If, as Beauchamp and colleagues suggested, this area is particularly important for processing tool motion (for review, see Beauchamp & Martin, 2007), our results would indicate that this processing includes knowledge about how tools and specific body parts (e.g. the arm and hand) typically move and interact together during use. That is, we believe our results suggest an important role for the pMTG in predicting object-mediated action outcomes, including how tools and body effectors are likely to move in both time and space, based on prior experience actually using, or, to some extent, seeing others use tools.

To summarize, our findings suggest that during the perception of object-directed actions the ventral stream is likely to play a prominent role in processing the meaning and interpretation of the action, presumably by integrating information about the motoric details of the action with stored knowledge about the object. Several areas, including the tool selective left pMTG and higher level object processing areas LO and the left vTO, were preferentially active for grasping actions that were consistent with the conventional use of tools. While other accounts remain possible, we view our findings as reflecting a special role for the ventral stream, as well as the tool-selective pMTG, in coupling stored perceptual and semantic knowledge about objects with procedural knowledge supporting their skilled use. These findings may extend to suggest that during actual tool use a complex interplay between ventral and dorsal streams must take place, with ventral stream areas providing critical input as to how an object should be engaged in accordance with stored semantic knowledge. Future research in our lab will look to provide new insights into how these interactions are mediated during actual tool use.

2.6. References

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Chapter 3

3. To use or to move: Goal-set modulates priming when grasping real tools.

3.1. Introduction

According to Gibson (1979), the content of visual perception includes a description of how the environment and objects within it can potentially impact our actions. The mere sight of a graspable object, for example, will partially activate motor programs for grasping. Tucker and Ellis (1998) asked participants to decide whether or not pictures of familiar graspable objects with handles were inverted or upright. Object handles were either facing left or right, and simple button-press responses were made with either the left or right hand. When objects were facing right, right hand responses were facilitated, and when objects were facing left, left hand responses were facilitated. These results were taken to indicate that handle orientation automatically gives rise to the activation of corresponding motor plans for grasping. These authors have since shown that such compatibility effects also work for the sizes of objects. Using a novel apparatus to simulate precision and power type grasping (Ellis & Tucker, 2000), they showed that small objects facilitate precision-type responses while large objects facilitate power-type responses (Tucker & Ellis, 2004). Again, the task, to decide if objects were man-made or natural, did not require explicit attention to the particular object features driving the effects, nor did it have anything to do with grasping. It appears as though the visual properties of objects important for grasping (e.g. size, orientation) automatically trigger the activation of corresponding motor representations.

The idea of motor affordances as integral to the visual perception of objects has also received some support at the neural level. Electrophysiological recordings in monkeys have shown that grasp-related neurons often respond to the visual presentation of objects, even in the absence of any movements (Murata et al., 1997; Murata, Gallese, Luppino, Kaseda, & Sakata, 2000; Rizzolatti et al., 1988; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). Moreover, for some of these cells, the motor and visual response properties closely match (e.g. cells that respond maximally to precision-type grasping, also respond maximally to the sight of small objects, which afford precision grasping). In human neuroimaging studies, sensorimotor areas show preferential activation for pictures of graspable (vs. non-graspable) objects (e.g. Chao & Martin, 2000; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007), and real objects within reachable (vs. unreachable) space (Gallivan, Cavina-Pratesi, & Culham, 2009). Also, in a recent study using a combined TMS and EMG approach, Buccino et al. (2009) showed that motor-evoked potentials recorded from hand muscles are modulated by the handle orientation of passively viewed objects; activity in the right hand was elevated when handles were oriented to the right, in accordance with a right-handed grasp.

The work we have discussed thus far indicate that object affordances relevant for grasping give rise to motor-related activity, and can influence unrelated motor responses, but what about the planning of real grasping actions? If object properties, like orientation, automatically activate corresponding motor plans, then grasping might be facilitated (primed) if preceded by an object that evokes consistent affordances. Indeed, Craighero and colleagues (1996) showed that grasping a simple bar is primed if preceded by a picture of a bar in the same orientation. However, Cant et al. (2005) failed to replicate such orientation priming effects, and argued that participants in the Craighero study were making memory-guided (not visually-guided) grasping, and this could account for the priming they observed. Still, other studies indicate significant priming effects with real visually-guided grasping using words as primes (e.g. Glover, Rosenbaum, Graham, & Dixon, 2004), and have shown priming in the context of action observations (e.g. Edwards, Humphreys, & Castiello, 2003; Gianelli, Dalla Volta, Barbieri, & Gentilucci, 2008). In short, available evidence indicates that grasping is sensitive to priming, but clearly more work is needed to better understand the particular experimental factors that are important (e.g. the nature of the task; the modality of primes).

Perhaps the strongest evidence that object affordances can lead to the activation of motor representations relevant for the planning of real grasping actions comes from those patients who demonstrate so-called ‘utilization behaviour’. Such patients are compelled to grasp and use familiar objects, even though they are not told to do so, and, indeed, even after they are instructed otherwise (Lhermitte, 1983; Shallice, Burgess, Schon, & Baxter, 1989). The disorder follows damage to frontal areas, and Lhermitte argued that it may reflect a release of control over parietal functions. Further, Riddoch and colleagues have shown that object affordances play an important role in triggering such impulsive grasping behaviours (Humphreys & Riddoch, 2000; Riddoch, Humphreys, & Edwards, 2000). In their task, a familiar cup with a handle is presented to the left or right of the patients' midline, and the instructions are as follows: if the cup is on the left, use the left hand to grasp it by the handle, if it is on the right, use the right hand. The patient, who has bilateral damage to medial frontal and anterior temporal areas and exhibits utilization behaviour, made frequent errors when the cup was on the left but the handle faced to the right. In this case the patient often incorrectly grasped with his right hand, as if handle orientation automatically evoked a grasp response which then served to override task instructions. Interestingly, such errors were only evoked when the task was grasping; when asked to point to handles instead, the patient performed without error. The findings show that object affordances can elicit grasping, and also suggest that task goals play a determining role (see also, Riddoch, Edwards, Humphreys, West, & Heafield, 1998).

Most studies of affordances have used familiar everyday graspable objects (although see, Symes, Ellis, & Tucker, 2006; Vingerhoets, Vandamme, & Vercammen, 2009), which may, in fact, strongly associate with multiple action plans. For example, a piece of fruit may afford a certain grasp style based on its size and shape, but it may also afford a different grasp style based on the way in which it is typically eaten (Gentilucci, 2002). Likewise, for familiar tools, grasping based on physical object properties, like handle size, shape, and orientation, may differ from grasping based on knowledge and intention of use (Daprati & Sirigu, 2006; Frey, 2007). Indeed, for some objects, hand configurations predicted from structure are at odds with those required for use (e.g. Buxbaum, Sirigu, Schwartz, & Klatzky, 2003; Klatzky, McCloskey, Doherty, Pellegrino, & Smith, 1987). For example, the structure of a piano or keyboard key affords a "pinch" interaction style for grasping, but the learned interaction style for use is in fact a "poke". Further, some patients show appropriate grasp scaling in accordance with object structure, but lack the kinematic features relevant for use (Carey, Harvey, & Milner, 1996; Randerath, Li, Goldenberg, & Hermsdorfer, 2009; Sirigu et al., 1995), while others show marked improvements when grasping familiar versus semantically-neutral objects

(Jeannerod, Decety, & Michel, 1994). Thus, for familiar tools, affordances may be based on structural properties, learned functional properties, or both (Valyear et al., 2007).

In fact, Bub and colleagues (Bub, Masson, & Cree, 2008), using a very clever approach, provide direct evidence for both kinds of affordances. They devised an apparatus, fitted with abstract object shapes used to simulate distinct hand-object interactions. Subjects were required to actually reach out and interact with the different elements of the apparatus, and each element required a distinct hand configuration to do so. In a training session, participants learned to associate different colours with the different response elements of the apparatus. For example, the colour red might instruct subjects to interact with the response element requiring a "poke" hand posture. Once trained, participants were presented with pictures of coloured familiar graspable objects, or object words, and were told to ignore the object and respond to colour. Critically, objects were chosen such that the actions they afforded were either consistent or inconsistent with those of the colour-cued hand configurations (see also, Bub, Masson, & Bukach, 2003). Moreover, the authors distinguished between affordances based on object structure, termed volumetric, and those based on learned use, termed functional. Thus, on any given trial, the colour-cued hand response could either match-up with the objects' volumetric affordance, its functional affordance, or neither. If such affordances automatically lead to activations of corresponding motor plans, then such activity should speed up responses on matched trials and slow down responses on non-matched trials. The authors showed exactly this, for both volumetric and functional matches, indicating that familiar objects can evoke both types of affordance effects.

In the current study, we focused on 'use-based' rather than 'structure-based' affordances and our main objective was to investigate how task goals and task setting modulate these effects. We used priming as a measure of affordances, and looked at real grasping actions, using familiar kitchen tools as our stimuli (Table 3.1). We had two tasks: (1) grasp-to-move (GTM), whereby subjects grasped a tool to move it from one location to another; and (2) grasp-to-use (GTU), whereby subjects grasped a tool to demonstrate its typical use. Tasks were either presented in separate blocks of trials (Experiment 1) or were randomly intermixed within the same block of trials (Experiment

2). Grasping was always preceded by a pre-view (prime) event, involving the simple visual presentation of a tool. Either the prime was the same tool as that which was then grasped (congruent trials), or the prime was a different tool (incongruent trials). If the mere visual presentation of a tool activates associated motor programs, then such activation may carry over to influence planning of subsequent grasping, and priming is expected for congruent trials.

Our interests were focused on whether or not such priming effects would depend on which task was being performed, and whether or not task setting, blocked or mixed, would also be important. For the GTU task, tool identity is important for action planning, and thus we predicted that priming would be observed. In contrast, for the GTM task, we predicted that grasping might be planned without processing tool identity, and priming was thus not expected. Notably, we took steps to minimize the metrical differences important for grasping across tools. We used tools with the same handle, such that grasp posture and grip scaling in the GTM task would in principle be comparable for all tools. As a secondary interest, this also gave us a chance to characterize the kinematics of grasping-to-use different tools without the confounding effects of using different handled tools. Of course, our tools differed in other physical aspects important for grasping, like overall size and weight distribution, factors that could also drive priming even in the GTM task. In addition, it is possible that grasping actions of any kind always involve some processing of identity, even in a strictly semantic sense (Gentilucci, 2002, 2003), regardless of specific goals and motor requirements. If this were the case, repeating tool identity would facilitate processing even in the GTM task, and priming is expected. Instead, we predicted that task goals would play a determining role, and priming was not expected for the GTM task. In contrast, the goals of the GTU task rely on access to tool identity, and thus priming was expected. Differences in priming for either task according to presentation setting, blocked (Experiment 1) versus mixed (Experiment 2), would be taken to reflect the influence of task set.

3.2. Experiment 1

3.2.1. Method

Participants

Twenty-three right-handed students from the University of Western Ontario participated in this experiment. All participants reported normal or corrected-to-normal vision and gave informed consent. The experiment took approximately 45 min and participants were either compensated financially or were given course credit.

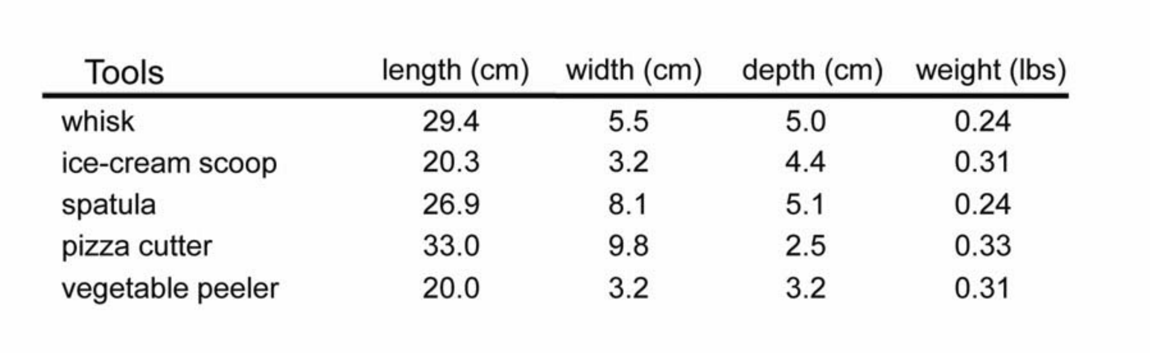
Experimental Setup and Materials

Two OPTOTRAK 3020 cameras (NDI, Waterloo, Ontario, Canada), monitored the position (at 100 Hz) of three infrared markers (IREDs) attached to the tip of the index-finger, the inside tip of the thumb, and the base of the index-knuckle (metacarpalphalangeal joint) of participants' right hands.

Participants were seated at a 1 m x 1 m table with a horizontally centred start button positioned 15 cm from the front edge of the table. Participants held the start button down with their right index finger and thumb lightly pinched together. A circular platform used to position tools was placed in front and to the right of participants. Vision was controlled using PLATO goggles (Translucent Technologies, Toronto, Canada), and hearing was controlled using headphones.

Table 3.1 lists the five different tools that were used. Importantly, all tools had the exact same handle.

Table 3.1. Tools



Tools	length (cm)	width (cm)	depth (cm)	weight (lbs)
whisk	29.4	5.5	5.0	0.24
ice-cream scoop	20.3	3.2	4.4	0.31
spatula	26.9	8.1	5.1	0.24
pizza cutter	33.0	9.8	2.5	0.33
vegetable peeler	20.0	3.2	3.2	0.31

Procedure

The sequence and timing of events within a given trial, and the two trial types are shown in Figure 3.1. Each trial comprised two successive events, a prime event followed by a probe event. Participants started each trial in the start position with no vision available. The goggles then opened for one second to reveal the prime object, (one of the five tools, Table 3.1), positioned in one of three positions on the presentation platform. Participants were instructed to simply view the (prime) tool. Next, the goggles closed for 3-4 seconds, accompanied by a continuous burst of white noise in the headphones. After this delay, the goggles again opened and participants' reached-to-grasp whichever (probe) tool was now on the platform, at a quick but comfortable pace. Critically, there were two types of trials. In a congruent trial, the same tool was repeated from prime-to-probe. In an incongruent trial, the tool was changed from prime-to-probe. The majority (~ 67%) of trials were congruent, so that the prime had some predictive value. To discourage subjects from simply 'darting out' to the same location on each trial, tool position was always varied from prime-to-probe events. The burst of white noise during the delay between prime and probe events served to mask any auditory cues that might have otherwise provided information about the type of upcoming trial and/or the particular tool to-be-grasped.

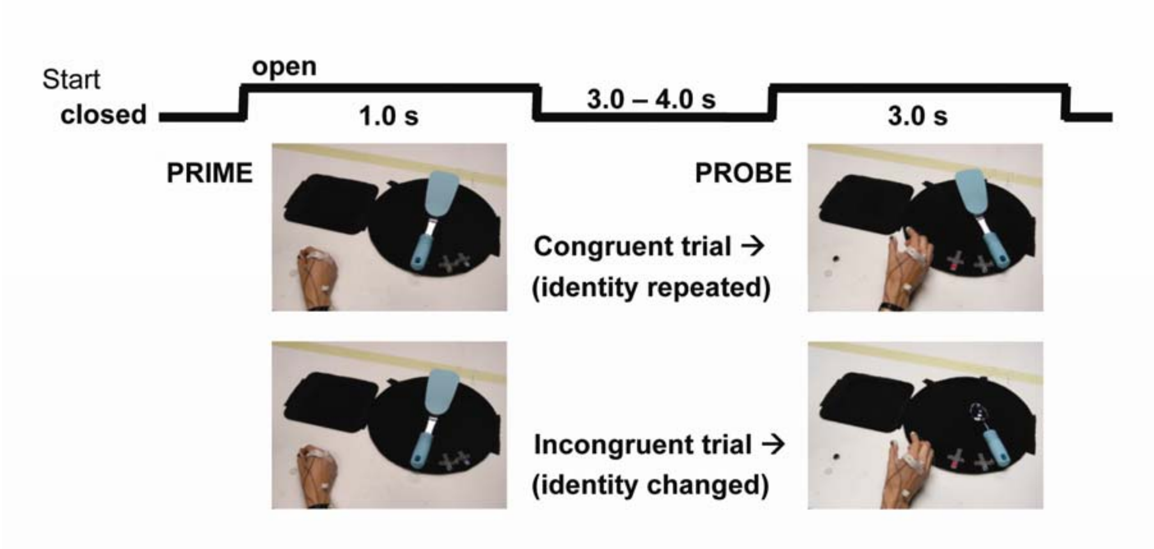


Figure 3.1. Trial types and timing. The top line represents the state of the LCD goggles and whether or not vision was available to participants. Prime events involved simply viewing tools while probe events required grasping. Tools were placed in three possible positions (29, 35, 39 cm from start), and position always varied from prime-to-probe events. Trials were either congruent or incongruent with respect to tool identity, and subjects were either grasping-to-move or grasping-to-use.

GTM and GTU were performed in two separate blocks of 90 trials (60 congruent, 30 incongruent). In GTM, probe events involved grasping tools, moving and placing them on a standard mouse pad, positioned 10 cm in front of the start button. In GTU, participants would grasp tools and then demonstrate two cycles of appropriate use (while over the mouse pad) before placing them down. Prior to testing, participants were shown each of the five different tools (Table 3.1) and the experimenter would demonstrate each of the expected actions. Note, however, that participants were told to carry out tool use actions in a way that was comfortable for them, not necessarily in the way that the experimenter had shown. All tools were shown, used, and paired with all other tools an equal number of times. Trials were presented in a randomized order, and balanced across all possible orientations for both prime and probe. Task order (GTM or GTU) was counterbalanced across individuals.

Data Processing

Release of the start button was used to calculate reaction times (i.e. time-to-movement onset). All other measures were derived using data from IREDs (see Table 3.2). Raw three-dimensional data for each IRED for each trial was filtered using a low-pass Butterworth filter (12 Hz-cutoff, 2^{nd} order). Instantaneous velocities in each cardinal dimension (x,y,z) were calculated for each marker for each time point and the resulting velocity profiles were filtered (low-pass Butterworth filter, dual pass, 8 Hz-cutoff, 2^{nd} order) and combined to create a vector velocity (i.e. three-dimensional) profile for each trial. Reaches were defined using the thumb marker, and were said to begin with the first of four consecutive vector velocity readings of greater than 20 mm/s where there was a total acceleration of 20 mm/s across the four points. Reaches were said to terminate with whichever of two conditions was first met: the first time the velocity dropped below 20 mm/s or the time at which the maximum x-position (lateral) value of the thumb marker was reached (within 1500 ms of movement onset).

When one of the markers was missing from view of OPTOTRAK cameras, we used translated data from other markers to fill in the missing time points. Specifically, for both the thumb and index-finger markers, missed data were filled with position translated data from the index-knuckle marker, and for the index-knuckle marker, data from the index-finger marker was used. When this could not be done, due to multiple missing markers at the same time, missing data were linearly interpolated.

Dependent Measures and Analysis

Trials were rejected for the following reasons: the start position of the index-finger marker was > 5 cm from the start button, the reach was too short in either duration (< 100 ms) or distance (< 10 cm in the x-dimension), a marker went missing for more than 100 ms, or the initial grip aperture (which was supposed to be pinched closed) was > 4 cm. This procedure resulted in 3% of trials being removed. In addition, we performed an outlier analysis on reaction times (for each individual and task) and movement durations (for each individual, task, and probe tool position) removing trials that were more than two standard deviations away from the mean. This procedure resulted in 9% of trials being removed. Finally, for the analysis of peak grip apertures and movement durations only, we then ensured that each participant had at least three repetitions of the actions performed in each task with each tool. In Experiment 1, two participants did not meet this criteria (in each case, too many trials were excluded due to the grip aperture being > 4 cm at start position).

Table 3.2. Dependent Measures

Dependent Measures	Unit	IRED marker(s)	Description
reaction time	ms		time between the onset of the probe event and the release of the start button
peak grip aperture	mm	thumb, index	maximum three-dimensional distance between the thumb and index markers
movement duration	ms	thumb	time from movement start to end of grasp

All dependent measures were entered into a three-factor task x trial type x probe tool identity (2 x 2 x 5) repeated measures analysis of variance (RM-ANOVA). Where significant, interactions were followed up with simple main effects single-factor RM-ANOVAs. Post hoc follow-ups to significant main effects and simple main effects compared all possible pairwise comparisons of the most relevant factor. All RM-ANOVAs were analyzed using the Greenhouse-Geisser correction for sphericity and taken to be significant at $P < 0.05$. Post hoc pairwise contrasts used the Bonferroni correction for multiple comparisons with a corrected $P < 0.05$ taken as significant.

3.2.2 Results and discussion

Reaction Times

As predicted, priming was specific to the GTU task; switching or repeating tools from prime-to-probe events had no impact on reaction times when the task was GTM (Figure 3.2; Table 3.3). Participants were also faster to initiate grasping for the GTM task.

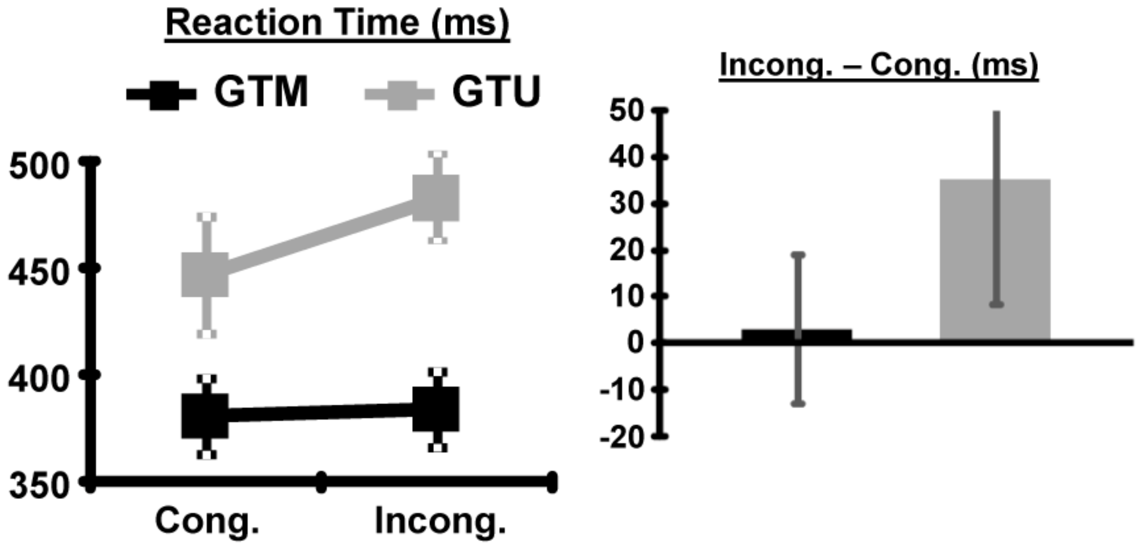


Figure 3.2. Task-specific priming (Experiment 1). Mean reaction times as a function of task and congruency (*left panel*). Congruent trials were initiated faster than incongruent trials, but only for GTU not for GTM, indicating that priming effects were specific to GTU. Priming is shown as the difference between reaction times for congruent versus incongruent trials according to task (*right panel*). Error bars reflect 95% confidence intervals based on the standard errors of the mean difference scores (incongruent-congruent) across individuals.

Table 3.3. Experiment 1 significant results (* indicates p < .05, ** indicates p < .001)

Experiment 1

Reaction Times (ms)

Interaction * task x congruency F(1, 22) = 6.01*

	congruent	incongruent	F-stat
GTM	381	384	F(1, 22) = 0.15, p = 0.70
GTU	447	482	F(1, 22) = **6.82***

Peak Grip Aperture (mm)

Interaction * task x probe identity F(3.2, 63.8) = 3.21*

	spatula	whisk	scoop	peeler	cutter	F-stat
GTM	46.7	47.7	46.5	46.9	47.4	F(2.2, 44.0) = 2.29, p = 0.07
GTU	52.0	50.9	51.4	49.7	51.2	F(3.0, 59.5) = **2.85***

For GTU, peeler < spatula, p = .064

Movement Duration (ms)

Interaction * task x probe identity F(3.2, 63.1) = 6.10**

	spatula	whisk	scoop	peeler	cutter	F-stat
GTM	581	589	586	587	588	F(3.0, 60.6) = 1.23, p = 0.31
GTU	579	583	551	546	569	F(3.2, 63.1) = **9.44****

For GTU, peeler << spatula, whisk; peeler < cutter; scoop << spatula; scoop < whisk

Kinematics

No effects of priming were evident in grasping kinematics. Analysis of variance revealed a main effect of task; wider peak grip apertures and shorter movement durations were associated with the GTU task (Figure 3.3; Table 3.3). In addition, there was a significant task by probe identity interaction for both peak grip apertures and movement durations (Table 3/3). For the GTU task, grasping patterns clearly differed as a function of tool identity, whereas for the GTM task, grasping was similar for all tools (Figure 3.3). To help visualize these differences further, we plotted the relative positions of the index finger, thumb, and knuckle markers in 3-D space at 10% increments of total movement durations for each tool for each task (Figure 3.4). These plots give us an idea of how the posture of the hand was oriented throughout the grasp trajectory as a function of task and tool identity.

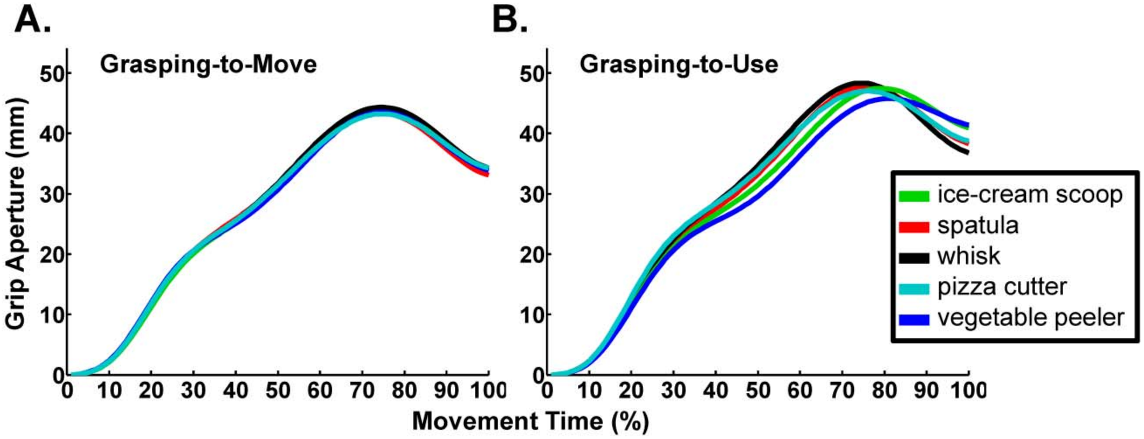


Figure 3.3. Grip aperture (Experiment 1). Grip aperture measures as a function of percent movement time, for each of the five tools for GTM (A) and GTU (B). Profiles for each individual tool are coloured as indicated in the legend. The hand opens and closes in much the same way for all five tools when grasping-to-move, but differently for different tools when grasping-to-use.

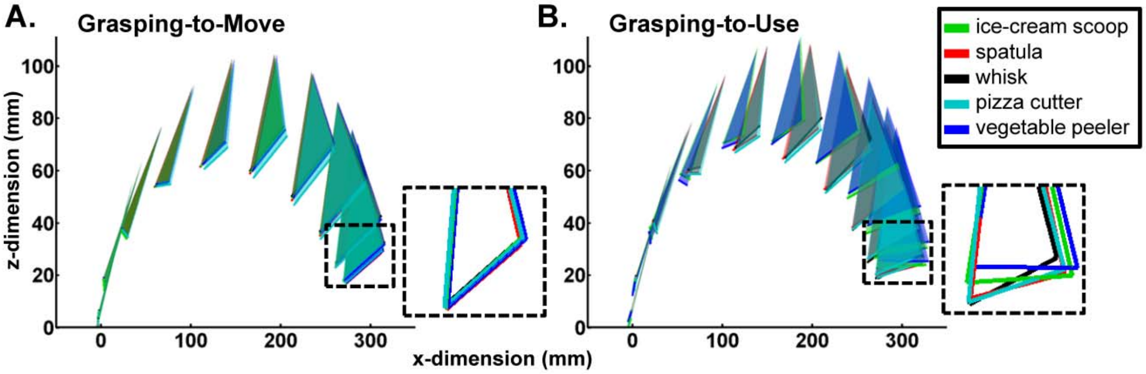


Figure 3.4 Grasp posture (Experiment 1). Plotted are the relative positions of the index finger, thumb, and knuckle markers in space, at 10% movement intervals, for each of the five tools, for GTM (A) and GTU (B). Plots for each individual tool are coloured as indicated in the legend. The x-dimension, or left-right direction, is plotted on the x-axis and the z-dimension, or up-down direction, is plotted on the y-axis. For each task, the final intervals of each grasp per tool are blown-up to facilitate comparisons. For GTU, the relative positioning of the finger and thumb markers, and hence the posture and orientation of the grasping hand, clearly differed for different tools at these later intervals. For GTM, however, the relative positioning of the markers was much the same for all tools.

To summarize, our predictions for Experiment 1 were verified. Priming was specific to the GTU task, and grasping kinematics differed between tasks. Participants took on a somewhat specific approach to grasping different tools for GTU, while all tools were grasped similarly for GTM.

3.3 Experiment 2

3.3.1. Method

Participants

Twenty-two right-handed students from the University of Western Ontario participated in this experiment. All participants reported normal or corrected-to-normal vision and gave informed consent. The experiment took approximately 45 min and participants were either compensated financially or were given course credit.

Procedure

GTM and GTU trials were presented together in a randomized order. Participants were cued auditorily, “move” of “use”, at the beginning of each trial (one second before the onset of the prime event) as to which task they had to perform. All other methods were identical to Experiment 1. Trial removal procedures resulted in 3% of data removed and outlier analysis resulted in 7% of data removed. Two participants were then excluded from further analysis for not having sufficient repetitions (three) of trials for each task for each tool.

3.3.2 Results and discussion

Reaction Times

GTM trials now showed sensitivity to priming; congruent trials reliably led to faster responses compared with incongruent trials for both tasks (Figure 3.5; Table 3.4). Main effects of task remained significant, although the differences were more pronounced when tasks were blocked separately. Participants appeared to have changed their motor strategies from blocked to mixed settings, and these changes gave rise to reliable priming effects in the GTM task. Priming was nontheless found to be significantly greater for GTU versus GTM trials (Table 3.4).

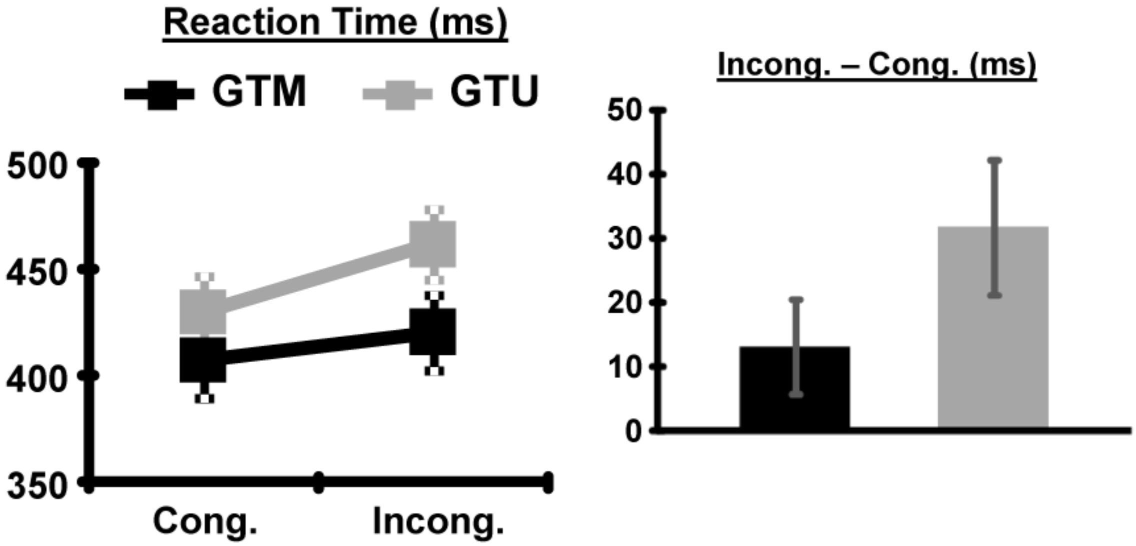


Figure 3.5. Priming (Experiment 2). Mean reaction times as a function of task and congruency (*left panel*). Congruent trials were initiated faster than incongruent trials, indicating significant priming effects for both GTM and GTU. The mean difference between congruent and incongruent trials, as a measure of priming, is also plotted for each task (*right panel*). Error bars reflect 95% confidence intervals based on the standard errors of these mean difference scores (incongruent-congruent) across individuals. Priming effects were significantly greater for GTU.

Also different from the blocked setting, we now found a significant task by probe identity interaction in reaction times (Table 3.4). When subjects had to perform the GTU task, the particular tool to be grasped had an impact on their reaction times. These findings provide further evidence that strategies changed across experiments; in this case, the effects may relate to trade-offs between the relative costs of programming specific kinematics and the time taken to initiate grasping.

Table 3.4. Experiment 2 significant results (* indicates p < .05, ** indicates p < .001)

Experiment 2

Reaction Times (ms)

Interaction * task x congruency F(1, 21) = 8.04*

	congruent	incongruent	F-stat
GTM	407	420	F(1, 21) = **12.4***
GTU	430	462	F(1, 21) = **36.6****

For GTM, congruent < incongruent

For GTU, congruent << incongruent

Interaction * task x probe identity F(3.4, 71.0) = 4.70*

	spatula	whisk	scoop	peeler	cutter	F-stat
GTM	412	421	405	404	415	F(3.1, 64.8) = 2.10, p = 0.11
GTU	434	429	449	448	442	F(3.2, 67.6) = **3.48***

For GTU, whisk < peeler

Peak Grip Aperture (mm)

ME * task F(1, 19) = 7.48*

GTM	GTU
46.9	49.1

Movement Duration (ms)

ME * task F(1, 19) = 9.54*

GTM	GTU
618	599

Kinematics

Similar to Experiment 1, participants reliably moved more quickly and opened their grasp wider for tools in GTU versus GTM trials (Figure 3.6; Table 3.4). However, interactions between task and tool identity, evident when the tasks were blocked, no longer reached significance in the mixed design (Table 3.4). The patterns remained the same, especially for different tools in the GTU task (Figures 3.6 and 3.7), but were less pronounced and/or more variable than observed when the tasks were blocked.

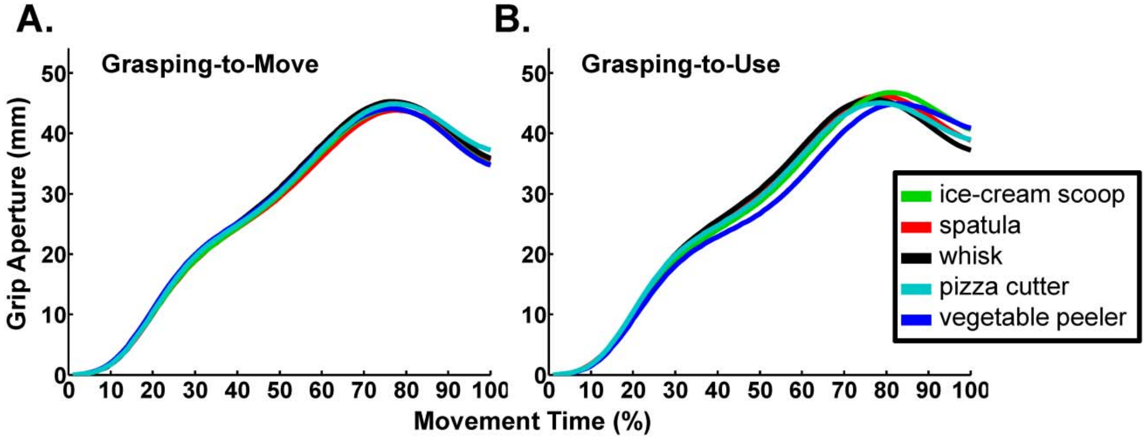


Figure 3.6. Grip aperture (Experiment 2). Grip aperture measures as a function of percent movement time, for each of the five tools for GTM (A) and GTU (B). Profiles for each individual tool are coloured as indicated in the legend

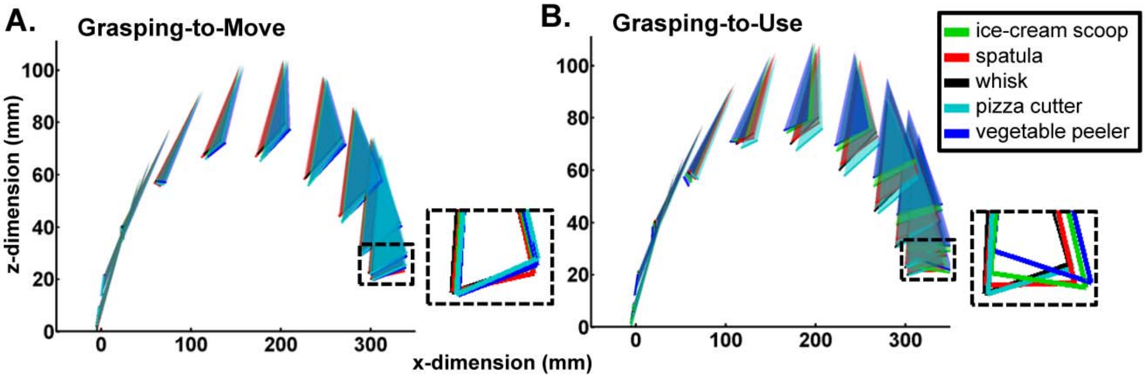


Figure 3.7. Grasp posture (Experiment 2). Plotted are the relative positions of the index finger, thumb, and knuckle markers in space, at 10% movement intervals, for each of the five tools, for GTM (A) and GTU (B). Plots for each individual tool are coloured as indicated in the legend. The x-dimension, or left-right direction, is plotted on the x-axis and the z-dimension, or up-down direction, is plotted on the y-axis. For each task, the final intervals of each grasp per tool are blown-up to facilitate comparisons.

3.4. Discussion

3.4.1 Priming and goal-set

When Gibson first described affordances (1979), he stressed that the kinds of actions an object would elicit would greatly depend on the goal state of the individual; for example, a fallen tree may afford sitting if one is tired, but may also afford standing if one is looking for a better view (Humphreys et al., 2009). In Experiment 1 we show that real grasping is differentially sensitive to priming depending on task goals; when the task was GTU, priming was evident, but when the task was GTM, priming was not (Figure 3.2). In line with our *a priori* predictions, priming effects appeared to follow the relative importance of tool identity to the particular goals and requirements of the task. We interpret these findings as evidence that grasping can proceed without the need to process object identity when the goal is to simply move an object aside. At a glance, such interpretations appear at odds with other studies that have shown effects of object semantics on grasping kinematics (Gentilucci, 2002, 2003; Gentilucci, Benuzzi, Bertolani, Daprati, & Gangitano, 2000; Glover & Dixon, 2002; Glover et al., 2004). However, in most of these studies the effects of semantics were mediated by words, which is different than testing for semantic effects mediated by the sight of objects. Also, in these previous studies semantic effects on grasping were driven by features such as object size or location, not learned function or use. We view our findings as convergent evidence that the functional and metrical aspects of grasping can be dissociated; both priming and the kinematics of grasping were dependent on the task. Previously, Riddoch et al. (Humphreys & Riddoch, 2000; Riddoch et al., 2000) showed that affordance effects in an individual with utilization behaviour depend on task; for the handle of a cup to evoke incorrect responses, the task had to be grasping (see also, Riddoch et al., 1998). These findings coincide nicely with ours, and suggest that task goals shape and determine affordances.

However, immediate task goals were not the only determining factor; when GTM and GTU trials were intermixed (Experiment 3.2), priming emerged for GTM trials as well (Figure 3.5). These findings, although at first surprising to us, are in fact quite consistent with the results of a previous study by Bub et al. (2003). In this work, participants were trained to respond to different colours by demonstrating different hand gestures, each of which fit with a specific learned object-use interaction style (e.g. a “poke” hand gesture). When participants were later cued to name objects on some trials and on others respond to colour, there were effects in the gesturing-to-colour responses based on whether or not the object in question shared the same hand configuration when used. However, in a separate experiment, when naming trials were not included no such effects were observed. Although not the focus of the paper, this finding was taken to indicate that affordances associated with the use of objects are not automatically evoked, but are instead only evoked when a certain extent of processing is, (or has been), directed to the object itself; in this case, recognition and retrieval of object names on separate trials did the trick. It seems that drawing attention to object identity on naming trials led to a ‘spill over’ of attention to these features on gesture trials. With attention to object identity in place, use-related affordances were evoked on gesture trials, and influenced response times accordingly. Our priming results for GTM, absent when tasks were blocked but evident when our tasks were put together, are in line with these findings. Attention to tool identity in GTU trials turned attention to these features in GTM trials, and, with attention to identity in place, priming effects emerged for GTM trials.

In this view, task goals modulate attention to particular object features, which in turn modulate corresponding affordances (and priming). Thus, affordance effects are determined by task goals insofar as task goals determine the allocation of attentional resources. If we expand this idea, and define the ***goal-set*** of an individual as that which is also determined by overall task setting and context, as well as immediate goals and intentions, then we can see how changes in setting can lead to changes in affordance effects, and this can explain why we observed priming for GTM trials in the mixed but not blocked experiments. In fact, there is a host of other evidence, nicely reviewed by Humphreys and colleagues (2009), to suggest that the goal-set, or action-state, of an individual indeed helps to shape processes of attention and selection. For example, Bekkering and Neggers (2002) asked participants to search for a target defined by its colour and orientation (e.g., find the red horizontal bar). Participants had to indicate the target by either pointing to it, or by grasping it. Eye movements during the search were made to distracters which shared the same orientation as the target much more often if participants were required to grasp versus point. It was as if the action-state of the individual influenced the ‘weighting’ of visual features in the display; in the case of grasping, orientation was weighted more strongly, presumably because orientation is more important for grasping than is object colour.

With these views in mind, our findings can be explained by differences in the way attention operates on (e.g. activates) affordances in accordance with the particular goal-set of the individual. Notably, however, our priming method may be limited in its capacity to detect affordances. For example, perhaps the presentation of a given tool as a prime leads to the activation of associated motor plans in both tasks, regardless of setting (blocked or mixed), but such activations then decay at different rates, or are differentially inhibited. Such differences could then impact priming and account for our results. In patients demonstrating utilization behaviour, the tendency to compulsively grasp and interact with objects is believed to reflect a failure to properly monitor and inhibit environmentally-driven processes (Lhermitte, 1983; Shallice et al., 1989). Lhermitte proposed that visual inputs activate parietal representations for actions, and that normally such activations are held in check by frontal control mechanisms. Damage to key frontal areas “releases the activity of the parietal lobe”, which then “tends to subject the patient to all external stimuli”, and utilization behaviour results. Our findings may reflect differences in the extent of such inhibitory control depending on task goals and overall task setting. When GTM trials were blocked, suppression of affordance-driven activity, specific to specific tools, may have allowed for more efficient responses. In contrast, in the context of the mixed design it may have been best to ‘allow’ such activations to unfold for both tasks. Switching inhibition of affordances on and off may have been inefficient in this context. Alternatively, perhaps affordance-driven motor plans need to be maintained in order to prime subsequent actions, and such maintenance in turn depends on the goal-set of the individual. In either case, corresponding differences in attentional mechanisms may be critical. Future studies may provide further insights as to which of these models is most likely.

3.4.2 Motor strategies and kinematics

In parallel with changes in priming from blocked to mixed designs, our findings also show evidence of other changes in general motor strategies across experiments. Some of these changes appear in line with previous work describing a homogenization effect, whereby responses to different trial types look more similar when presented together versus separately (e.g. Rastle, Kinoshita, Lupker, & Coltheart, 2003; Song & Nakayama, 2007). For example, in a study by Song and Nakayama (2007), two reaching tasks, one ‘easy’ and one ‘hard’, were compared across different methods of presentation. When the tasks were presented separately (blocked), easy trials led to faster reaction times than hard trials, as might be expected. However, when the tasks were presented together (mixed), as either alternating or random sequences, the differences between easy and hard trials disappeared. In particular, reaction times were extended for easy trials *and* shortened for hard trials, reflecting the so-called homogenization effect. If we compare our results from Experiment 1 (blocked) with Experiment 2 (mixed), reaction times for GTM appear to be lengthened in the mixed design, while reaction times for GTU appear to be shortened, in line with this homogenization pattern. Song and Nakayama (2007) concluded that participants implicitly took on different states of motor readiness when tasks were presented as mixed versus blocked. They also showed that explicit knowledge of upcoming trial types could not be used to reset the system to its optimal strategy. That is, in both their blocked and alternating conditions participants had full knowledge of upcoming trial types, and yet the alternating condition looked much like the randomized condition. They concluded that differences in strategy between blocked and mixed conditions appeared to be governed by a passive cumulative learning process tuned to recent trial history, not to do with the explicit predictability of future events (see also, Whitwell & Goodale, 2009; Whitwell, Lambert, & Goodale, 2008). In our Experiment 2, due to the task cuing before each trial begins, our participants also have explicit knowledge of upcoming trial types, and yet they also fail to make full use of such knowledge to prepare their actions accordingly. That is, if we assume that the blocked setting (Experiment 1) gives rise to the most optimal strategies for a given trial type, then the strategies employed in the mixed setting (Experiment 2) can be considered less optimal.

Further evidence that strategies changed across our experiments is indicated by the significant task by tool identity interaction in reaction times, specific to the mixed setting (Table 3.5). Only in Experiment 2 did participants take different amounts of time planning grasping-to-use actions according to the particular tool being grasped. And, most intriguing, the tool that stands out here, the vegetable peeler, is the tool that elicits the most distinct pattern of grasping kinematics. We believe these findings indicate a change in the way subjects carried out the GTU task in the mixed setting. First, we should clarify our stance that reaction times do indeed reflect the planning of actions, including (at least in part) the programming of specific kinematic details. Indeed, Klatzky and colleagues (Klatzky, Fikes, & Pellegrino, 1995; Pellegrino, Klatzky, & McCloskey, 1989) provide evidence that when functionally interacting with objects, participants plan appropriate hand configurations prior to initiating movements. Similarly, previous work with both grasping and tool use indicate that goal postures are predicted in advance of preceding movements (Bongers, Michaels, & Smitsman, 2004; Cohen & Rosenbaum, 2004; Rosenbaum, van Heugten, & Caldwell, 1996). With this in mind, if we compare reaction times for the GTU task from Experiment 1 (blocked) to Experiment 2 (mixed), participants seemed to have spent less time planning these actions in the mixed setting. If, as we suspect, this effect reflects a change in strategy, perhaps the peeler action, by virtue of its relatively distinct kinematics, was more difficult to adjust to this new strategy.

Why did the peeler action result in such distinct kinematics? Our account is that for all tools, the particular pattern of grasping reflects anticipation of upcoming features of the movements to be performed. In the case of the peeler, what appears to stand out most from the other tool actions with respect to post-grasp kinematics is the act of turning the handle over. That is, the peeler was always placed with its blade facing up, so that to properly perform the action participants should turn the tool over so that the blade faces downward. Participants usually did this in time with the final stages of grasping; the 3D plots of the thumb and finger positions in space appear to reflect this pattern (Figures 3.4 and 3.7). The thumb most often contacts the top surface of the handle while the index finger hooks to the far side and under, in line with the mechanics of the turning action. Rosenbaum and colleagues (Cohen & Rosenbaum, 2004; Rosenbaum et al., 1996) have shown that where and how participants grasp objects depends on the next steps of actions, and in particular anticipated end-states. Similarly, when participants grasp the same objects for different purposes, grasping kinematics differ and early steps of actions reflect the particular mechanics and demands of later steps (Ansuini, Giosa, Turella, Altoe, & Castiello, 2008; Ansuini, Santello, Massaccesi, & Castiello, 2006; Armbruster & Spijkers, 2006; Marteniuk, MacKenzie, Jeannerod, Athenes, & Dugas, 1987). Ansuini and colleagues (2008) show, for example, that changes in finger joint angles were unique for grasping a water bottle in order to pour from it, and appeared to reflect anticipation of the particular dynamics needed to carry out the pouring action. Likewise, Friedman and Flash (2007) demonstrate that force transmission patterns during functional grasping are compatible with the specific requirements of the task. Finally, Randerath et al. (2009) provide evidence that performance in functional grasping predicts performance in actual tool use. Thus, the differences we observed in grasping when moving versus using, and between different tools during our GTU task, most likely reflects differences in the kinetics of the movements to follow, as consistent with predictive models of motor control (e.g. Flanagan, Bowman, & Johansson, 2006; Rosenbaum et al., 2009).

3.4.3 Concluding remarks

Relatively few studies have looked at the priming of actual grasping actions using familiar objects, and, to our knowledge, we are the first to explore how object identity can differentially prime grasping depending on the greater goals of the task. Our findings indicate that task specific goals as well as overall task setting determine the goal-set of an individual, which in turn determines object affordances and priming, most likely by modulating processes of attention and selection. Beyond the physical properties of objects, knowledge and intention of use provide a mechanism for which affordances and the priming of actions may operate. One of the more exciting directions for future research is a continuing interest in the potential interactions between detailed kinematics of actions and priming. While our findings showed no evidence of priming effects on in-flight kinematic measures of grasping for either task, other studies have shown that the features of prime events can impact such details (e.g. Glover et al., 2004). Further, it is sensible to expect that such effects would be short lived (Jax & Rosenbaum, 2007, 2009), so that future studies with shorter delays between prime and probe events may indeed show learned object-specific priming effects in the kinematics of grasping. The present findings suggest that such effects would track with task goals and task setting.

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Chapter 4

4. Neural priming of tool use

4.1. Introduction

Tool use is ubiquitous and essential to human life, culturally universal, and common to hunter-gatherer and modern advanced societies alike. In a single day, we perform countless interactions with objects, typically without much thought or conscious deliberation. And yet, according to multiple lines of evidence in the fields of psychology and neuroscience, tool use must rely on complex interactions between highly specialized and functionally dissociable brain areas, organized within a widely distributed network of cortical and subcortical regions (Johnson-Frey, 2004; Rothi, Ochipa, & Heilman, 1997). Clearly, understanding the neural mechanisms underlying this network is a great challenge for neuroscientists, but continuing efforts in this area promise to reveal fundamental elements of human brain function and cognition (Iriki & Sakura, 2008; Johnson-Frey, 2003b; Washburn, 1960). At the core of common tool use is memory and mechanical understanding. Memory for objects, memory for actions, and an understanding of the mechanical properties of objects, and how these properties can aid in achieving specific goals. Despite over 100 years of prolific neuropsychological work in this area, and more recently the application of advanced neuroimaging methods, a clear picture of the brain mechanisms underlying tool use has yet been established. Indeed, current cortical theories of tool use highlight important gaps in understanding (e.g. Buxbaum & Kalenine, 2010; Frey, 2007). For example, it remains unclear how the brain transforms information supporting object recognition to recruit and implement appropriate action plans.

Challenges inherent in the study of real actions with neuroimaging methods such as fMRI have undoubtedly held back progress in this area. This is not to say that previous neuroimaging studies related to tool use have not significantly furthered our understanding; indeed, many valuable studies have been carried out, and convergence of activity patterns across a wide range of disparate paradigms implicate a core network of areas spanning temporal, parietal, and frontal cortices as important for tool use knowledge (Johnson-Frey, 2004; Lewis, 2006). However, given that actual tool manipulation has been scarcely explored, exactly how well activations reported correspond with those areas needed for real tool use planning and execution is not yet clear. Of the few studies that have used real tools, comparisons were made against conditions that either involved no object manipulation (Hermsdorfer et al., 2007; Imazu et al., 2007), no overt action (Higuchi et al., 2007), or, quite specifically, the use of chopsticks to pick up objects versus grasping with the hand (Inoue et al., 2001). With this approach, it is difficult to determine if resultant activity reflects processes specific to tool use per se, or differences in motor complexity, duration, spatial extent, somatosensory feedback, or a combination of such factors.

The current design manages to solve these difficult challenges. We use a novel variant of repetition suppression (RS) that we refer to as neural priming, which ultimately compares trial types involving the same motor outputs. Participants grasped and used real mini-sized familiar kitchen tools in accordance with the basic kinematic features of corresponding tool-specific actions. Actions matched the basic movement patterns tied to real tool use according to known identity and function (Figure 4.1C). Most importantly, action (probe) events were immediately preceded by visual preview (prime) events showing either the same or different tool as that which was then used. Neural priming was predicted to correspond with less BOLD activity for trials involving repeated tools at prime-probe events (Tool Repeated, TR) compared with trials involving different pairs of tools (Tool Changed, TC). Thus, on either side of this comparison the same actions were performed, the only difference being the relationship between prime (visual) and probe (action) events. In other words, with this method, neural priming effects are mediated purely visually, although directly related to the planning and execution of stored tool use.

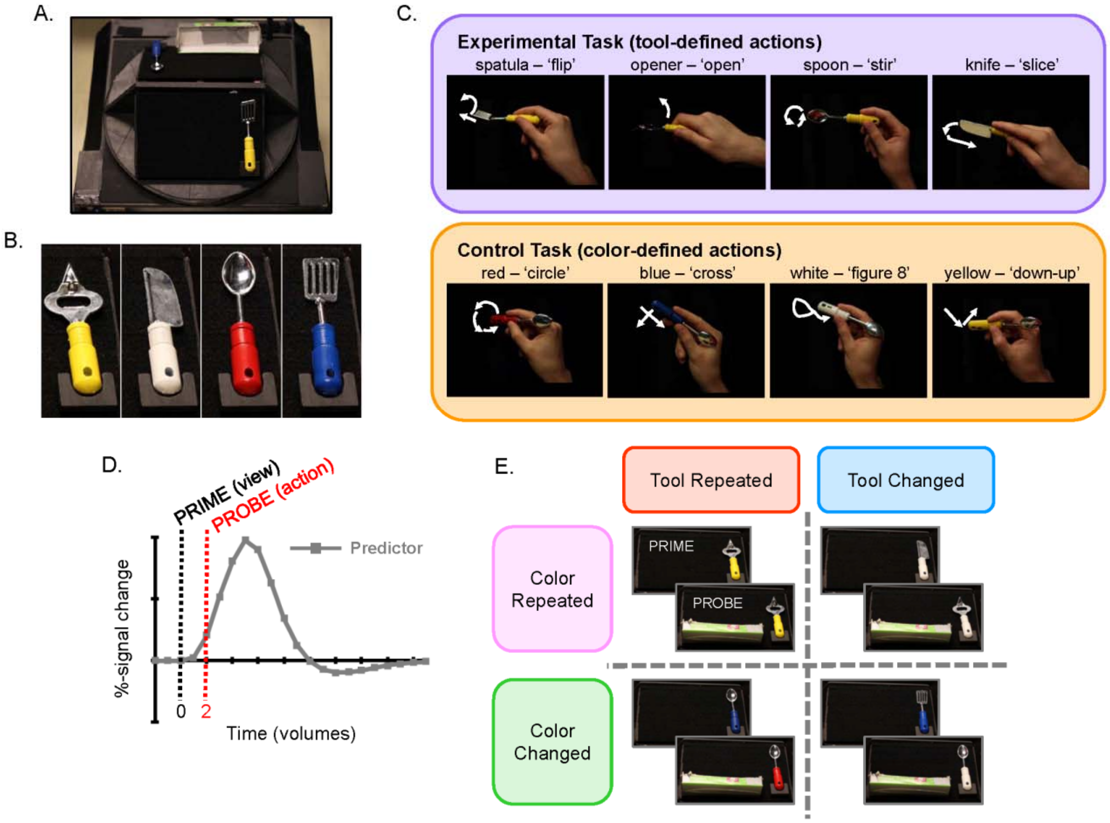

Figure 4.1. Methods. **A.** An overhead view of the grasping platform and turntable apparatus used to present tools to participants in the scanner. Both presentation sides can be viewed, the prime side showing a yellow spatula in position, and the probe side showing a blue spoon in position. On the probe side, a small box was used for participants to drop tools in after they had completed their actions. **B.** Examples of tools (bottle opener, knife, spoon, and spatula) and handle colours (yellow, white, red, and blue). **C.** In the Experimental Task, participants grasped and used tools according to identity (i.e. the basic movement features of these actions were consistent with those of actual tool use). Actions are shown with arrows drawn to indicate basic movement features. In the Control Task, participants grasped and used tools according to arbitrarily learned associations matching handle colour to a specific set of movements. **D.** For each trial, prime and probe events were modelled with a single predictor function aligned to the start of the prime event convolved with Brain Voyager QX "two-gamma" hemodynamic response function designed to estimate BOLD response characteristics. **E.** Shown are examples of the four possible combinations of prime-probe tool identity and handle colour. For Experimental runs, the critical trial types were Tool Changed (TC) and Tool Repeated (TR), and priming was expected to correspond with TC > TR. For Control runs, the critical trial types were Colour Changed (CC) and Colour Repeated (CR), and priming was expected to correspond with CC > CR.

Less BOLD activity in this context, as with other RS designs, is thought to reflect better metabolic efficiency when successive events activate closely overlapping neural processes (Grill-Spector, Henson, & Martin, 2006). In this case, tools presented as prime events are expected to partially activate corresponding motor plans related to learned use. Repetition of the same tools at action events, TR trials, will thus result in overlap of neural processing, and reduced BOLD activity is predicted. In contrast, by definition, prime-probe events for TC trials involve different tools, and will thus activate different motor plans. The theoretical basis for these predictions stems from the concept of motor affordances (Gibson, 1979): that the vision of objects alone naturally involves some activation of corresponding motor representations. This theory has received support from multiple disciplines, including monkey neurophysiology (Murata et al., 1997; Murata, Gallese, Luppino, Kaseda, & Sakata, 2000; Rizzolatti et al., 1988; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990), human neuroimaging (e.g. Chao & Martin, 2000; Grezes, Armony, Rowe, & Passingham, 2003), human neuropsychology (Lhermitte, 1983; Shallice, Burgess, Schon, & Baxter, 1989), and behavioural studies with neurologically healthy individuals (e.g. Tucker & Ellis, 1998). More recently, beyond the physical properties of objects, we and others have provided support for tool 'use-based affordances' that correspond with motor plans related to learned function and use (Bub, Masson, & Bukach, 2003; Bub, Masson, & Cree, 2008; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007).

Previous neuroimaging studies using RS have typically involved events of the same stimulus-response modality, and few have looked at real object manipulation tasks (although see Chong, Cunnington, Williams, Kanwisher, & Mattingley, 2008; Dinstein, Thomas, Behrmann, & Heeger, 2008; Kroliczak, McAdam, Quinlan, & Culham, 2008). Thus, the current study is unique in that it deals with real actions with real tools, and, critically, prime-probe events involve different response modalities: prime events involve viewing tools while probe events involve viewing and acting with tools. Detection of priming is predicted to reflect increased efficiency in the neural mechanisms underlying retrieval and implementation of stored tool use plans. Thus, these activations will reveal those areas critical to learned tool use planning and execution.

Importantly, to make such claims about the specialization of areas for learned tool use, it is necessary to demonstrate that neural priming is specific to tool-action associations. Less activity for TR versus TC trials could in principle reflect a general effect of prime stimuli correctly versus incorrectly cuing subsequent actions, independent of tool use specialization per se. If this were the case, then other types of congruent versus incongruent stimulus-action associations should lead to the same effects. To test this, we included a Control task whereby participants grasped the same tools used in the Experimental task, but instead of performing actions according to tool identity and function, actions were performed according to arbitrary associations based on handle colour of tools. These action associations, along with the Experimental task, were learned and practiced prior to scanning, and involved distinct hand and wrist movements along distinct spatial trajectories (Figure 4.1C). The Control task was performed on separate runs, interleaved with Experimental runs. For Control runs, trials with repeated handle colours, Colour Repeated (CR), would signal overlapping motor plans, while trials with different handle colours, Colour Changed (CC), would signal different motor plans, and priming in this task was thus predicted to correspond with CC > CR activations.

4.2. Results and discussion

4.2.1. Neural priming of tool use

The comparison TC > TR for Experimental runs identified four distinct areas at reliable statistical thresholds (Figure 4.2 A-D): left anterior intraparietal/inferior parietal, left dorsal precentral, left ventral precentral, and right intraparietal/superior parietal.

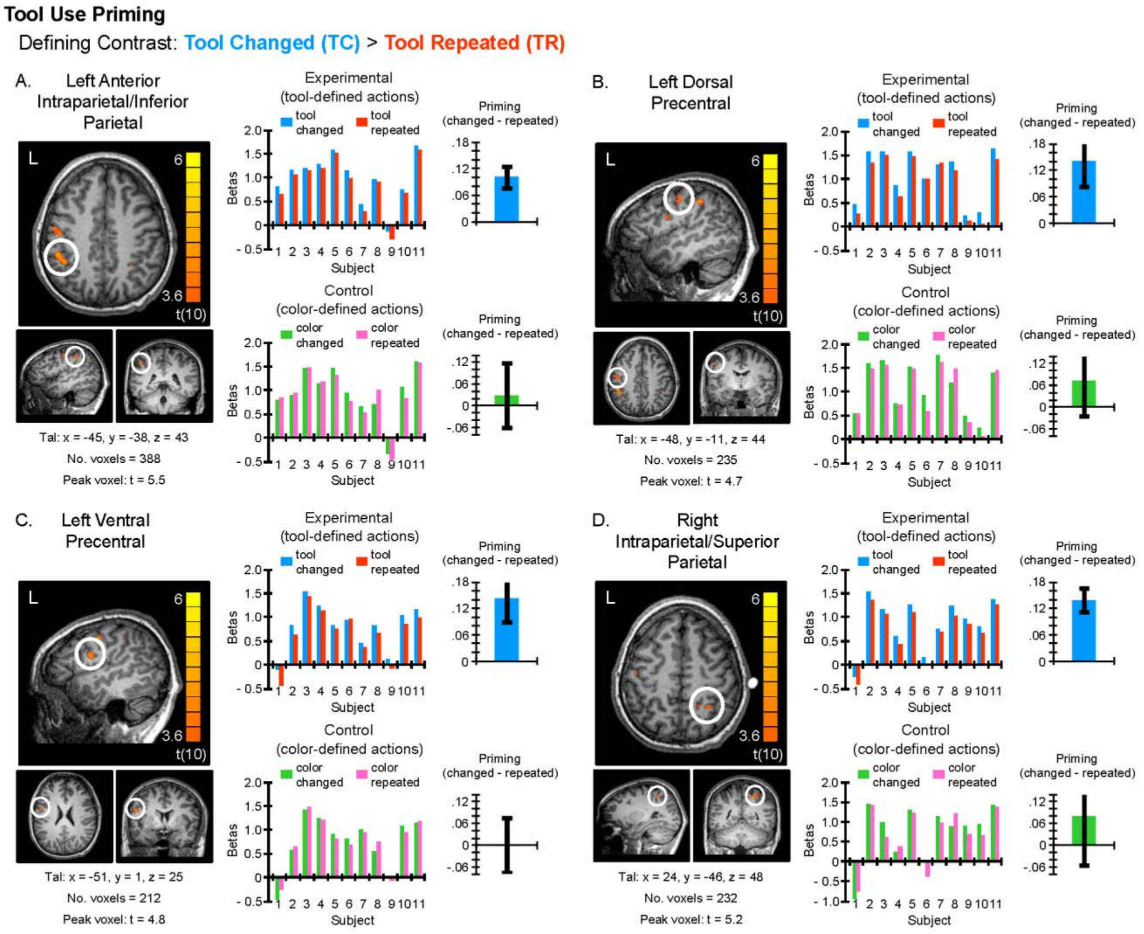

Figure 4.2. Priming of tool use. Activation maps based on the contrast TC > TR for Experimental runs, set to reliable statistical thresholds (t = 3.6, p < .005; cluster-sized corrected, min = 135 mm^3, p < .05) based on group random effects general linear model. Four distinct areas are identified (A-D). For visualization purposes, beta weights per individual per trial type are shown for each of the areas, and the group mean difference between TC-TR activation levels is shown as a measure of priming with 95% confidence intervals indicated. Beta weights per individual per trial type for Control runs indicate no reliable differences between trial types; neural priming effects in these areas were specific to tool-action associations and Experimental runs.

Priming effects in these areas did not generalize to colour-action associations for Control runs, but were specific to tool-action associations and Experimental runs (see Figure 4.2). The findings provide neural evidence for learned use-based affordance effects; experience using tools shapes robust associations between tool identity and action schema, such that vision of tools can activate corresponding motor plans. Re-activation of shared processes following repeated tools in TR trials results in less BOLD activity compared with TC trials. Localization of these effects to the areas identified indicates a relatively selective, mainly left-lateralized parietofrontal circuit. These areas play an important role in the retrieval and/or implementation of stored tool-specific action plans; neural priming effects specific to Experimental runs indicate functional specialization for learned tool use.

Activations showing tool specific priming effects correspond well with previous tool-related imaging studies, based on a wide range of disparate paradigms (Lewis, 2006), but also appear to highlight a more selective network than that which is typically specified. First, while left superior parietal cortex is most commonly reported, we detect priming effects within lateral anterior intraparietal cortex, more closely aligned with inferior parietal cortex. Notably, in two previous studies, when planning aspects were separated from execution of tool use pantomimes, more inferior versus superior parietal areas were isolated (Fridman et al., 2006; Johnson-Frey, Newman-Norlund, & Grafton, 2005). Also, tasks involving explicit retrieval of manipulation versus functional knowledge of tools selectively activate inferior parietal areas (Boronat et al., 2005; Canessa et al., 2008; Kellenbach, Brett, & Patterson, 2003). Such findings are consistent with our interpretations of the current results: that tool specific priming corresponds with access to and implementation of stored action plans. Note also that more inferior versus superior parietal areas for learned actions is consistent with several recently articulated theories of posterior parietal function which posit a separation of inferior from superior parietal cortex based on a number of factors, including tool use as specific to left inferior parietal lobule (Frey, 2007; Jeannerod & Jacob, 2005; Rizzolatti & Matelli, 2003). Second, many previous tool-related imaging studies report activations more closely aligned with the ventral visual pathway (e.g. left posterior middle temporal and mid-fusiform cortex), whereas we find no evidence of tool use priming in ventral stream areas. Compared with the current paradigm involving real actions with real 3D tools, previous studies have used tasks and/or stimuli that may have tapped into more perceptual/conceptual aspects of tool knowledge (for review, see Lewis, 2006), which could be particularly important in driving the activity in temporal areas (Martin & Chao, 2001). Still, we and others have previously argued that tool use necessarily involves access to ventral stream resources (Creem & Proffitt, 2001; Milner & Goodale, 1995, pp. 202-204; Valyear & Culham, 2010), and the current findings, showing robust priming for tool use in parietofrontal areas in the absence of concurrent effects within temporal areas, appear to work against such a model. Indeed, although there is some support for a direct, non-semantic route to learned actions (Riddoch, Humphreys, Coltheart, & Funnell, 1988; Riddoch, Humphreys, Heslop, & Castermans, 2002; for review and computational model, see Yoon, Heinke, & Humphreys, 2002), that the ventral stream is not at all important for planning tool use is difficult to reconcile with other findings (e.g. Carey, Harvey, & Milner, 1996; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000). Alternatively, our neural priming paradigm may bias detection of changes at the level of inputs (e.g. Tolias, Smirnakis, Augath, Trinath, & Logothetis, 2001), such that comparable changes in outputs may have been missed. Clearly, further investigations are needed to clarify the importance of ventral stream areas in planning learned tool use.

That priming effects in left inferior parietal and frontal areas reveal processes related to procedural memory stores for tool use is consistent with previous research on ideomotor apraxia. These patients have lost the ability to carry out learned actions with tools, hypothesized by many to reflect the loss of procedural representations which normally specify the particular details of tool use actions (Buxbaum, 2001; Heilman, Rothi, & Valenstein, 1982; Liepmann, 1980; Rothi et al., 1997). Lesion overlap studies point to both left inferior parietal and inferior frontal cortex as the most common sites of damage (Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005; Goldenberg & Spatt, 2009; Haaland, Harrington, & Knight, 2000). Priming effects specific to tool use in the current study were detected in both of these areas. Together the findings converge to implicate left inferior parietal and frontal cortices as specialized for the storage and retrieval of learned tool use actions. Notably, the presence of concurrent effects in a more dorsally located left frontal area, as well as right intraparietal/superior parietal cortex, suggests that these regions are additionally important. We can only speculate why lesion subtraction studies with apraxic patients do not tend to also highlight these areas, but perhaps this discrepancy indicates a cooperative but non-critical role for these areas in the healthy brain. In other words, unless damage here also coincides with damage to either inferior frontal or inferior parietal areas, compensation is possible and ideomotor apraxia is not typically observed. Previous imaging studies involving tool use pantomimes have also noted dorsal frontal activations (for review, see Johnson-Frey, 2004; Lewis, 2006), and comparisons with more perceptually oriented tasks (e.g. tool picture viewing) suggest that right intraparietal activations may be specific to tool-related tasks involving actual motor outputs (see Lewis, 2006).

4.2.2. Neural Priming of Control Actions

The comparison CC > CR for Control runs identified three distinct areas at reliable statistical thresholds (Figure 4.3 A-C): left ventral prefrontal, left posterior calcarine, and bilateral ventral medial occipital.

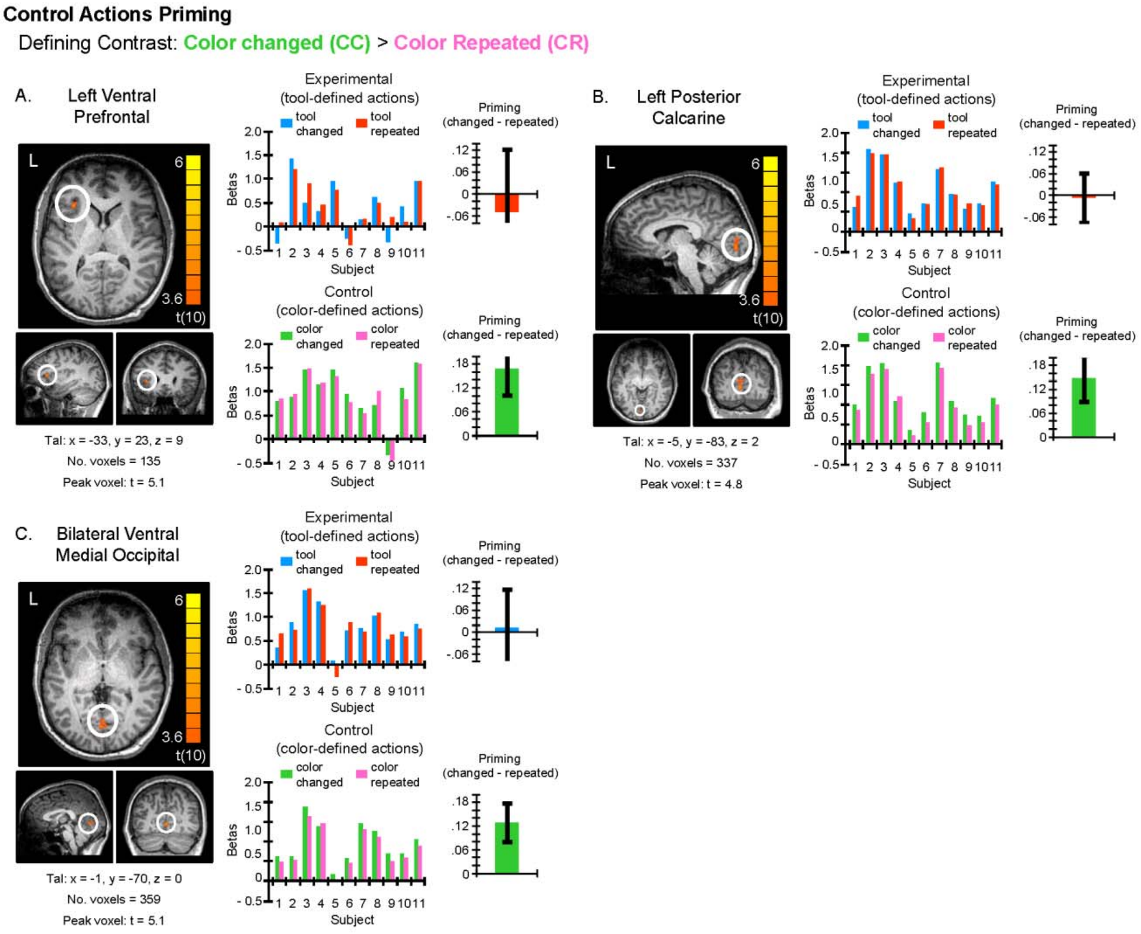

Figure 4.3. Priming of control task. Activation maps based on the contrast CC > CR for Control runs, set to reliable statistical thresholds (t = 3.6, p < .005; cluster-sized corrected, min = 135 mm^3, p < .05) based on group random effects general linear model. Three distinct areas are identified (A-C). For visualization purposes, beta weights per individual per trial type are shown for each of the areas, and the group mean difference between CC-CR activation levels is shown as a measure of priming with 95% confidence intervals indicated. Beta weights per individual per trial type for Experimental runs indicate no reliable differences between trial types; neural priming effects in these areas were specific to colour-action associations and Control runs.

Priming effects in these areas were specific to Control runs and colour-action associations; no indication of priming in these regions for Experimental runs was observed (Figure 4.3). This pattern of selectivity suggests a specific role for these areas in mediating the colour-defined Control actions. Mohr et al. (2006) report left inferior prefrontal cortex as selectively active in encoding and maintaining colour (versus spatial) information over a delay period. More recently, Yee et al. (2010) find greater delay activity for colour versus shape in what appears to be the same left inferior prefrontal region, and the strength of activity in this area was related to better performance on the colour task. Both studies provide support for a selective role for this region in encoding, storing, maintaining, and/or manipulating colour relevant task information. Notably, both studies also showed concurrent colour-specific activations within posterior medial occipital areas, and, as Mohr and colleagues (2006) proposed, left ventral prefrontal cortex “might control the rehearsal of colour information through a cross talk with more posterior visual areas”. Thus, our findings showing neural priming specific to colour-action associations within left ventral prefrontal and posterior occipital areas fit well with this previous work. This circuit appears particularly well suited for mediating behaviours based on arbitrary mappings according to object colour; in our case, left ventral prefrontal cortex may hold colour-defined rules in mind and coordinate with early visual areas to plan and carryout actions accordingly.

4.2.3. Tool-action Associations and Experience-dependent Plasticity

To account for tool use specific priming, we favour two interrelated hypotheses. The first puts an emphasis on the relative strength of tool-action associations. Pairings between tools and their associated actions tend to be particularly well established, built up over the life span, with relatively continuous reinforcement, not only through the performance of actual actions with tools, but also through the observation of others using tools, and through the gradual development of conceptual knowledge stores about tools and tool use actions. In other words, the specificity of neural priming within parietofrontal cortices corresponds with the overlearned nature of tool-action associations; only with sufficient experience and reinforcement do stimulus-action associations come to be represented within this circuitry to the extent that stimuli (tools) alone will trigger partial activation of motor plans. The second hypothesis highlights the role of ecologically valid outcomes. Tools are used to achieve specific goals, real world aims with meaningful outcomes, to the benefit of the user. In this way, tool-action pairings are themselves coupled with ecologically important behavioural outcomes, and this factor may be crucial in ‘gaining a position’ within parietofrontal neural machinery. Recent evidence implicate inferior frontoparietal areas as coding the goals and outcomes of actions, rather than specific motor mechanisms, such as the particular effectors or kinematics used to achieve those goals (Andersen & Buneo, 2002; Bonini et al., 2010; Fogassi et al., 2005; Hamilton & Grafton, 2008; Umilta et al., 2008). Of course, both accounts may be valid, and, in fact, interactions between these factors may be particularly critical: sufficient experience and continuous reinforcement paired with true ecologically meaningful outcomes together may comprise the key features underlying the specificity of neural priming for tool use within the parietofrontal areas identified.

In contrast, the colour-action associations that make up our Control task are neither well established nor ecologically meaningful. It is true that following instructions accurately, like those required by our colour-action task, does have real ecological value in the sense that socially, it is often advantageous to adhere to the requests of others; and in the case of our experiment, participants were certainly encouraged to learn these associations and were ultimately given monetary compensation for their participation. But still, there is something clearly different about the explicit, inherent rewards that are routinely paired with real familiar tool use, and those that go along with performing the colour-defined actions we introduced to participants in the current experiment. Thus, in our hands, it is fair to say that the arbitrarily assigned colour-action associations that comprise our Control task differed critically in how they are paired with real world meaningful outcomes, such as successfully feeding and clothing oneself. As for the strength of these associations, colour-action pairings were newly learned, with no correspondence to pairings that occur in real life. Thus, clearly the strength of these associations differed from those of our tool use task. Indeed, we view the pattern of priming effects specific to Control runs and colour-action associations as in part reflecting the temporary nature of these associations; it made sense for participants to hold in mind these pairings only temporarily, and evidently, they recruited a completely different set of areas to do so. Priming in left ventral prefrontal cortex may, in particular, reflect the holding of rules in mind, while concurrent effects in early visual areas may relate more directly with bottom-up components of the task (i.e. in distinguishing between different handle colours). In other words, we interpret this collection of activations as reflecting the coordination of both top-down (left ventral prefrontal) and bottom-up (early visual) mechanisms.

To conclude, we identified a selective, mainly left-lateralized parietofrontal circuit showing neural priming specific to familiar tool-action associations. Specificity of priming for tool use in these areas reflects a form of experience-dependent plasticity, whereby continuous pairings of tools with actions gives rise to use-based affordances: visually-driven activations of motor representations for learned use. That such effects instantiated within left inferior parietal and frontal cortex converges with previous neuropsychological and neuroimaging evidence; these areas are particularly important in the retrieval and implementation of learned tool use. The current design controlled for various confounds that plagued previous imaging studies of tool use and the findings have provided a more selective account than was previously available. Tool-use priming within left inferior parietal cortex is consistent with recent arguments for its uniquely human specialization for tool use (Peeters et al., 2009), following disproportional expansion of inferior parietal cortex in human evolution (Bruner, Manzi, & Arsuaga, 2003; Eidelberg & Galaburda, 1984, as cited in Johnson-Frey, 2003a, p.206).

4.3. Experimental Procedure

4.3.1. Subjects

Eleven right-handed individuals with normal or corrected-to-normal vision participated in the study. None of the participants had any prior history of neurologic or psychiatric illness. All subjects provided informed consent in accordance with the guidelines approved by the University of Western Ontario Health Sciences Review Ethics Board.

4.3.2. Stimuli and presentation setup

Figure 4.1B shows the different tools and handle colours that were used. The complete set included repeats of each exemplar, for a total of 32 items. Tools were presented using the platform and turntable apparatus shown in Figure 4.1A. Two Velcro-covered sides were used to attach tools and allowed for the independent presentation of prime and probe events within a trial. On the probe side only, a small cardboard box was attached to the lower part of the workspace, used to catch tools in after subjects had completed their actions. The platform was specifically adjusted for each individual so that tools and the workspace could be comfortably viewed without the use of a mirror and so that tools could be easily grasped and used with minimal movement of the arm. Specifically, the setup allowed participants to grasp and use tools without the need to lift their elbow from the bed or move their upper arm or shoulder. Tools were presented in the lower right quadrant of the workspace. Participants were instructed to fixate a small light-emitting diode (LED) that was attached to an adjustable plastic stalk positioned directly above where tools were presented. For both prime and probe events, tools were made visible by brief (300-ms) illumination of a superbright white LED attached to a second adjustable stalk. The experiment was otherwise carried out in complete darkness.

4.3.3. Tasks

Experimental and Control tasks were performed in separate runs. Each run comprised 16 trials. A given trial was made up of the following events: a visual prime event involving 300 ms illumination of a tool, followed by a 2700 ms delay with no vision, followed by a second tool illuminated for 300 ms (Figure 4.1D). Illumination of the second tool signalled the action (probe) event, in which subjects reached, grasped, and used whichever tool was shown and then placed it in the 'catch box' before returning to the rest position to wait for the next trial to begin. From the onset of the probe event, there was a 16.5 s delay period before the next trial began.

On a given trial, prime-probe events either involved the same or different tools, with either the same or different coloured handles (Figure 4.1E). Each possible combination of these trial types was shown 4 times per run, arranged so that actions events were equally represented within a run, evenly distributed across trial types. For Experimental runs, handle colour was irrelevant and participants performed actions according to tool identity; whereas for Control runs, tool identity was irrelevant and participants performed actions according to handle colour (Figure 4.1C). For each task, actions were minimal-amplitude motions, involving mostly the wrist, fingers and thumb, approximately 3-4s in duration. Participants performed a minimum of 3 Experimental (with an average of 4.2 runs per subject) and 3 Control runs (with an average of 4.1 runs per subject). Eight distinct run orders were created for each Experimental and Control runs, and all possible combinations of prime-probe pairings were equally represented across orders. Different run orders were evenly distributed across individuals, randomized for presentation order within individuals, always following an interleaved sequence (e.g. Control-Experimental-Control, or vice-versa).

4.3.4. Pre-scan training

Prior to scanning (max 1 week, min 2 days), participants took part in a behavioural training session. The purpose of this session was to familiarize participants with tools, trial types, events and timing, and to learn the colour-action pairings for the Control task. Another important goal was to closely specify and practice the particular actions that were to be performed in the scanner, for both Control and Experimental tasks. The problems associated with movements of the head while in the scanner were thoroughly explained, and participants understood that their hand actions should not involve movements of the upper arm or shoulder, and that their head should be kept still at all times. Minimal-amplitude actions were stressed, emphasizing the use of only the wrist and fingers. And, actions were trained to be performed quickly but smoothly, finishing in approximately 3-4s.

After initial discussions about the task and stimuli had took place, participants performed 16 trials of each Experimental and Control actions, presented in separate blocks, balanced for trial type and action type within a block. Trial types and timing were the same as used in the actual fMRI experiment, except trials were not spaced so far apart; participants dimply signalled the experimenter to initiate new trials once ready. The same turntable apparatus as used in the scanner was used to present tools (Figure 4.1A), and LCD goggles were used to control participants' vision. For these first 32 trials, actions were performed with visual feedback to allow participants and the experimenter to more easily comment on and adjust actions if needed (e.g. to suggest smaller amplitude movements; to suggest particular finger placements, etc.). After these two blocks of trials were performed, two additional blocks of 40 trials per task were performed, this time with no visual feedback of actions, as in the fMRI experiment (i.e. tools at both prime and probe events were only made visible for 300 ms). Actions and trial types were equally represented and evenly distributed within blocks, and block order was counterbalanced across individuals. For the Experimental task, no differences in reaction times were evident when Tool Repeated (M = 412 ms, SEM = 19.9 ms) and Tool Changed (M = 416 ms, SEM = 24.5 ms) trials were compared, $t(10) = 0.20$, $p = 0.85$. Likewise, for the Control task, no differences between Colour Repeated (M = 416 ms, SEM = 34.7 ms) versus Colour Changed (M = 411 ms, SEM = 30.1 ms) trials were evident, $t(10) = 0.13$, $p = 0.90$.

4.3.5. Imaging parameters

Imaging was performed on a 3 Tesla Siemens TIM MAGNETOM Trio MRI scanner. The T1-weighted anatomical image was collected using an ADNI MPRAGE sequence (time to repetition = 2300 ms, TE = 2.98 ms, field of view and matrix size = 192 x 240 x 256, flip angle = 9°, 1 mm isotropic voxels). Functional MRI volumes were collected using a T2*-weighted single-shot gradient-echo echo-planar imaging (EPI) acquisition sequence (time to repetition = 1500 ms, slice thickness = 4 mm, in-plane resolution = 3.3 mm x 3.3 mm, time to echo (TE) = 30 ms, field of view = 211 mm x 211 mm, matrix size = 64 x 64, flip angle = 75°, and acceleration factor (integrated parallel acquisition technologies, iPAT) = 2 with generalized auto-calibrating partially parallel acquisitions (GRAPPA) reconstruction). We used a combination of parallel imaging coils to achieve a good signal-to-noise ratio and to enable direct viewing without mirrors or occlusion. We tilted (~30° degrees) the posterior half of the 12-channel receive-only head coil (6-channels) and suspended a 4-channel receive-only flex coil over the anterior-superior part of the head. Each volume comprised 28 contiguous (no gap) axial-oblique slices, spanning from the most superior point of cortex through ventral fusiform cortex to include approximately two-thirds of cerebellum, providing near whole brain coverage; volume acquisition space included anterior temporal poles but excluded parts of orbital prefrontal cortex.

4.3.6. Data preprocessing and analysis

Imaging data were preprocessed and analyzed using Brain Voyager QX version 2.1.0.1532 (Brain Innovation, Maastricht, The Netherlands). Each functional was assessed for subject head motion by viewing cineloop animation and by examining Brain Voyager motion-detection parameter plots after running 3-D motion correction algorithms on the untransformed two-dimensional data. No abrupt movements were detected in the animations and no deviations larger than 1 mm (translations) or 1° (rotations) were observed in the motion correction output. Motion correction was performed using BV QX intra-session alignment options (involving resampling with sinc interpolation) with the reference volume taken as the closest volume to the T1-weighted anatomical scan. Error trials (i.e. where the participant may have fumbled with the object or performed the incorrect instruction) were examined off-line from videos recorded using an MR-compatible infrared-sensitive camera that was optimally positioned to record the participant’s movements during functional runs (MRC Systems GmbH). However, due to equipment failure, recordings were available for only 5 participants in the group. No trials from these participants contained errors.

Functional data were preprocessed with linear trend removal and underwent high-pass temporal frequency filtering to remove frequencies below three cycles per run, and aligned to anatomical volumes, which were then transformed into standard stereotaxic space (Talairach & Tournoux, 1988). Data were spatially smoothed for group analysis using a Gaussian kernel of 6 mm (full-width at half-maximum).

Trials were defined as four volume (6 s) events starting at the onset of prime events (Figure 4.1D). For Experimental runs, trial types were either Tool Repeated (TR) or Tool Changed (TC), and for Control runs, trial types were either Colour Repeated (CR) or Colour Changed (CC). Predictor functions for each trial type for each run were convolved with Brain Voyager QX “two-gamma” hemodynamic response function designed to estimate the spatiotemporal characteristics of the BOLD response. A group defined random effects general linear model (GLM) was used for analysis of both Experimental (minimum 3 runs, average 4.2 runs per subject) and Control runs (minimum 3 runs, average 4.1 runs per subject). Each run was z-transformed prior to

GLM analysis. Resultant activation maps were set to a statistical threshold of $t = 3.6$, $p < .005$, uncorrected for multiple comparisons. Maps were then corrected using BV QX cluster-level statistical threshold estimator which was found to indicate a minimum cluster size of 135 mm^3, corrected at $p < .05$. To evaluate specificity of priming defined areas, Beta weights per individual per trial type for either Control (Figure 4.2) or Experimental (Figure 4.3) runs were extracted from identified areas, and condition means were compared using paired t-tests at a significance threshold of $p < .05$, Greenhouse-Geisser corrected.

4.4. References

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Chapter 5

5. General Discussion

Broadly speaking, the goals of my thesis were to gain new insights into the neural and behavioural mechanisms underlying learned tool use. My approach focused on the activation of tool use representations in response to viewing and using tools (Project 2 and 3) and in response to observing tool use grasping (Project 1). Neural recording studies in monkeys reveal that viewing objects or object directed actions activates neurons underlying motor programming of object grasping and manipulation (Chapter1, section 1.3.1). Neurons in both anterior intraparietal (area AIP) and ventral premotor (area F5) cortex respond to viewing objects (canonical neurons) and viewing object-directed actions (mirror neurons), and this activity coincides with the motor properties of these cells for object grasping and manipulation. My studies were designed so that response selectivity for tools (Projects 2 and 3) and tool use grasping (Project 1) would indicate sensitivity to ***learned*** features of tools not accessible without access to stored knowledge.

In Project 1, I used fMRI to visualize brain activity in response to viewing tool use grasping. Movies of grasping actions that were typical of how tools are normally grasped for use (Typical Grasping, TG) were compared with atypical grasping that would not allow for easy use (Atypical Grasping, AG). Differential activity was taken to indicate sensitivity to learned aspects of tool use grasping. We found preferential activity for viewing TG movies in a collection of areas closely aligned with the ventral visual pathway; however, contrary to our expectations, no such preferential activity was observed in parietofrontal areas thought to underlie learned motoric aspects of tool use.

In Project 2, behavioural priming of tool use grasping was examined and compared across two types of tasks: grasping-to-use (GTU), where participants grasped and demonstrated the use of tools, versus grasping-to-move (GTM), where participants grasped and moved tools. Actions were preceded by a visual preview (prime) event involving the presentation of a single tool, either congruent or incongruent in identity to that which was then acted with. A reaction time advantage for congruent trial types was taken to indicate priming. Tools had identical handles and thus priming did not reflect facilitation of processing related to structural object properties important for grasping, but instead was related to knowledge of identity and learned use. In a first experiment, we found that when GTU and GTM tasks were presented separately, priming was detected for the GTU task only. We also found that grasping kinematics split apart according to tool identity when the task was GTU but not GTM, revealing robust differences in the way the hand shaped to grasp tools according to intention and use. A second experiment involving both GTM and GTU tasks randomly intermixed in the same block of trials revealed priming effects for both tasks. This finding indicates the importance of goal-set in shaping effects of priming, likely driven by differences in the allocation of attentional resources. Differences in attention to particular object features, in this case tool identity, modulate affordances driven by those features which in turn determines priming.

In Project 3, I presented a new imaging method to study real tool manipulation that controls for various confounds that have plagued previous fMRI studies of tools (as discussed in Section in 1.4.2.). The paradigm is a neuroimaging variant of the behavioural priming approach used in Project 2 and follows directly from the theory of use-based affordances developed from Valyear et al. (2007). With a visual priming paradigm I am able to selectively probe the neural correlates of learned tool use. My general approach relies on well established neuroimaging findings known widely as stimulus specific repetition suppression; yet, my design is unique in that it involves a visual-only event followed by a visual-action task. To demonstrate specificity of priming for learned tool use, I introduced a control task whereby actions were guided not by tool identity but instead by arbitrarily learned associations with colour. The results show specificity for tool use priming in a selective mainly left-lateralized network of parietofrontal areas. Neural priming of tool use is taken to reflect a form of experience-dependent plasticity, driven by continual reinforcement of tool-action pairings.

My discussion is divided into four main sections. First, I consider my findings with respect to the ventral stream and stored conceptual knowledge of tools (section 5.1). The question of ventral stream importance for tool use is addressed in light of the findings from each project in turn (section 5.1.1), followed by an expanded discussion of the evidence for and against the importance of explicit conceptual knowledge in planning and using tools (section 5.1.2). Second, I discuss behavioural (section 5.2.1) and neural (section 5.2.2) priming of tool use, Projects 2 and 3 respectively. Both types of priming are thought to reflect the activation of tool-specific motor plans implicitly triggered by the visual presentation of tools (i.e. use-based affordances). Third, section 5.3 provides a summary of both sets of neuroimaging findings from Projects 1 and 3, followed by a consideration of two interrelated theoretical themes in light of these new findings: schema theory of tool use and divided parietal streams for action (section 5.3.1). Finally, I conclude with specific suggestions as to the most important and promising future directions that follow directly from the findings of the current thesis (section 5.4).

5.1. Conceptual object knowledge and the ventral stream

5.1.1. Is the ventral stream important for tool use?

The findings from Project 1 (Chapter 2) showed a collection of areas within the ventral visual pathway as preferentially active for observing typical tool use grasping (TG) (Figure 2.5). While this was not what we had in mind when we set out with this experiment, this pattern of specificity falls in line with thinking about the ventral stream as important for conceptual knowledge of objects and tools. Just as TG actions make sense with respect to ‘how’, they make sense with respect to ‘what’; that is, these actions fit with the way tools are normally grasped for use (how) insofar as the tools themselves are known and can be recognized (what). In essence, this feature of tool use, the necessary marriage between ‘what’ and ‘how’, is exactly what I looked to exploit; only my sights were more narrowly focused on the procedural side of things – hoping to activate associated parietal regions by way of implicit motor simulation. As Scott Frey so cleverly states in the title of his recent review paper on the cortical basis of tool use: “What puts the how in where? Tool use and the divided visual streams hypothesis” (Frey, 2007). The title is both a question and an answer; ‘what’ refers to the ventral stream and ‘where’ refers to the dorsal stream, and thus the suggestion is that the ventral stream works with the dorsal stream to contribute and help mediate the ‘how’ of tool use.

Prior to Project 1, I had not thought of such processing within the ventral stream arising implicitly. In our task participants were not asked to evaluate movies with respect to conceptual content in any explicit sense – they were asked to detect relatively infrequent instances of repeated movies; a task that was intended to simply keep subjects attending to movies, rather than impose any particular processing demands. And yet, simply watching and attending to videos led to robust differences in ventral stream activity according to how tools were grasped. Specifically, TG gave rise to greater activity compared with atypical grasping (AG) even though participants were not told to explicitly evaluate grasp type. Since this project, a new imaging study by Roberts and Humphreys (2010) involving the viewing of object pairs positioned correctly versus incorrectly for action showed strikingly similar findings. Correct action positioning is when an 'active' object, like a corkscrew, is facing a 'passive' object, like a wine bottle, so that interaction between the pair of objects is immediately possible. The assignment of 'active' and 'passive' relates to how the two objects influence one another when used together, where the active object of a pair is used to change the state of the passive object. In this way, active-passive object pairs can be shown as properly or improperly positioned for action. Roberts and Humphreys (2010) found that such positioning selectively influenced the strength of activity within the ventral stream; when pairs of objects were correctly positioned for action, activations within a relatively large swath of ventral stream cortex showed stronger responses compared with when those same objects were positioned incorrectly for action. Preferential activity was seen bilaterally in lateral occipital temporal cortex, corresponding with LOC, although the effects were much stronger in the left hemisphere, extending inferiorly to include fusiform cortex exclusively in the left hemisphere. Notably, these position effects were evident even when participants were not directly attending to object pairs. Clearly these findings match well with ours; where Roberts and Humphreys (2010) show implicit ventral stream coding for learned object-object positions for action, we show implicit ventral stream coding for learned hand-object positions for action. Further, as with our findings, Roberts and Humphreys (2010) found no concurrent effects in visuomotor areas of the dorsal stream. They conclude that their ventral stream effects reflect "a ***visual*** response to the possibilities of action" (Roberts & Humphreys, 2010, p. 1547) not governed by motor-related influences from parietofrontal areas. We also find that although parietal areas were more responsive for grasping versus reaching movies, activity was the same for typical and atypical tool grasping. Together both sets of findings indicate that, at least in the realm of perceptually driven events, the dorsal stream is agnostic to the learned functional relationships between stimuli for action.

Note that ventral stream responses to such learned relations may not reflect conceptual knowledge processing or retrieval in an explicit sense, but rather may reflect statistical regularities built-up from perceptual experience with ‘the way the world is’. That is, perceptual systems may very well be sculpted by the kinds of visual consistencies, patterns, and instances normally present in the natural world (Geisler, 2008; Schwarzkopf & Kourtzi, 2008; Simoncelli & Olshausen, 2001). Perhaps such shaping includes influences from the regularities of everyday living, which include how objects are normally manipulated and used, and how multiple objects typically interact and are arranged (Humphreys et al., 2009). According to this account, our findings indicate that seeing a hand grasp a tool in a way consistent with such regularities, consistent with everyday interaction, gives rise to greater metabolic activity within the ventral visual pathway.

What is not immediately clear in this account is why the rise in metabolic demand/consumption? Why would a match in perceptual consistency lead to greater activation in the perceptual system; one might just as easily predict that processing would unfold more efficiently, and thus with less metabolic consumption and less BOLD activity. The explanation I put forth in Chapter 2 suggested that with this better perceptual fit, activations in the ventral stream tend to spread, both locally within neighbouring populations of cells making up distinct processing modules (e.g. area LO), and more distally, to other modules within the network. The example I provided is that seeing a garden shovel grasped properly may activate other semantic associates like dirt and flowers. This argument extends to other information types, like predicted or implied motion, and, in accordance with the organizational principles laid down by Simmons and Barsalou (2003), even low-level visual areas encoding simple visual features that show overlap in ‘conceptual space’ may be more strongly activated. This account explains the widespread distribution of effects we detected, not only within high level object areas, but also motion area MT+ and more posterior occipital foci (Figure 2.5).

Whatever the driving mechanism, in my view, the sensitivity to conceptual aspects of tool use grasping within the ventral stream is consistent with the model of tool use and the two visual streams put forth by Milner and Goodale (1995, pp. 202-204; see also Milner & Goodale, 2006, p. 231). In this view, tool use involves the cooperation of both streams, and what is more, the ventral stream is thought to play a specific role in both object and action selection. Alongside identification and selection of particular tools for action, the ventral stream is thought to flag the part of a tool to be grasped (e.g. its handle). It follows that the conveyance of such information is essential to the specification of functional features of tool use grasping. That is, as I have shown empirically with Project 2 (Chapter 3), functional grasping of tools involves computation of a complex array of anticipatory kinematic features in accordance with predicted kinetics of upcoming action components. Ventral stream inputs are thought to be vital to the specification of such details. Milner and Goodale were also clear that prior to the implementation of actual motor outputs by dorsal stream areas, praxis-specialized areas within inferior parietal cortex would need to do their part. What exactly this role is, and how it unfolds at the neural level, represents a fundamental missing link in contemporary cortical theories of tool use.

Keeping with the current focus, how do my findings from Projects 2 and 3 integrate with this model of ventral stream involvement for tool use? Recall that while the dorsal stream is thought to operate on a moment-to-moment timescale, ventral stream processes are thought to operate over much longer timescales (Chapter 1, section 1.2.1). Differing timescales translate into contrasting predictions about priming: while functions of the ventral stream are expected to show sensitivity to priming, functions of the dorsal stream may not. At the most conservative end of this view, real actions are programmed from the bottom-up, based only on information currently available to the system, not subject to prior events, and thus not expected to show priming. In an earlier study, we provided evidence for this conservative account by showing no indication of behavioural priming in accordance with repeated versus non-repeated object orientation in a real grasping task (Cant, Westwood, Valyear, & Goodale, 2005). Conversely, with the same setup, stimuli, and timing of events, a naming task, dependent on ventral stream function, showed robust evidence of priming. Garofeanu et al. (2004) used a more traditional repetition-priming paradigm whereby a set of common objects were shown in a study phase followed by presentation in a test phase along with ‘new’ objects, not shown during study. Priming was observed for repeated objects in the test phase when the task was naming, but not for grasping. The findings support the view of visuomotor processes as reliant on moment-to-moment computations, relatively insensitive to priming, whereas object recognition is fundamentally dependent on memory, highly sensitive to priming (see also Kroliczak, Westwood, & Goodale, 2006). Notably, the concept of priming and real actions is not without its opponent views (e.g. Craighero, Fadiga, Umilta, & Rizzolatti, 1996; Jax & Rosenbaum, 2007); it appears as though the picture of priming and actions depends greatly on the specific details of experimental design (for relevant discussion, see Kroliczak et al., 2006, p. 140). Nevertheless, if we accept that in general, ventral stream processing is more susceptible to priming than is dorsal stream processing, my findings from Project 2 showing robust priming for grasping-to-use tools provides support for the idea that familiar tool use involves ventral stream contributions. Conversely, when participants performed the grasp-to-move (GTM) task priming was much less evident (Figure 3.5), and in the case of Experiment 1 altogether absent (Figure 3.2). This pattern is consistent with the idea that the GTM task can be performed based entirely on dorsal stream function, without ventral stream involvement. With respect to the model outlined in the General Introduction (section 1.4), differential priming for the grasp-to-use (GTU) versus the GTM task is consistent with the distinction between systems for grasping based on learned object properties, as aligned with a lateral-IPL pathway and the ventral stream, versus structural object properties, as aligned with a medial-SPL pathway and the dorsal stream (Figure 1.3).

It is important to recognize that this separation of priming according to task was not completely rigid, but instead showed sensitivity to whether or not tasks were presented together, in a mixed task setting, or in separate blocks, in a single task setting. In the mixed setting, both GTM and GTU trials showed priming. How do these findings fit with the model of distinct pathways to grasping? In Chapter 3, I discussed the findings with respect to attention and affordances. The motor system takes on unique strategies depending on both immediate action goals and overall context, including task setting (blocked or mixed). I used the term ***goal-set*** to capture these adjustments in behavior and underlying motor strategies. The complete set of findings from both experiments can be explained by the idea that goal-set determines the specific allocation of attentional resources which in turn determine affordances and priming. In the mixed setting, priming for the GTM task reflects attention to tool identity and function, spilled over from the need to attend to these features in GTU trails. Under the model of distinct routes to grasping, these findings may indicate a shared attentional system. With attention to tool identity in place, priming unfolds even for GTM trials. Alternatively, when trial types were intermixed, perhaps the brain's solution was to simply perform both tasks with the same route to grasping; namely, the lateral-IPL route specialized for functional grasping and tool use. That this route can actually penetrate the programming and control of motor outputs for grasping is evidenced by the findings from optic ataxic patient AT (Jeannerod, Decety, & Michel, 1994). Recall from Chapter 1 (section 1.4.1), this patient showed improved grasp scaling for familiar versus semantically-neutral objects.

Finally, how do my findings from Project 3 fit with the model of ventral stream involvement for tool use? Right away, lack of neural priming effects in ventral stream areas appears at odds with an account of ventral stream importance for tool use planning. Areas important for retrieval and implementation of stored tool-specific action plans were expected to show reduced BOLD activity for Tool Repeated (TR) compared with Tool Changed (TC) trials. We identified a selective network of parietofrontal regions that followed this pattern, and left parietal activations were localized to lateral intraparietal cortex overlapping with IPL, in line with its proposed specialization for tool use and the two action route model of PPC. If ventral stream input is an important component of the lateral-IPL system, why then did ventral stream areas not also show neural priming of tool use? Rather than reject the model of ventral stream importance in tool use altogether, which would be difficult to reconcile with previous findings (e.g. Carey, Harvey, & Milner, 1996), I looked to explain these findings by considering the proposed underlying nature of BOLD-based priming effects more closely. The theory posits that priming (reduced BOLD) comes about when successive events activate overlapping neural processes. In the case of my experiment, repeated tool identity will activate more of the same neurons than when identity is changed, and given the context of the tool use task, some of this activity will underlie the retrieval/implementation of tool-specific action plans. We can break the process down further and consider the expected ventral stream responses to both the prime and probe events in turn. Vision of prime events activate neural populations coding tool identity, and volleys of action potentials are sent forth to inferior parietal areas to communicate this message; evidence for such parietal activity for viewed tools in the absence of overt action is clear from my previous imaging findings (Valyear et al., 2007) as well as others (Chao & Martin, 2000). At the onset of probe events, the same processes unfold, except, of course, this time retrieval and execution of motor plans is explicit, as the actions themselves are then actually carried forth. Although an obvious oversimplification, if we define this as an activation loop between ventral and inferior parietal areas, we can say that ventral stream components represent primary senders of information while parietal components represent primary receivers. As I suggest in Chapter 4, this difference between output and input roles may have important consequences at the level of detection of activation changes. Previous findings indicate that BOLD activity is more strongly correlated with local field potentials which reflect the inputs-to and local processing within an area versus single and multi-unit spiking activity which reflect long-range outputs (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001; Logothetis & Wandell, 2004). Thus, activation changes due to repeated tool identity may be detected at the level of inputs to an area (inferior parietal cortex) but missed at the output level (ventral stream areas).

The above hypothesis gains support from the following study by Tolias et al. (2001). The authors used an fMRI adaptation paradigm to measure direction selective responses to motion stimuli in macaque monkeys. Motion stimuli moving in a single constant direction were shown continuously for several seconds. This is called the adaptation phase, where motion responsive neurons selective for the presented direction of motion will show decreased firing (i.e. adaptation). Direction selectivity is then measured by introducing a change in direction of motion. A corresponding increase, or ‘rebound’ from the adapted level of activity then indicates sensitivity to motion directionality. Notice that the logic of this paradigm is essentially the same as what I called neural priming in Project 3; repeated events lead to decreased activity in an area(s) of interest, which is detected and measured by comparison with non-repeated or changed events[3]. Tolias and colleagues found that area MT showed a robust rebound from BOLD adaptation, indicative of strong motion directionality. The findings matched well with previous neurophysiological studies showing that spiking activity in a high proportion of MT neurons indicate direction selectivity (Albright, 1984; Maunsell & van Essen, 1983). What was surprising, according to BOLD measurements area V4 showed even greater direction selectivity than MT, even though according to neurophysiology much fewer neurons show direction selectivity in V4 (Desimone & Schein, 1987). To account for this discrepancy, the authors explained that such apparent direction selectivity may come about as a consequence of the dense connectivity between direction selective neurons in MT and non-directionally selective neurons in V4. In other words, the activation changes in V4 reflect changes at the level of inputs, proposed to stem from changes in output firing from MT. This account was also used to explain higher than expected direction selectivity in others visual areas such as V1. The findings highlight key differences between classic neurophysiological investigations focused on spiking activity of neurons and BOLD imaging, where imaging is highly sensitive to network dynamics and may be biased to detect activity at the level of inputs and local synaptic events.

Priming effects aside, the model of ventral stream involvement in tool use predicts that activation in ventral stream areas will rise and fall in time with tool use planning and execution. As a simple test of this prediction, I performed a whole-volume voxel-wise contrast of action events (either Experimental or Control) versus rest. Ventral stream activity was detected bilaterally, although with a strong left hemisphere prevalence. Two distinct hotspots were evident in left temporo-occipital cortex, one lateral and anterior (Figure 5.1A) and one more inferior near fusiform cortex (Figure 5.1B). For both areas, the activation time course shows a rise onset consistent with visual responsiveness to prime events, followed by a more pronounced increase in time with

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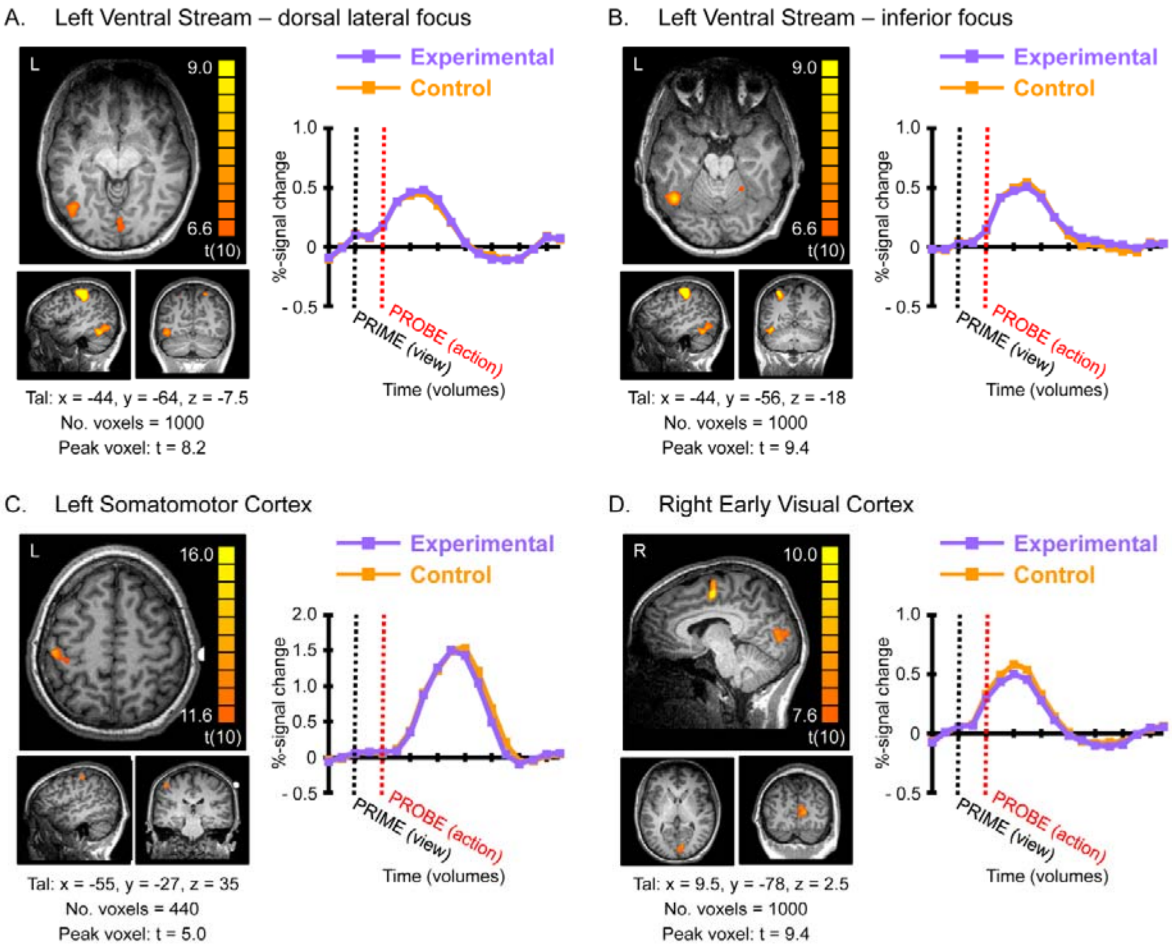
[3] Indeed, the terms fMRI adaptation, repetition suppression, and neural priming have all been used interchangeably n neuroimaging research; although, adaptation usually indicates that blocks of repeated events were used rather single repeats as with event-related designs.

action (probe) events. For comparison, activation in an area overlapping with somatomotor cortex shows a much later response onset, consistent with distinct motor-driven activity (Figure 5.1C). As with ventral stream areas, early visual cortex was activated early on, in sync with the onset of prime events (Figure 5.1D). Further analyses according to trial types showed no indication of priming in ventral stream areas for either tool use and Experimental runs or colour-defined actions and Control runs. Activation time courses also indicate similar responses to both Experimental and Control tasks. Nonetheless, elevated BOLD activity in concert with prime and action events was clearly evident. Although minimal, this provides some support for the hypothesis that tool use involves the ventral stream.



A. Left Ventral Stream – dorsal lateral focus

Tal: x = -44, y = -64, z = -7.5
No. voxels = 1000
Peak voxel: t = 8.2

B. Left Ventral Stream – inferior focus

Tal: x = -44, y = -56, z = -18
No. voxels = 1000
Peak voxel: t = 9.4

C. Left Somatomotor Cortex

Tal: x = -55, y = -27, z = 35
No. voxels = 440
Peak voxel: t = 5.0

D. Right Early Visual Cortex

Tal: x = 9.5, y = -78, z = 2.5
No. voxels = 1000
Peak voxel: t = 9.4

Figure 5.1. Non-specific task-related activity (Project 3). Activation maps were generated from the contrast of Experimental and/or Control actions > rest, based on group random effects general linear model. The goal of this additional analysis was to determine if ventral stream areas were activated by tool use. Two distinct foci in the left ventral stream were identified (**A-B**) at reliable statistical thresholds (t = 6.6, p < 1.0 x 10^{-4}; cluster-sized corrected, min = 162 mm^3, p < .05). The strongest activity based on this contrast was revealed in left somatomotor cortex (**C**), and for additional comparison, activity is shown for early visual cortex (**D**). Averaged activation time courses are shown for each area, based on a maximum selection of 10 mm^3 set of active voxels centred on the local activation peak. No differences between Experimental versus Control actions are evident in any of these areas. Notably, the onset of activity is much earlier in both ventral and early visual areas compared with left somatomotor cortex. The results indicate elevated ventral stream activity in time with action events. As shown, ventral stream activations were much stronger in the left hemisphere, revealed bilaterally only at reduced thresholds.

Further, it may well be significant that ventral stream activations were so strongly left lateralized. Typically, objects activate ventral stream areas in both hemispheres to much the same degree; but, tools as a category selectively activate left posterior middle temporal gyrus (pMTG), as shown in our Localizer results of Project 1 (section 2.3.2; Figures 2.2A-B, 2.4). Comparison revealed partial overlap between this tool selective pMTG and the dorsal lateral ventral stream activity we observed when participants performed real actions with tools (Figure 5.2). Such a finding provides additional support for the idea of ventral stream involvement in tool use. Selectivity for tools in pMTG has been shown with many different kinds of tasks and defining contrasts (Lewis, 2006); this area may represent a convergence point whereby multiple information types from separate modalities are integrated (e.g. Beauchamp, Lee, Argall, & Martin, 2004). We show a very consistent spatial relationship with this area and areas LO and motion area MT+ in individuals; tool selective pMTG sits just anterior and lateral to both areas (Figure 2.4). Although speculative, its position is well suited to mediate integration and exchange of information between dorsal and ventral pathways. On the basis of preferential responses to tool versus body motion, Beauchamp and colleagues (Beauchamp, Lee, Haxby, & Martin, 2002) proposed that tool selective pMTG may play a specialized role in processing the typical motions of tools in action (Beauchamp & Martin, 2007). We extend these findings in Project 1 to show preferential activity for TG versus AG movies (Figures 2.2A-C), and suggest that coding in this region may integrate hand and tool motion. Activation of this area in time with our tool use task in Project 3 may indicate additional contributions to real tool use; however, we cannot exclude the possibility that this activity may also simply indicate visual responses to tools in general.

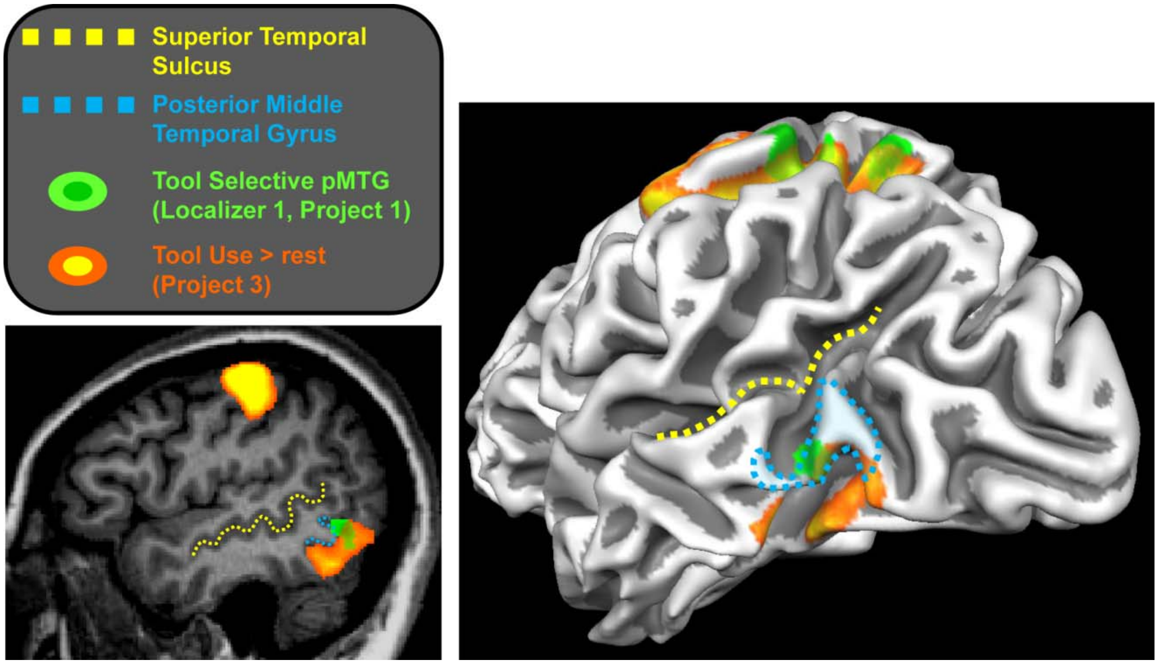


Figure 5.2. Ventral stream activity for real tool use overlaps with tool-selective pMTG. Activity for real tool use (Project 3, Figure 5.1A) is shown in yellow-orange while activity selective for viewing pictures of familiar tools versus bodies, non-tool objects, and scrambled images (Project 1, Figures 2.2A-B, 2.4) is shown in green. Activity for both maps are based on group averaged results in standardized space shown on a single individuals' anatomical MR image (left) and 3D cortical reconstruction (right). Overlapping activation suggests partial correspondence between tool-selective pMTG and ventral stream activity for real tool use. Superior temporal sulcus (yellow) and posterior middle temporal gyrus (blue) are marked for anatomical reference.

In my view, several lines of evidence suggest possible correspondence between particular neuron types in monkey STS and this tool selectivity observed in human pMTG. Response characteristics of certain STS neurons indicate multimodal integration of sights and sounds of actions (Barraclough, Xiao, Baker, Oram, & Perrett, 2005). Human pMTG shows selectivity for both viewing and hearing tools in action (Beauchamp et al., 2004; Lewis, Brefczynski, Phinney, Janik, & DeYoe, 2005). STS neurons show high level selectivity to viewing the actions of others (Barraclough, Keith, Xiao, Oram, & Perrett, 2009; Perrett et al., 1989; Perrett, Mistlin, Harries, & Chitty, 1990), including not only response specificity for particular action outcomes but also conjoint sensitivity to the direction of an actor's gaze, consistent with encoding of action intentionality (Jellema, Maassen, & Perrett, 2004; Jellema & Perrett, 2006). In Project 1, I observed differential activity for viewing typical versus atypical grasping actions in tool selective pMTG (Figure 2.2A-C), consistent with an area showing sensitivity to action intentions. Finally, as I covered in section 1.3.2, tool use learning in monkeys gives rise to extensive changes in the physiology of neurons in anterior IPS (Iriki, Tanaka, & Iwamura, 1996; Ishibashi et al., 2002), in parallel with the emergence of new incoming connections stemming from areas within STS (Hihara et al., 2006). New connections are thought to carry forward visual information important for skilful tool use. Others have shown differential coding in STS neurons in responses to the monkey's own movements with and without an object in hand (Hietanen & Perrett, 1993, 1996).

I would argue that these response similarities between tool selective pMTG in humans and STS areas in monkey suggest possible functional correspondence. Importantly, with other functionally defined areas in monkey STS, others have noted more posterior correspondence in humans (Orban, Van Essen, & Vanduffel, 2004). For example, motion areas MT/MST in the macaque are situated within the STS (Van Essen, Maunsell, & Bixby, 1981), whereas in humans, MT+ is located further back, in middle temporal cortex at the junction of inferior temporal and lateral occipital sulci (Dumoulin et al., 2000). These differences have been attributed to the great expanse of inferior parietal cortex in human brain evolution (Bruner, Manzi, & Arsuaga, 2003; Holloway, 1996), which is thought to have 'pushed around' existing areas; in the case of STS, expansion appears to have forced many areas backward (Orban et al., 2004). Such evidence is consistent with my argument for putative functional overlap between cell types identified in monkey STS and human tool selective pMTG. Monkey STS neurons may represent important functional precursors in human brain evolution, present in a common hominid ancestor, necessary for further development and specialization of advanced tool use. With the massive expansion of inferior parietal cortex these cells may have migrated posteriorly, to take up position in and around posterior middle temporal cortex; an area which appears to be a critical part of the human cortical network specialized for complex tool use (Lewis, 2006).

Upon concluding, is the ventral stream important for tool use? While my current findings are merely suggestive on this front, evidence sides with the view that ventral stream contributions are indeed important. Results from Project 1 are most clear, but since the task was only tool action viewing, extension of these findings to real tool use is necessarily speculative. Project 2 shows that priming unfolds more robustly for grasping tools when the goal is to demonstrate their use (versus grasping-to-move only); results that can be taken as support for preferential ventral stream involvement for tool use. Finally, although neural priming of real tool use was not observed in ventral stream areas in Project 3, activity was seen in time with action events, and left lateralization showed overlap with tool-selective activity in pMTG (as defined in Project 1). Overall, my findings provide indirect support for the account of ventral stream involvement in learned tool use; considerable room for progress in this area remains. Given that the model of ventral stream contributions to tool use makes clear predictions about the flow of information from ventral to inferior parietal areas, future experiments using methods designed to capture functional interactions between brain areas may be particularly fruitful. For example, ERP/EEG imaging allows for high resolution mapping of temporal dynamics and thus may be particularly well suited to test this account. The paradigms developed here should be transferable to such an approach. For example, perhaps tracking the time course of neural events for grasping-to-use versus grasping-to-move tasks with ERP would reveal early ventral stream involvement specific to the tool use condition. Finally, transcranial magnetic stimulation (TMS) techniques may also be particularly informative. Stimulation of ventral stream areas, like area LO or tool-selective pMTG, may selectively disrupt grasping-to-use tools, and/or the priming thereof. Further, combined with detailed tracking of kinematics of functional grasping (Project 2, Chapter 3), TMS to ventral stream areas at different times during the planning of tool use actions may give rise to different effects. Again, the kinds of tool use tasks I have developed in Projects 2 and 3 may be well suited for transfer to investigation with such an approach. In brief, the topic of ventral stream importance for tool use planning and implementation is ripe for future experimentation and discovery. I hope that my current findings will provide a springboard for which these future experiments may propel forward.

5.1.2. Is explicit conceptual knowledge important?

While I have taken a stance in favour of ventral stream importance for tool use, I have not been overly clear about the content of information likely to be sent forth to inferior parietal areas. Beyond visual recognition of tools, is explicit declarative conceptual knowledge needed for tool use? The most powerful insights with regards to this topic have undoubtedly come from the study of patients with semantic deficits. The picture that has emerged, however, is not so clear cut.

Sirigu et al. (1991) describe a patient with associative agnosia who is utterly puzzled about the identity and function of most common objects, but nonetheless can sometimes manually gesture how those same objects are typically used. Notably, the patient showed great appreciation of object mechanics; a comment from the patient while visually exploring a safety pin is particularly telling in this regard: “You open on one side, stick something on it, close it, and it stays in. I can tell you how it works, but I don’t see its exact use. I don’t think I’ve seen one like this before, it is not a very common object” (Sirigu et al., 1991, p. 2555). MRI scans showed bilateral damage to anterolateral temporal cortex (anterior temporal poles, aTP). Buxbaum and colleagues (1997) studied a patient with semantic dementia (SD) who also suffered from bilateral damage to aTP. Despite profound semantic impairments, the patient showed surprisingly good performance in gesturing the proper use of objects, and in some cases even showed seemingly spared knowledge of conventional function (e.g. when demonstrating the use of a toaster, the patient also mimed the insertion of bread). Further, on tests of multiple object use, he scored much better than expected, even with objects he was impaired with when tested for declarative conceptual knowledge. Finally, another SD patient studied by Lauro-Grotto et al. (1997) also showed impaired conceptual object knowledge, but performed well when tested on a food preparation task requiring multiple steps and the combined use of different tools and utensils. The patient showed worse performance on semantic tests involving verbal versus visual materials, and the authors proposed a fractionation of semantic knowledge into separate modality-specific systems. Seemingly normal tool use skills were thought to reflect the patient's spared visual semantic system. Consistent with these three cases, other reports indicate that SD patients are competent with tasks of daily living and may play sports and engage in various hobbies, all of which involve the skilled use of objects (Graham, Lambon Ralph, & Hodges, 1997; Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden, Griffiths, & Neary, 1996). Altogether, the message appears to indicate that intact conceptual knowledge is not necessary for tool use.

The findings from two papers by Hodges and colleagues (2000; 1999), however, suggest differently. In their initial study (Hodges et al., 1999), these authors tested two SD patients with bilateral aTP damage and a single ideomotor apraxic patient with posterior parietal damage on tool naming, picture matching to functional associates, actual object demonstrations of use, and a novel tool use task. The novel tool use task (designed by Goldenberg & Hagmann, 1998) involved retrieval of a cylindrical object from a casing by selecting and using a novel tool from a choice of three tools, where only one of these available tools would allow for proper interaction and retrieval of the cylinder. The task relies on mechanical understanding of the fit between tool and cylinder end (a hook-ended tool will work for a loop-ended cylinder), referred to as mechanical problem solving by Goldenberg and Hagmann (1998) who showed that such a task was dependent on the integrity of PPC. Consistently, the parietal patient tested by Hodges et al. (1999) was unable to solve the novel tool use task; the patient was also poor at familiar tool use, but did well with naming and functional associates. Conversely, both temporal lobe patients were severely impaired on naming and matching tools with functional associates, but performed flawlessly with the novel tool use task. Critical to the current discussion, both patients scored badly with familiar tool use. Moreover, for those instances where SD patients showed reasonably good tool use performance, success was either due to residual sparing of conceptual knowledge or was based on a gradual process of trial and error, dependent on preserved mechanical problem solving. With this latter strategy, performance was better with those tools for which the relationship between structure and function was particularly transparent; for which function and use could be deduced from an appreciation of structural mechanics. The authors concluded that "conventional use of objects depends on additional conceptual knowledge for which inferotemporal brain structures appear to be critical" (Hodges et al., 1999, p. 9447).

In a follow-up study, Hodges and colleagues (2000) extend these initial findings with more extensive testing of both tool use and semantic performance in a larger group of 9 SD patients. Again, patients were shown to be impaired with actual tool use, and their performance was highly correlated with scoring on semantic tests; those objects that were used correctly tended to be the same objects that patients showed some residual conceptual knowledge of. With explicit reference to the two visual streams hypothesis, the authors highlight that SD involves extensive ventral stream damage (see p. 1924, and also referenced Mummery et al., 2000), and conclude that:

> Under these circumstances, the functioning of the (intact) dorsal pathway must become increasingly isolated, leaving patients still able to solve mechanical problems such as the novel tool task, but gradually depriving them of the normal ability to use familiar objects in the conventionally correct, conceptually determined, fashion. (Hodges et al., 2000, p. 1924)

To account for the occasional sparing of seemingly normal tool use ability and success with daily living, sports, and hobbies, the authors described five factors that may allow for reasonable compensation in the face of conceptual knowledge impairments. Alongside of residual conceptual knowledge of objects and intact mechanical reasoning, they point out that experience and familiarity, including premorbid familiarity, with particular tools is likely to be important. As a fourth factor, they suggest that whether or not patients are personally familiar with tools and contexts, surroundings and settings, is also likely to be important. Notably, in a more recent study (Bozeat, Ralph, Patterson, & Hodges, 2002), patients were found to perform better when tested with their own personal items. Finally, as a fifth factor, the authors suggest that affordances, defined as an automatic process of motor evocation driven by the inherent structural properties of objects, distinct but likely related to mechanical problem solving skills, may also play a role. The confluence of all of these factors may help support relatively normal object use in patients with SD and other forms of semantic impairment. The cortical events underlying tool use in the neurologically healthy individual are supposed to greatly benefit from access to stored conceptual knowledge; in particular, when it comes to carrying out conventional use of tools.

The idea of affordances and mechanical reasoning as a route to action that may circumvent the need for explicit semantics overlaps with the dual route to action hypothesis of Riddoch and colleagues (Riddoch, Humphreys, Coltheart, & Funnell, 1988). On the basis of various patient dissociations (Pilgrim & Humphreys, 1991; Riddoch, Humphreys, Heslop, & Castermans, 2002; Riddoch, Humphreys, & Price, 1989), and, more recently, added support from tests with normal individuals (Rumiati & Humphreys, 1998; Yoon & Humphreys, 2007), these authors suggest that two independent routes to learned actions exist, a semantic route and a non-semantic visual route. The visual route to action is reliant on what they called stored structural descriptions of familiar objects. This element of stored knowledge within the direct visual route is different from the ideas of affordances or mechanical reasoning, which typically do not involve stored representations. The visual route to action has access to stored structural descriptions of familiar objects, as an independent form of learned object knowledge. Such content is presumably represented within higher order visual object areas of the ventral stream.

Notably, Buxbaum and colleagues (1997) also theorized about an affordance-based account of preserved tool use abilities in patients with SD. However, since the SD patient they studied (discussed above) showed some access to conceptual content about the contextual relations between objects and their conventional use, Buxbaum and colleagues argued that structural affordances alone could not account for this spared performance. Instead, they reasoned that some form of conceptual knowledge must have been spared in this patient, not accessible by declarative means. They proceeded to suggest that conceptual knowledge tapped into by the performance of natural actions can separate from that of explicit declarative representations. To be clear, according to their view, it is not so much the content of conceptual knowledge that is separable, but rather the accessibility of that content; with natural tool use, a confluence of activity from multiple sources (e.g. visually driven affordances) may allow for access to conceptual knowledge not otherwise accessible via explicit declarative means. In other words, task itself may interact with accessibility of stored knowledge.

The picture is more complex with consideration of the condition known as conceptual apraxia. Liepmann (1980) first described this condition in a patient that behaved quite differently from what he classified as ideomotor apraxic. Rather than showing problems carrying out the motor aspects of actions, this patient was seen to make odd errors of substitution (e.g., using a razor as a comb). Liepmann considered the problem to reflect a loss in the patient's ability to internally conceptualize the idea or purpose of tool use, and thus termed the condition ideational apraxia. In his view, the disorder was a result of damage to a system distinct from that underlying ideomotor apraxia; he wrote that ideational apraxia "is determined through diffuse damage of the brain, but particularly through lesions on the left in the transition from parietal to occipital lobe, lying more in the latter" (Liepmann, 1980, p. 80). In more recent times, the disorder is known as conceptual apraxia, to emphasize the conceptual aspects of the underlying deficits and to distinguish it from ideational apraxia which is now more often associated with motor sequencing problems (Poeck, 1983). The errors of a conceptual apraxic patient are fundamentally different from those of an ideomotor apraxic individual (De Renzi & Lucchelli, 1988; Ochipa, Rothi, & Heilman, 1989). They may use the wrong tool to perform actions, like attempting to eat soup with a knife, often omit critical steps in multi-step actions, like leaving out the coffee grinds when making coffee, or they may perform the correct movements with tools but in the wrong location, like combing movements with a comb but near the midline of the body. They are often confused about the goals of a particular action and fail to appreciate how a given tool can provide an advantage in fulfilling those goals. When faced with a problem, like when trying to drive a nail into a piece of wood, these patients fail to see how a hammer would be helpful (Raymer & Ochipa, 1997). Perhaps most important to what I have discussed thus far, conceptual apraxia separates from generalized semantic deficits (Ochipa, Rothi, & Heilman, 1992). Patients can typically name objects and point to objects by name, and, also different from SD patients, conceptual apraxic patients are deeply impaired with tasks reliant on mechanical problem solving (Ochipa et al., 1992; Raymer & Ochipa, 1997). In short, a consideration of conceptual apraxia reveals additional layers of complexity germane to neural systems underlying tool use.

The above discussion is not only relevant to the broader picture of tool use and its cortical basis in humans, but also more pointedly to the interpretation of ventral stream activity in my real tool manipulation task in Project 3 (Figure 5.1, 5.2). Does this activity reflect access to conceptual content of tool knowledge? On each trial, participants must visually recognize tools and call up correct actions from memory. With what has been discussed thus far in mind, to do so it seems unlikely that the brain would need to access deep conceptual knowledge of the declarative type. Instead, a more direct (and efficient) route from tool recognition to stored action plans may have been utilized. This seems especially likely since my task involved a limited set of four different tools, tools were highly familiar, and tool-specific actions were practiced before scanning. The need for explicit access to stored conceptual knowledge on a trial by trial basis would seem unnecessary. This may explain why aTP activity was not detected even with the simple comparison of action events versus rest[4]. Instead, I suspect that in my tool use task ventral stream contributions may be somewhat minimized; activity in these areas may reflect a relatively superficial tool recognition process, essentially involving visual discrimination between the four possible tool types, and a fast feed-forward of ‘results’ to inferior parietofrontal areas for action plan retrieval and implementation. A minimized role for the ventral stream in my tool use task may have also contributed to the lack of

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[4] In general, anterolateral temporal pole (aTP) activity has not typically been reported in previous imaging studies of tools, even with more explicit semantic tasks (e.g. Boronat et al., 2005). This leads to a puzzling disconnect between the findings from patient work and those from neuroimaging. What is likely a contributing factor is that these areas are more susceptible to signal artifacts with fMRI; close to the air-tissue interface near orbital frontal cortex, the MR signal is simply more variable in these voxels. Many potentially relevant studies have not actually scanned these areas for such reasons. However, I was sure to include these areas in my coverage in Project 3. Moreover, I found no obvious evidence of unreliable signal in these areas and no indication of BOLD signal changes (up or down) in time action events. Thus, it appears as though these areas were indeed not engaged in my tool use task.

priming seen in these areas. This hypothesis need not contradict the idea that ventral stream contributions are necessary for specifying how to grasp tools for use; instead, such specifications may instantiate at the level of inferior parietal cortex, which may decode the message from ventral stream areas to trigger appropriate action outputs. More generally, the identification of multiple routes to stored action plans has broad implications for theorizing about how the brain may support tool use differently depending on the particular action scenario (Rothi, Ochipa, & Heilman, 1997). Access to deep conceptual knowledge may often be unnecessary.

5.2. Affordances for tools

Central to my thesis are the findings that action plans and the motor system can be activated by the mere presence of visual stimuli. Contrary to classic views of the motor system, current evidence strongly indicates that even primary motor areas may automatically specify visual stimuli according to their potential for action, in confluence with higher order goals and intentions (Cisek & Kalaska, 2010). With grasping, visual object properties register with corresponding motor representations; object size, shape, and orientation activate parietofrontal neurons coding these features for the purpose of controlling the hand accordingly for grasping (Murata, Gallese, Luppino, Kaseda, & Sakata, 2000; Rizzolatti et al., 1988; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). When this correspondence is driven by structural object features, I have used the term “structure-based affordances”. One of the goals of both Projects 2 and 3 was to test the following hypothesis: for familiar tools, affordances reflect the activation of motor plans not accessible by way of structural object properties alone, but instead reliant on prior experience (i.e. memory). I distinguish these as “use-based affordances”, to indicate that visual-to-motor correspondence is necessarily driven by knowledge of tool identity, function, and use.

In the previous section, I emphasized how tool actions likely depend on inputs from ventral stream sources, important for the specification of object identity, and perhaps, in certain cases, other conceptual aspects of stored tool use knowledge. This dependency on ventral stream input contrasts with the planning and control of other kinds of actions, like grasping in order to simply pick up an object, or to move it from one place to another. Likewise, use-based affordances likely depend on ventral stream inputs, while structure-based affordances do not. As Neisser pointed out: “to see that something affords posting letters, we must first identify it as a mailbox, and that’s a job for the categorizing systems – for re-cognition” (1992, p. 11, as cited in Buxbaum et al., 1997).

But, this aspect of use-based affordances is only half the story. A second major theme of my thesis focuses on the receiving end of this output; according to the model of distinct parietal streams for action (Figure 1.3), a left lateral-IPL stream should mediate the retrieval and implementation of stored tool-specific action plans. Use-based affordances for tools should manifest at the level of left IPL.

5.2.1. Behavioural priming of tool use

Project 2 (Chapter 3) provides behavioural evidence consistent with the hypothesis of use-based affordances for tools. Reaction times for grasping-to-use were reliably shortened (primed) when preceded by a visual preview of the particular tool to be used. The effects were not attributable to structural properties relevant for grasp scaling according to handle size or shape, as all tools had identical handles. Rather, priming was driven by information relevant for tool use, carried forward by the specific identity of tools. Detailed kinematic tracking revealed distinct patterns of grasping according to tool identity, in accordance with the specific kinetics of the actions that followed. In other words, the characteristic movements defining particular tool use actions were reflected in the patterns of grasping kinematics leading up to those movements.

For comparison, priming and kinematics were tested in a grasping task not requiring explicit access to functional knowledge of use; the grasp-to-move (GTM) task. Following the model of distinct parietal streams to action, I supposed that while the grasp-to-use (GTU) task would be carried out by the lateral-IPL stream, the GTM task would be carried out by the medial-SPL stream (Figure 1.3). Recall from Section 1.4.1, the medial parietal stream corresponds with the classic dorsal pathway described by Milner and Goodale (1995), tuned to object properties directly accessible to vision like size and shape, and not stored properties like identity and function. The medial stream provides fast efficient motor programming when access to stored object knowledge is unnecessary. Consistent with this basic scheme, Experiment 1 showed no evidence of priming for the GTM task, and grasping kinematics were similar for different tools (Figures 3.2-3.4). This clearly contrasted with results from the GTU task, where robust priming was evident and grasping kinematics were distinct for different tools. The findings were consistent with the model of separate underlying systems for grasping-to-use versus grasping-to-move (Daprati & Sirigu, 2006; Johnson & Grafton, 2003).

Separation between GTU versus GTM tasks was less evident when this experiment was repeated with both tasks presented in the same block of trials, in a mixed presentation setting (Experiment 2, section 3.3; Figures 3.5-3.7). Priming and thus sensitivity to tool identity was now revealed for the GTM task as well. As I have already discussed (section 5.1.1), separate underlying systems may still accommodate such findings, by either supposing a common pool of attentional resources, or by supposing that in the mixed setting one system took control of both tasks, namely the lateral-IPL system sensitive to tool identity. My results indicate that priming of real grasping is sensitive to task and task setting, both of which are likely to shape how target object features are attended, which in turn will determine affordances and priming. In my view, this was the clearest most important contribution of the study.

In light of these findings, several prior studies may have underestimated the importance of task-driven attentional factors. A number of studies have used words to show that grasping is sensitive to semantic processing even when such information is irrelevant to the grasping task. For example, Glover et al. (2004) showed that reading the names of familiar objects that varied in size (e.g. “apple” versus “grape”) just prior to grasping had a predictable impact on subsequent grip aperture measures, especially early on in the course of grasping. Similarly, a study by Gentilucci et al. (2000) showed that words printed on objects can influence grasping kinematics. When the word “far” versus “near” was present, participants made faster movements independent of actual object location (although the effects were more evident for the far object location). Since actually grasping more distant objects reliably leads to faster movements (Jeannerod, 1988), the findings were taken to indicate that word meaning had an implicit impact on movement programming. Movements were also slowed when word and actual object location were mismatched. The findings were extended to grip aperture measures, influenced accordingly by the words “small” versus “large”. In both studies (Gentilucci et al., 2000; Glover et al., 2004), even though word reading was irrelevant to grasping, word meaning had an impact on action programming. The findings were taken to suggest that information regarding object meaning is automatically taken into account when programming otherwise unrelated actions. However, I would suggest that reading itself necessarily requires orientation of attention to explicit declarative semantics. This may have inadvertently imposed a shift in the way actions were programmed. Different routes to action are evident from various patient findings (Rothi et al., 1997). Optic apraxic individuals can gesture to words and other verbal material describing tools, but cannot gesture to the visual appearance of those same tools. Conversely, optic aphasic individuals can gesture to visually presented tools, but can only name those tools if presented non-visually (e.g. via verbal description). When grasping unfolds in the context of reading words, participants may implicitly engage in a more semantic route to action programming than they would have engaged otherwise. This possibility may extend also to other modes of input, such as with auditorily conveyed object names as primes. In a task involving auditory priming of newly learned name-object associations, Kroliczak et al. (2006) found no evidence for priming with grasping but priming was evident for naming and perceptually based size estimations. Whether this kind of insensitivity to auditory-based priming of grasping with object names would hold with familiar objects is not clear. Certainly the findings of Glover et al. (2004) discussed above with written object names as primes would suggest otherwise.

Other studies, not with words, may have also underestimated how attention as a function of task could have influenced their findings. For example, Tucker and Ellis (1998; 2004) report automatic affordance effects when viewing pictures of familiar graspable objects, but in each case, the task required access to learned object semantics (upright versus inverted Tucker & Ellis, 1998; man-made versus natural object categorization Tucker & Ellis, 2004). Attention to semantics may have influenced task-set and mode of action programming, helping to drive affordance effects. Put differently, with action affordances and priming, cross-talk between semantic and action systems may be particularly sensitive to relatively subtle details of task and task setting.

Previous findings indicate that the action-state of an individual, or what I have referred to as goal-set, can influence the way object attributes are visually perceived (Humphreys et al., 2009). In my discussion in Chapter 3, I gave the example of a search task where differing effects of distractor attributes were observed according to the type of action subjects were asked to perform (Bekkering & Neggers, 2002). When asked to acquire target objects by grasping (versus pointing), participants made less erroneous saccades to distracters of the wrong orientation, as if attention to orientation as an object attribute was made more selective in accordance with goal-set. Affordances are tuned to and defined by object attributes. If goal-set modulates the saliency of object attributes, it follows naturally that goal-set will modulate affordances and priming, as my findings indicate. In a fascinating case study presented by Humphreys and Riddoch (2001), a patient with unilateral neglect was found to perform better in a search task when the target object was defined by its function ("find the object you could drink from") versus its name ("find the cup") or even a salient perceptual feature ("find the red object"). The goal-set of the patient influenced the detectability of visually presented objects. When the patient was in the state-of-mind to use an object, oriented towards its function, objects were more easily spotted. Further, these enhanced search effects were modulated by whether or not the handles of target objects were orientated toward or away from the patient; search was best when the handle faced toward the patient, as to make affordances for grasping more salient. Important for my main argument, these affordance effects were only evident when the search task was defined by function not by object name; further evidence of how goal-set determines the impact of object affordances. In other studies by this group (Humphreys & Riddoch, 2000; Riddoch, Humphreys, & Edwards, 2000) it was shown that impulsive erroneous grasping of objects in a patient with utilization behavior was not only dependent on the saliency of affordances, but also on the patient's goal-set as defined by the nature of the (action) task for which they were engaged. Together the findings fit with the main message of Project 2 – object affordances and priming depends on an interplay between task-defined action goals and corresponding attention-selection demands (see also Pavese, Coslett, Saffran, & Buxbaum, 2002).

To conclude, priming of grasping represents a relatively underexplored topic in cognitive behavioural science, and this is particularly true for grasping involving different goals and intentions. The importance of specific modality (e.g. visual vs. auditory), information content (e.g. structure vs. function), information format (e.g. words vs. pictures; pictures vs. real objects), timing between prime and probe events, and how these many factors may interact to modulate action priming is yet poorly understood. With functional grasping and tool use, it is of interest to determine if identity-based priming, as I have shown with Project 2, may extend to priming by way of functional associates (e.g. priming of grasping-to-use a peeler by the sight of a potato) or other kinds of conceptually based associations. New insights as to the types of information which best lead to priming will help constrain future models of tool use planning and execution. Such insights will also help explain patient findings in this area, which, as we have seen, often manifest as complex patterns of deficits and preserved functions (section 5.1.2). Also, continuing efforts to characterize detailed kinematics of movements alongside priming may uncover fundamental relationships between priming and motor programming. In my mind, this represents one of the more important lines of pursuit; does action priming actually reflect facilitation of motor plans at the level of programming specific kinematics?

5.2.2. Neural priming of tool use

At the neural level, object affordances translate to the activation of motor areas. Project 3 uses a novel fMRI priming paradigm to find evidence of motor activity underlying learned tool use by the visual appearance of tools. Vision of a particular tool is expected to activate corresponding motor plans for use, following my hypothesis of use-based affordances (section 1.4.3, Valyear et al., 2007). If after a short delay the same tool is shown again and used, motor programs supporting its use will have already been activated (primed) and overlapping neural processes will translate to better metabolic efficiency and reduced BOLD signal. If a different tool is shown for use, new motor programs will be activated, which lead to a relative increase in energy demands and resultant BOLD activity. This is the fundamental logic of the neural priming paradigm. Greater activity for Tool Changed (TC) versus Tool Repeated (TR) trials is predicted for areas involved in the recruitment and implementation of stored tool use plans.

We identified four distinct areas showing the predicted pattern of activity indicative of neural priming of tool use: left inferior parietal lobule (L-IPL), left dorsal precentral (L-dPreC), left ventral precentral (L-vPreC), and right superior parietal lobule (R-SPL) (Figure 4.2). Specificity of tool use priming in these areas was verified by comparison of priming with colour-defined actions and Control runs. If neural priming was driven by consistent versus inconsistent cuing of action plans in general, independent of familiar tool use, then greater activity is expected for Colour Changed (CC) versus Colour Repeated (CR) trials. Instead, only when actions were cued by tools, mapped onto learned tool-defined action plans, did neural priming in this parietofrontal circuit unfold. Selectivity for tool-action associations indicates specialization of these areas for learned tool use, and neural priming indicates experience-dependent plasticity. Specialization and procedural memory for tool use in left inferior parietofrontal cortex converges nicely with findings from both neuropsychology and neuroimaging studies of apraxia and tool use (Johnson-Frey, 2004). Schema theories posit that as tool use learning unfolds procedural memory representations are developed, specifying the spatiotemporal characteristics of skilled actions (see also section 5.3.1). That damage to left inferior parietal and/or frontal cortex often leads to selective impairments in these learned motoric aspects of tool use is taken as evidence that these areas normally represent a specialized repository for procedural memories underlying tool use (Buxbaum, 2001; Heilman, Rothi, & Valenstein, 1982; Rothi et al., 1997). My findings coincide nicely with these schema theories. Keeping with the focus of affordances, neural priming also indicates that the visual properties of tools are tightly coupled with stored action programs, presumably as these procedural representations are built-up and shaped through experience. Established connections ultimately translate visual recognition of tools to partial activation of corresponding motor plans for use, even in the absence of overt actions. In other words, neural priming reflects experience-dependent plasticity of parietofrontal representations underlying tool use; the emergence of visual response properties consistent with the hypothesis of use-based affordances.

What is the functional significance of such experience-dependent affordances; why would such a mechanism have evolved? In my view, visuomotor affordances are likely to represent a neural-behavioural adaptation designed to provide more efficient motor responses to overlearned and/or particularly important stimulus-action pairings. They provide a fast route from visual stimuli to the most likely of appropriate motor responses based on prior experience. It is easy to appreciate how such a mechanism could offer a survival advantage. For example, monkeys learn to associate the visual appearance of threatening stimuli, like the sight of a snake, with a powerful fear-avoidance response. Such behavior is not innate, but learned through experience (Schiller, 1952). Once learned, fast efficient triggering of appropriate action plans by way of visual-to-motor affordances would be an adaptive mechanism that would provide a clear survival advantage. In other words, affordance properties of motor-related neurons offer a 'short circuit' to appropriate learned behavioural outcomes. In humans, affordances for tools may reflect a hold-over of this natural tendency to link stimuli to their most commonly associated action plans at the neural level; it follows that mappings of tools-to-actions would correspond with conventional motor plans for use.

How might use-based affordances for tools be mediated at the neural level? In the General Introduction I provided coverage of the neurophysiology of both grasping and tool use in monkeys (section 1.3). Within the neural circuitry underlying the control of grasping, (anterior intraparietal area AIP and ventral premotor area F5), the response properties of canonical neurons offer a mechanism for which motor affordances tied to structural object properties may be instantiated (Jeannerod, Arbib, Rizzolatti, & Sakata, 1995). Visual responses code object size, shape, and orientation in alignment with corresponding motor requirements for grasping. At the same time, Iriki and colleagues report remarkable changes in the physiological properties of anterior intraparietal neurons after tool use training (Iriki & Sakura, 2008; Iriki et al., 1996). Tool use-based affordances could be mediated via the modification of canonical neurons. Tool use training could modify both the visual and motor response properties of neurons with canonical-like response features. If motor encoding was modified to represent learned procedural aspects of tool use, and visual responses aligned accordingly, tool use-based affordances would be supported. Unfortunately, to my knowledge, direct comparisons between tool-use modified and canonical neurons for grasping in AIP have not been reported. Notably, alongside changes in the receptive field properties of bimodal neurons in anterior IPS, tool use training was also found to induce visual responses in other neurons previously unimodal prior to training (discussed most thoroughly in Hihara et al., 2006, p. 2637). Such dramatic examples of training-induced neural plasticity suggest that modification of canonical neuron response properties in AIP is possible. Also noteworthy, when Ishibashi et al. (2000) tested tool trained monkeys with novel objects that were very different in shape to that of the rake (e.g. spherical objects), monkeys never attempted to use these novel objects to try and retrieve out-of-reach food rewards. In contrast, when presented with novel rake-like objects, similar in basic shape but different in colour and physical dimensions from that which had been used for training, after only brief hesitation monkeys proceeded to use these new rakes with success. Thus, monkeys learned to selectively associate the visual appearance of rake objects with the act of retrieving food items. Interestingly, movements with new rakes were somewhat clumsy, as if, as the authors had suggested, monkeys failed to adjust for differences in rake lengths and weight distributions. Instead, they appeared to implement the exact same motor outputs as they had learned with the trained rake. This suggests a very tight correspondence between the visual appearance of rakes and the stored kinematic programs defined during training. Although speculative, such correspondence could be conveyed via modified canonical neuron mechanisms, transforming visual features of tools to learned motor plans for use.

In Chapter 4, I provide two complementary accounts of parietofrontal selectivity of neural priming for tool use. My first hypothesis highlights the relative strength of tool-action associations. Such pairings are built up over the life span, with relatively continuous reinforcement, not only through the performance of actual actions with tools, but also through the observation of others using tools, and through the gradual development of conceptual knowledge stores about tools and tool use actions. Conversely, Control actions involve newly learned colour-action pairings, with no correspondence to associations that occur in real life. My second hypothesis relates to the ecological importance of common tool-action pairings. Tools are used to achieve specific goals, real world aims with meaningful outcomes. Recent evidence implicate inferior parietofrontal regions as coding the goals and outcomes of actions, rather than specific motor mechanisms, such as the particular effectors or kinematics used to achieve those goals (Andersen & Buneo, 2002; Bonini et al., 2010; Fogassi et al., 2005; Hamilton &

Grafton, 2008; Umilta et al., 2008). Action associations that coincide with ecologically valid behavioural outcomes may be a prerequisite to lasting encoding within parietofrontal areas. Again, this contrasts with arbitrarily assigned colour-action pairings, which are not routinely matched with real world goals outside the confines of our particular experiment. To perform our Control task participants were likely to have only kept colour-action rules in mind temporarily. The particular pattern and distribution of neural priming effects for colour-action associations and Control runs is likely to reflect such a strategy. Specifically, I hypothesized that activity within left ventral premotor cortex may reflect rehearsal and maintenance of colour-defined rules, while concurrent effects in early visual areas may relate more directly with distinguishing between different handle colours (as consistent with findings from Mohr, Goebel, & Linden, 2006; Yee, Roe, & Courtney, 2010). In contrast, extensive experience and continuous reinforcement paired with true ecologically meaningful outcomes together may comprise the key features underlying specificity of neural priming for tool use within the parietofrontal areas identified.

Lastly, my findings in Project 3 appear to have important implications for future patient rehabilitation programs. Bozeat and colleagues (2004; 2002) studied a patient with semantic dementia who was unable to use many common objects following loss of object conceptual knowledge and meaning. However, the patient showed dramatic improvements in object use following repeated exposure to the same object exemplars (Bozeat et al., 2002), and, in a second study with a new set of tools, similar improvements in tool use were observed after a simple training program was implemented involving brief demonstration of appropriate object use by an experimenter (Bozeat et al., 2004). Tool use learning was thought to indicate that “repeated use of a specific object establishes a set of automatic, stereotyped responses that are triggered by that particular object without activation of, or reliance on, general semantic knowledge” (Bozeat et al., 2004, p. 353). The authors stressed that this learning corresponds with learning at the level of procedural memory representations. Such an account overlaps remarkably well with my own conception of what use-based affordances for tools in parietofrontal areas are likely to represent. The author’s note that after four weeks from training, the patient’s performance shows some regression, and emphasize that with regular reinforcement and practice rehabilitation would likely be lasting, and perhaps even permanent. They conclude that such a training program “may provide a rare opportunity for improvement in the face of this progressive disease: a glimmer of hope while many other cognitive functions are deteriorating” (p. 362). If the neural mechanism of such learning and recovery were to map onto use-based affordances as represented within parietofrontal areas, tracking the emergence of neural priming effects with a longitudinal fMRI approach as healthy individual learn the use of novel tools would provide a powerful template for which to guide rehabilitation strategies. Differences in the strength and/or onset of priming effects in accordance with difference in training strategies could be used as an index to predict the effectiveness of training strategies with patients. Testing of SD patients with a tool use fMRI priming paradigm such as the one I have designed in Project 3 may also be helpful. Indeed, a convergent behavioural training and fMRI approach may provide compelling evidence as to the neural basis of patient recovery with using tools after profound loss of conceptual knowledge and object meaning. Such a direction for this research would be of clear importance, not only in the sense of improving the daily lives of patients with SD, but also in its potential to reveal new insights as to the cortical mechanisms underlying tool use in the healthy brain.

5.3. Summary of neuroimaging findings

Figure 5.3 provides a schematic summary of the brain areas identified in Projects 1 and 3. Shown are those areas activated by my primary contrasts of interest. For Project 1, temporo-occipital areas were preferentially activated for viewing tool grasping typical of use compared with grasping that was atypical of use. Activations were observed in both hemispheres, although more anterior lateral activations in posterior middle temporal gyrus and more inferior activity in fusiform cortex were specific to the left hemisphere. For Project 3, priming of tool use was identified within parietofrontal areas, mainly in the left hemisphere with right hemisphere activity exclusive to an area within SPL.

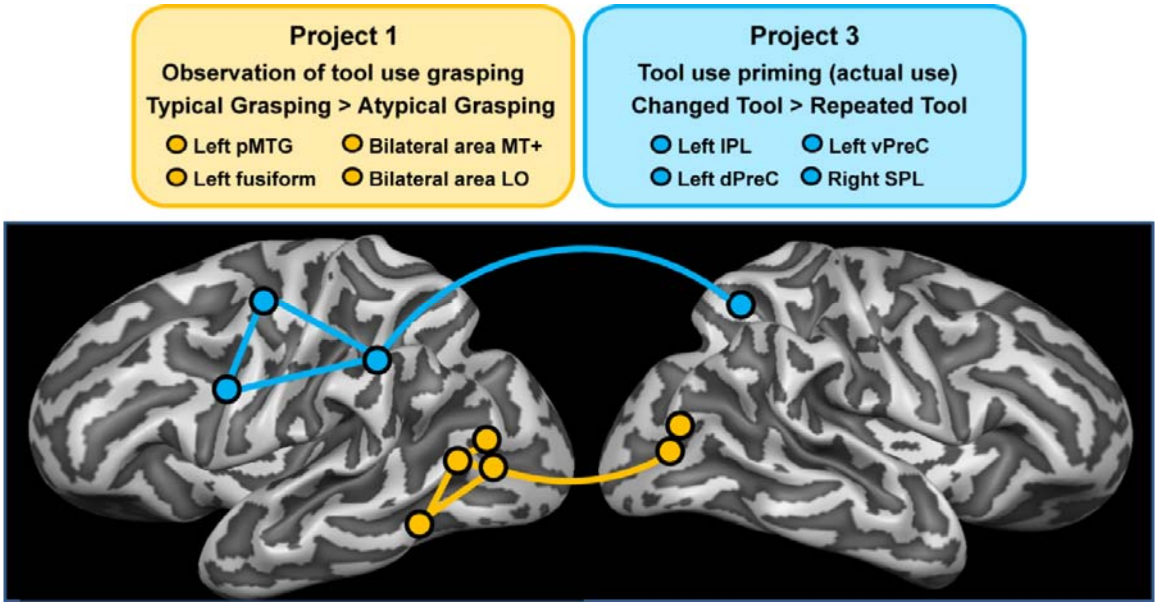

Figure 5.3. Summary of neuroimaging findings. Project 1 revealed preferential activity for viewing tool grasping actions typical of use (orange) in several distinct lateral temporo-occipital foci. Activity was seen to overlap with bilateral motion area MT+, and object area LO of the ventral visual pathway. The effects were more prominent in the left hemisphere, extending to include more lateral anterior cortex overlapping with posterior middle temporal gyrus and more inferior to include posterior mid-fusiform cortex. Project 3 revealed neural priming of tool use (blue) in left anterior intraparietal cortex, overlapping with inferior parietal lobule, left dorsal and ventral premotor areas within precentral cortex, and a single right hemisphere focus within intraparietal cortex overlapping with superior parietal lobule.

My summary of findings fits rather well with the results of a recent meta-analysis of tool-related neuroimaging results from 35 studies involving 64 paradigms (Lewis, 2006). In his summary, Lewis distinguished a “tool-use motor skill network” from a “conceptual and semantic network”. The motor skill network included critical nodes within SPL and IPL, dorsolateral premotor and ventral premotor cortices. The network was represented bilaterally but with clear left-hemisphere prevalence in the strength and extent of reported activations. Conversely, the conceptual tool network comprised left inferior frontal gyrus, left pMTG, and bilateral fusiform cortex. According to this organization, my findings from Project 1 overlap with the conceptual tool network while my findings from Project 3 overlap with the tool use production network.

This separation makes intuitive sense given that Project 3 involved the performance of real actions and thus may be expected to activate motor areas for tool use most strongly, while Project 1 involved passive viewing of tool-related action movies and thus may be expected to activate perceptual areas for tool use most strongly. However, as I have discussed at length throughout the thesis, learned tool use is thought to involve the integration of both stored motor and conceptual knowledge. Cooperation between ventral and parietofrontal areas is expected. Instead, the basic summary of my findings suggests separate systems, with little evidence of cooperation between them. Responses to observed tool use grasping showed preferential activity in ventral but not parietofrontal areas, while planning and carrying out real actions with tools showed activation priming in parietofrontal and not ventral stream areas.

In line with the distinctions emphasized by Lewis (2006), I suggest that this apparent disconnect between parietofrontal and ventral stream systems reflects: i) the particular paradigms I used to identify areas, and, more importantly, ii) the fundamentally different functional contributions of each system. The ventral stream is tuned to learned conceptual aspects of tools, sensitive to action viewing, uncovered by preferential activations for typical versus atypical tool use grasping. In contrast, parietofrontal areas are tuned to learned procedural aspects of tool use, untapped by neural priming of real familiar tool use actions. As I have elaborated on in section 5.1, these findings do not necessarily indicate that actual tool use does not involve ventral stream areas, or that conceptual knowledge of tools is unimportant when planning tool use actions. But rather, neural priming by repetition of tool identity in the context of real tool use may preferentially uncover parietofrontal contributions, as more intimately connected with motor plan retrieval and output. I suggest that further experiments are needed to clarify the importance of ventral stream regions and conceptual tool use knowledge.

In my General Introduction I reviewed evidence for a theory of divided parietal streams to action which separates a left lateral-IPL stream from a bilateral medial-SPL stream (section 1.4). The lateral-IPL pathway is connected with ventral stream areas and is thought to mediate learned aspects of tool use while the medial-SPL pathway is thought to mediate online visuomotor control. In concert with this basic distinction, schema theories of tool use propose a specialized role for left IPL in storage and recruitment of procedural memory representations underlying learned actions. In this section, I consider these concepts in light of my new findings.

5.3.1. Left inferior parietal specialization

Schema theory

Perhaps the single most important contribution of my thesis is that it provides compelling evidence of memory for tool use within parietofrontal areas. Given that neural priming was specific to tool use and did not also emerge for colour-defined actions, the most parsimonious explanation is that these effects operate at the level of memory for tool use. Activity in parietofrontal areas showing tool use priming is thought to reflect processing underlying retrieval of stored tool-specific action plans. Processing is made more efficient and neural priming unfolds when actions are preceded by information regarding the correct tool to be used. Neural priming in parietofrontal areas is not attributable to correct action cuing in general, or else similar BOLD reductions would have been detected for repeated colour trials for Control runs, where actions were cued by colour. Instead, priming effects were specific to tools and tool use actions. Such specificity is best accounted for as evidence for the activation of memory-based representations, shaped by extensive experience using tools.

These conclusions match closely with schema theories of tool use. Such accounts posit that procedural memories of learned actions are stored cortically. In the case of tool use, this encoding specifies how tools are used motorically. The origins of these ideas trace back to the work of Hugo Liepmann at the turn of the 20th century. For Liepmann, procedural memory stores for tool use, what he called “movement formula”, were thought to encode “knowledge of space-time sequences”, which specify the “course of the procedure to be realized” (Liepmann, 1980, p. 43). The central concept and importance of stored motor schema is nicely captured by the following statement from Rothi and colleagues (Rothi et al., 1997):

> To acquire skilled motor behaviour implies that the central nervous system stores information that the individual has previously experienced and that this stored information expedites future behaviour. Therefore, rather than portions of the process being reconstructed *de novo* with each experience, they may be called up from memory and reutilised. We use the term "processing-advantage" to describe the assistance provided by a system that can be called upon to reconstitute previously constructed programs (Rothi et al., 1997, p. 33).

That specificity of neural priming for tool-action and not colour-action pairings relates to experience-dependent plasticity intersects directly with this argument for stored motor schema. Only overlearned tool-action associations and not newly learned colour-action associations mapped onto stored programs in parietofrontal areas.

My findings identify a primarily left-lateralized circuit including left IPL, left inferior (L-vPreC) and superior lateral frontal (L-dPreC) activations centred within precentral cortex, and an area of activity within right SPL. That activity in left IPL corresponds with procedural memory stores underlying tool use is predicted from existing models of ideomotor apraxia (IM) that narrowly implicate left IPL as the cortical area underlying storage of tool use schema (Buxbaum, 2001; Heilman et al., 1982; Rothi et al., 1997). According to the model of Rothi et al. (1997), IM as a result of left inferior frontal damage reflects disrupted access to stored schema in left IPL. Functional connectivity between these two key areas is vital for praxis and learned tool use. Such a model nicely supports my interpretation of neural priming for tool use in these areas. I consider concurrent neural priming in L-dPreC and R-SPL as evidence for a more expansive interactive network important for retrieval and implementation of stored motor plans. The complete circuit overlaps with part of the tool use production network specified by Lewis (2006), commonly activated in tasks involving tool use pantomimed actions (Johnson-Frey, Newman-Norlund, & Grafton, 2005; Lewis et al., 2005) as well as real tool use (Inoue et al., 2001).

In a neuroimaging experiment involving tool use pantomimed actions, Johnson-Frey and colleagues (2005) were able to separate planning related activity from activity corresponding with actual motor outputs. Further, tool use plan-related activations were identified in individuals, which allowed for detailed characterization of function-anatomical correspondence. Activation peaks were most commonly observed within left supramarginal gyrus, and this was independent of which hand was used to perform upcoming actions. In contrast, tool use pantomime execution-related parietal activity was sensitive to which hand was used, and was distinctly more anterior to plan-related activity (see also Fridman et al., 2006). Tool use priming in L-IPL appears close to the location of plan-related activity from Johnson-Frey et al. (2005, left hand: x = -40, y = -43, z = 40, right hand: x = -40, y = -44, z = 39). Such correspondence is consistent with my interpretation of neural priming for tool use as directly related to the retrieval of stored tool use plans.

Finally, tool use priming activity in L-IPL was more anterior, ventral, and lateral to tool-selective activity identified in Project 1 with our “Localizer 1” paradigm (Figure 2.2D-E), as well as that revealed in our previous study (Valyear et al., 2007). More anterior-lateral activity for priming real tool use actions versus category selectivity for viewing tool pictures may reflect closer ties to motor stores. Recently, Stark and Zohary (2008) identified a posterior-to-anterior continuum of visual-to-motor response specificity in IPS during tool grasping, with more posterior areas tied to tools (and their location in the visual field) and more anterior areas tied to the hand used for grasping. More anterior lateral localization of neural priming in L-IPL may correspond with more motorically driven parietal areas, consistent with my account of this activity as related to recruitment and implementation of learned procedural schema for tools.

Divided parietal streams theory

According to several recent models of PPC in action, a laterally oriented pathway projecting to inferior parietal lobule (lateral-IPL stream) is specialized for tool use, distinguished from a medial pathway running through parieto-occipital cortex to superior parietal lobule (medial-SPL stream) devoted to basic online visuomotor control (section 1.4.1., Figure 1.3).

While tool use priming in left IPL is consistent with this model, my findings in Project 3 provide only partial support for this distinction between lateral and medial parietal streams to action. First, the model predicts concurrent effects in the ventral stream, which, as I have already discussed (section 5.1), was not observed; only non-specific task correlated activity was evident in ventral stream areas (Figure 5.1). Second, the model of separate parietal streams does not predict R-SPL specificity for tool use actions. Indeed, neural priming for tool use in R-SPL seems directly at odds with this account. I have considered that this activity somehow relates to spatial attention; that perhaps this area is important in the control of attention, and in the case of the tool use task participants preferentially attend not only to the area of space where tools are presented, but also to the upper part of this space in particular, so that tool identity can be recognized and distinguished. When tools are repeated, perhaps this process is made more efficient (e.g. shorter duration of underlying neural events) and BOLD activity is reduced. However, it is unclear why the same logic would not also apply to Control actions, where attention should then be preferentially directed to space where tool handles are presented, and repeated colour trials should afford the same reduced processing demands. I have also considered that perhaps this area somehow relates to the activation identified by Gallivan et al. (2009) who showed that right superior parieto-occipital cortex shows selectivity for objects in reachable space. This activity was thought to reflect processing related to encoding an object’s potential for action. However, the focus of activity found in that study was medial and posterior to the R-SPL activity I detected, and again it is unclear why such an account would only hold for Experimental actions. If R-SPL activity was related to processing an objects’ potential for action, why would priming show selectivity for the Experimental task only? Instead, I see no compelling reason why this R-SPL activity should be considered different from neural priming for tool use observed in left IPL, vPreC, and dPreC areas. Finally, and perhaps most relevant, my approach was one-sided with respect to the model in question; my aim was to identify areas underlying stored knowledge of tool use, not to also exploit regions more distinctly engaged in online visuomotor control. The purpose of my Control task was to provide a set of actions that were comparable in kinematic complexity and processing demands as compared with Experimental tool use actions. To test this particular model more directly, learned tool use should be compared with an action task requiring more precise or elaborate online control. While tool use should activate lateral-IPL areas, the more demanding online visuomotor task should activate medial-SPL areas. Such an experiment highlights the importance of continuing efforts to develop improved methods for tracking kinematics while in the scanner, alongside behavioural kinematic testing with mock-MR-scanner setups to closely mimic the unique constraints of the scanner environment.

Previous neuroimaging work has shown that pantomimed tool use activates left IPL independent of the hand used to perform actions (Bohlhalter et al., 2009; Johnson-Frey et al., 2005; Kroliczak & Frey, 2009). This contrasts with other actions like grasping, which typically show stronger anterior intraparietal (AIP) activity contralateral to the hand used to perform grasping (Begliomini, Nelini, Caria, Grodd, & Castiello, 2008; Culham, Cavina-Pratesi, & Singhal, 2006; Culham et al., 2001; Stark & Zohary, 2008). These findings have been taken as support for a variant of the divided parietal streams model whereby separate systems are thought to underlie object grasping versus tool use (section 1.4.1) (Daprati & Sirigu, 2006; Johnson & Grafton, 2003). Again, tool use is thought to correspond specifically with left inferior parietal areas. In Figure 5.4, I compared the location of tool use priming in L-IPL with an estimated location of grasping area AIP based on the average Talairach coordinates reported from eight published studies of grasping (see Figure caption). The area I detected showing tool use priming is distinctly lateral to the estimated location of AIP, consistent with the model of separate parietal systems for tool use versus grasping. However, partial overlap between areas is also evident, and this approach can only provide rough indication; further clarification is needed involving comparisons between grasping-defined and tool-use-defined activity in single subjects

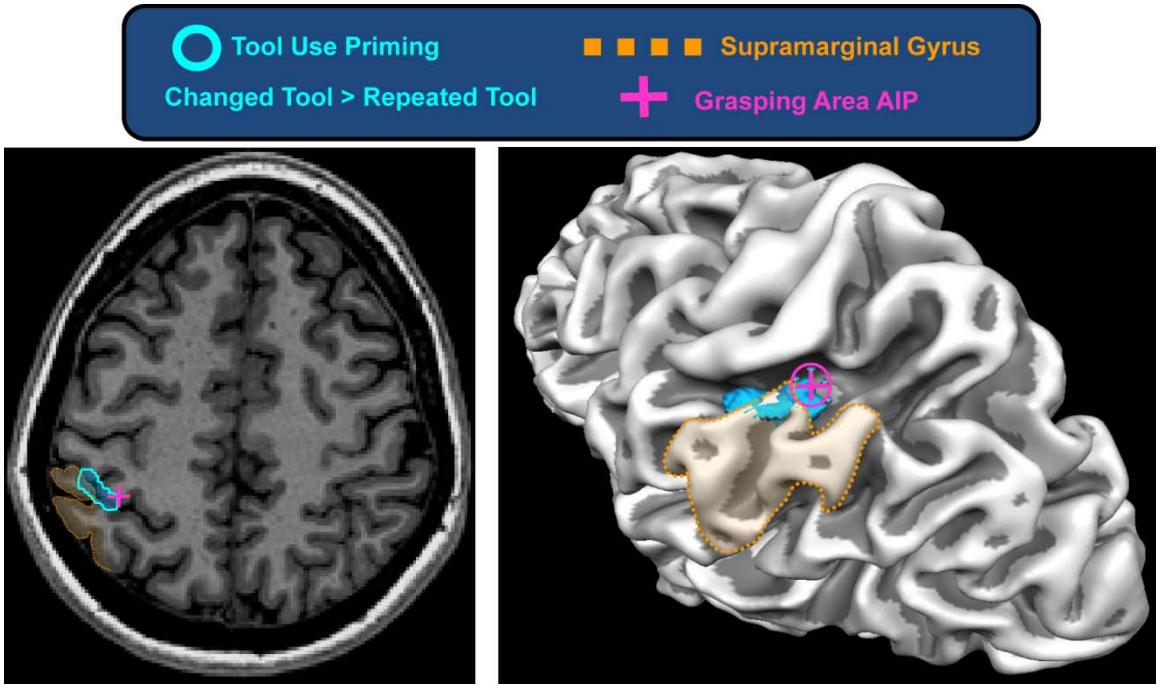

Figure 5.4. Comparison of grasping area AIP with tool use priming. Shown in cyan is the boundary of the L-IPL activation showing tool use priming in Project 3 (see Figure 4.2A). The pink crosshairs represent the mean Talairach coordinates of area AIP from eight published fMRI studies of real grasping (Begliomini, Caria, Grodd, & Castiello, 2007; Binkofski et al., 1998; Cavina-Pratesi, Goodale, & Culham, 2007; Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005; Grafton, Arbib, Fadiga, & Rizzolatti, 1996; Kroliczak, Cavina-Pratesi, Goodman, & Culham, 2007). The extents of the crosshairs represent 95% confidence intervals (x = -35 to -41, y = -37 to -45, z = 39 to 49) shown for posterior-anterior (x) and lateral-medial (y) directions.

Overlapping theories

Distinctions between lateral-IPL and medial-SPL systems directly intersect with schema theories of tool use. It is the stored aspects of left IPL that readily distinguish the functions of this system from SPL areas devoted to visuomotor control. Presumably, alongside this special role in stored action schema, the left IPL has unique ties to ventral stream areas. Such connections presumably offer an exchange between conceptual knowledge stores and procedural knowledge stores. While inputs from neural sources underlying conceptual knowledge provide a means to activate stored tool use plans, feedback connections allow procedural memory stores to enrich the content of conceptual knowledge stores. In contrast, SPL areas are supposedly tuned to dynamic aspects of action programming and control, thought to transform incoming sensory information to motor outputs from the bottom-up, *de novo*, and not based on stored representational knowledge. My findings show some consistency with these accounts; namely tool use priming within L-IPL and preferential activity within the ventral stream for observing typical versus atypical tool use grasping. However, distinct roles for medial-SPL versus lateral-IPL with respect to visuomotor control versus learned tool use require further clarification.

Worth noting, dexterous tool use requires both aspects - retrieval of stored action plans and dynamic visuomotor control mechanisms based on the situational specifics of a given action (Buxbaum, 2001). That is, for example, stored schema for hammering is not predicted to specify the particular kinematic or force requirements for a specific hammer, or for a given set of spatial constraints, but rather would only specify the gross ‘invariant’ movement features of hammering. Consider the act of pantomiming a hammering action without a hammer in hand. In this case, obviously only the basic invariant features of hammering would be called to action. It is these invariant features of learned actions that comprise procedural memory for tool use, generalizable across different tool exemplars, stored within left IPL. Real tool use requires additional computations related to dynamic features of actions and tools. Presumably such computations are carried out within the medial-SPL stream to action. It follows that real tool use must involve cooperation between lateral-IPL and medial-SPL streams[5].

Future imaging studies will hopefully find ways to test more and more natural tool use tasks, not only involving real tool manipulation but also actual interactions between tools and their recipients. According to the above account, the inclusion of more dynamic aspects of tool use is predicted to involve more medial-SPL systems. Close tracking of kinematic measures of actions while in the scanner will be important for analysis and interpretation of such experiments. A combined schema and divided parietal streams theory predicts that while the activation of medial-SPL areas should correlate with various kinematic measures, left lateral-IPL activity should correlate with tool use experience and procedural familiarity.

5.4. Future directions

Progress in research usually follows such that with every new insight, new unknowns are revealed. The current thesis is no exception. My findings make several new and important contributions, but also generate new hypotheses that require further clarification. I will conclude with a discussion of the most important areas of future research that follow directly from the current findings.

5.4.1. Linking behavioural and neural priming of tool use

I found that preceding tool use with a visual preview of the tool to be used leads to reliable behavioural priming, measured as shortened reaction times to initiate movements (Project 2). Time to movement onset is known to be a sensitive measure of action planning (Klatzky, Fikes, & Pellegrino, 1995; Rosenbaum, van Heugten, & Caldwell, 1996), and thus behavioural priming of tool use is taken to reflect facilitation of motor planning. I also found that preceding tool use with a visual preview of the tool to

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[5] Of course, many other areas including cerebellum, basal ganglia, premotor, supplementary, and primary motor cortices are also important for skilled action. In fact, even dynamic aspects of learned actions are likely stored as motor plans once sufficient skill is reached. For example, learned motor sequences may be partially stored in supplementary motor area (Watson et al., 1986), and dynamic internal models underlying the acquisition of novel tool use skills may be represented and stored in cerebellar cortex (Imamizu et al., 2000; 2003).

be used leads to reliable neural priming, measured as reduced BOLD activity (Project 3). Neural priming of tool use was specific to four distinct parietofrontal areas, including left inferior parietal cortex, previously implicated in the storage of learned tool use plans (Rothi et al., 1997). Neural priming was taken to reflect increased efficiency in the activation and implementation of such plans. Thus, my two sets of findings are complementary; behavioural priming reflects less time needed to plan actions while neural priming reflects less brain activity underlying action plan retrieval. Shortened temporal duration of neural firing has been hypothesized to account for BOLD priming effects (Grill-Spector, Henson, & Martin, 2006; James & Gauthier, 2006). It is possible that such a mechanism may underlie both behavioural and neural priming of tool use.

To make this connection stronger, behavioural and neural priming of tool use should be looked at concurrently, in the same experiment. At the moment, Project 3 shows neural priming of tool use independent of behavioural priming. Ideally, the same tool use actions should be compared inside and outside the scanner. Such comparison would allow for behavioural priming to be tracked at the neural level. Presumably the same brain areas identified in Project 3 would show neural priming, but would other areas also show effects? Further, would the strength of activation priming correspond with the strength of behavioural priming? With such an experiment in hand, new and important steps could be made toward understanding both behavioural and BOLD-based priming of tool use. It is possible that multiple mechanisms are at play, some which correspond with behavioural and kinematic differences in action planning, and some of which are independent of such.

In Project 2, I found behavioural priming for the grasping-to-move (GTM) task (Experiment 2; Figure 3.5) despite the fact that these actions involve similar kinematics according to different tools. Conversely, effects with the grasp-to-use (GTU) task were accompanied by robust differences in grasping according to tools. Participants took on a highly strategized approach that appeared to reflect an optimal path to grasping tools according to the next steps of actions. An fMRI version of this experiment would presumably reveal priming in the same areas showing tool use specific priming in Project 3. But, would the magnitude of BOLD priming according to task match that of behavioural priming? Would such correspondence be evident in all areas of this network, or only in specific areas? This experiment would help tease apart potential relationships between kinematic complexity of action programming, behavioural priming, and fMRI priming of grasping and tool use.

As follow-up study to Project 3, it would also be of interest to test tool-defined and colour-defined actions in the same runs. Would the same areas again show task-specific priming, and which brain areas would show activity changes selective for task switch periods? That is, with task cuing spaced far enough apart in time from action events, brain areas important for executive control may be separated from areas showing: i) stimulus (tool/colour)-specific priming, and ii) those more directly involved with action output.

Finally, conjoint behavioural and fMRI priming studies provide a powerful approach to address new questions. As noted previously, new insights into brain mechanisms underlying learned tool use may be gained by exploring the types of information that lead to behavioural priming. Contributions of conceptual knowledge stores to tool use planning may be addressed by testing for priming based on functional associative knowledge (e.g. testing if a potato or carrot primes the use of a vegetable peeler). Parallel fMRI priming experiments may reveal neural sources of conceptual content. Different modalities (e.g. auditory versus visual) and format (e.g. words/pictures versus real objects) of prime stimuli may also reveal distinct brain networks involved. Comparison with lesion studies of patients showing modality-specific tool use deficits (e.g. De Renzi, Faglioni, & Sorgato, 1982) would help validate existing models of tools use (e.g. Rothi et al., 1997) as well as inform new ones. With a better understanding of the multiple routes to learned action, perhaps new and improved patient rehabilitation programs could be developed, tailored to individual patient profiles according to which pathways are likely spared.

5.4.2. Procedural motor learning

My findings in Project 3 were taken to indicate activation of stored procedural representations for tool use. That is, tool use specific priming in parietofrontal areas was taken to indicate visually driven (primed) activations of use-dependent motor representations, what I have called use-based affordances. I have tried to indicate how evidence from neurophysiological studies of grasping and tool use in monkeys make this account feasible; anterior intraparietal neurons are modified following tool use training, and other presumably nearby neurons important for grasping show visual selectivity for particular object properties (affordances). Further, at least some of the areas showing priming, namely left inferior parietal and frontal cortex, correspond well with neuropsychological evidence which implicate these areas as critical to storage and implementation of learned tool use schema. Still, direct links between procedural motor learning and tool use priming are missing. How might such links be established?

Future studies will need to track motor learning of novel object-defined actions, using either behavioural-kinematic or force-kinematic measurements. A large enough set of new object-action (tool use) pairings must be established showing reliable, tractable patterns of behavioural changes throughout stages of procedural learning. Further, new tool use actions must be appropriate for fMRI. Procedural learning should be established behaviourally in a mock-MR setup, with the same subject configuration and space constraints as experienced in the scanner. Once behavioural measures of motor learning were established, transfer to fMRI can be used to track concurrent changes in brain activity.

Changes in brain areas underlying motor learning would be expected to correspond with changes in behavioural measures. Comparison between early and late instances of the same tool use actions could be used to demonstrate such changes. Areas overlapping with acquired motor skill would be expected to show preferential responses to late, more practiced trials, corresponding with robust levels of motor refinement. Conversely, areas important for the initial stages of tool use learning may show stronger activity to early, less practiced trials. An advantage of this approach is that it allows for comparisons between trials involving similar motor outputs (i.e. same actions). A disadvantage is that these trials are necessarily tied to different time periods within and across runs. Order effects not related to differences in tool use learning may superimpose on effects of interest. Fortunately, order effects related to novelty, task difficulty, attention, or non-specific habituation each predict that activation should decrease over time (i.e. early > late trials). Areas underlying procedural skills should show the opposite pattern (late > early trials). In particular, areas underlying storage of procedural tool use plans (e.g. left IPL), should show a shift to greater activity as tool use actions become more refined. Further, different tool use actions may be included that have different time courses of procedural learning. Tool-action pairings that take longer to acquire procedural expertise may be contrasted with pairings that are more quickly acquired. In this case, activity should correspond with stages of procedural learning rather than extent of previous exposure (early versus late). This would be a way to control for potential confounds due to order effects. Finally, if instances of common tool use were also included, then both early and late trials of these types should activate representations overlapping with stored tool use schema.

A priming version of this experiment is then simple to employ. Priming in parietofrontal areas identified in Project 3 is predicted only for well established object-action associations, after procedural learning had reached a robust level of sustained skilled performance.

It should be acknowledged that such an endeavour would not be easy. Establishing a novel tool use set that provides distinct and reliable behavioural markers of procedural motor learning would be a great challenge. Transfer to fMRI would require new advanced methods to track behavioural kinematics in the scanner; available, but uncommon to most MR units. Plasticity at the neural level may also take more than a single fMRI session to establish, requiring multiple sessions to identify. Still, if successful, the upshot of such a project would be of clear importance for future models of tool use, procedural motor learning, and experience-dependent cortical plasticity in general.

5.5. Conclusions

Together, the set of neuroimaging findings from Projects 1 and 3 highlight distinctions between systems important for tool use. Project 1 uses a perceptual task involving the viewing of actions and highlights temporo-occipital areas while Project 3 uses a real action task and highlights parietofrontal areas. Findings from Project 1 show sensitivity to learned object-action associations in perceptual but not visuomotor areas. Findings from Project 3 show the reverse pattern, activation priming for learned tool use in parietofrontal but not temporo-occipital areas. Differences are thought to reflect both the driving influence of task as well as distinct functional roles of each system.

Project 2 also indicates the importance of task; behavioural priming of grasping tools depended on both task and task setting. These effects were interpreted as changes in goal set and motor strategy, which in turn determined affordances and priming. Future progress in this area will benefit from a clearer understanding of the relationships between behavioural priming of tool use and actual motor programming (e.g. kinematics). As an imaging paradigm, the priming approach has clear advantages for studying the production of complex actions - good control over concerns about comparisons between actions that greatly differ in kinematics. Combined behavioural and fMRI action priming studies hold great promise for new discoveries in understanding human tool use.

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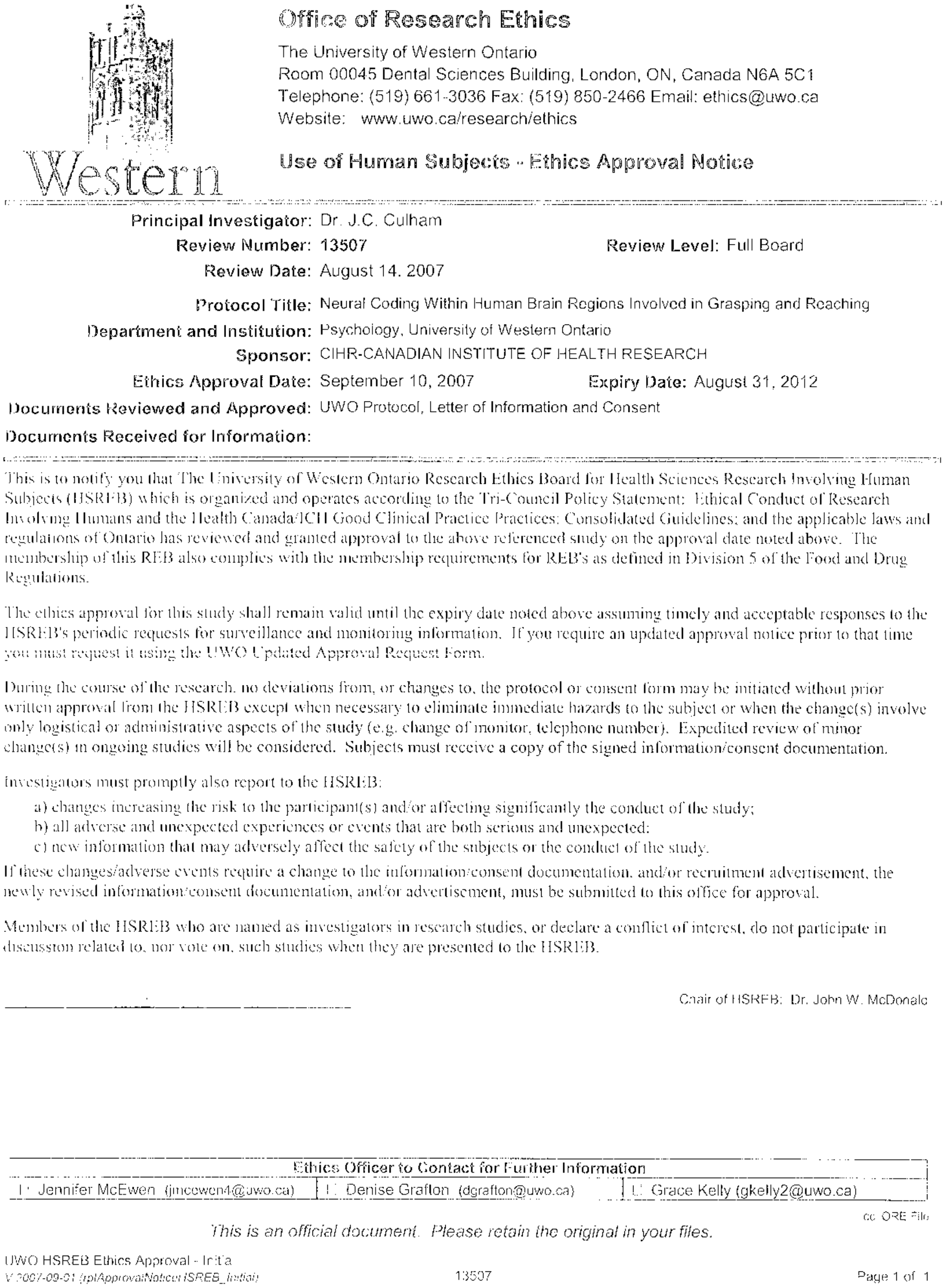
Appendix A



Office of Research Ethics
The University of Western Ontario
Room 00045 Dental Sciences Building, London, ON, Canada N6A 5C1
Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
Website: www.uwo.ca/research/ethics

Western

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. J.C. Culham
Review Number: 13507 **Review Level:** Full Board
Review Date: August 14, 2007
Protocol Title: Neural Coding Within Human Brain Regions Involved in Grasping and Reaching
Department and Institution: Psychology, University of Western Ontario
Sponsor: CIHR-CANADIAN INSTITUTE OF HEALTH RESEARCH
Ethics Approval Date: September 10, 2007 **Expiry Date:** August 31, 2012
Documents Reviewed and Approved: UWO Protocol, Letter of Information and Consent
Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB: Dr. John W. McDonald

Ethics Officer to Contact for Further Information		
☐ Jennifer McEwen (jmcewen4@uwo.ca)	☐ Denise Grafton (dgrafton@uwo.ca)	☐ Grace Kelly (gkelly2@uwo.ca)

cc: ORE File

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UWO HSREB Ethics Approval - Initial
V.2007-09-01 (rptApprovalNoticeHSREB_Initial) 13507 Page 1 of 1

13507

SECTION 1 PROJECT REGISTRATION

1.1a	Project Title
Neural Coding Within Human Brain Regions Involved in Grasping and Reaching	
1.1b	Sponsor or Agency Reference Number or Identifier if known.
Canadian Institutes of Health Research (CIHR) operating grant [MOP 84293]	

1.2	Is this a US Food and Drug Administration (FDA) monitored study?	YES	
		NO	X

1.3		**Start Date**	Sept. 1, 2007
		End Date	Aug. 31, 2012

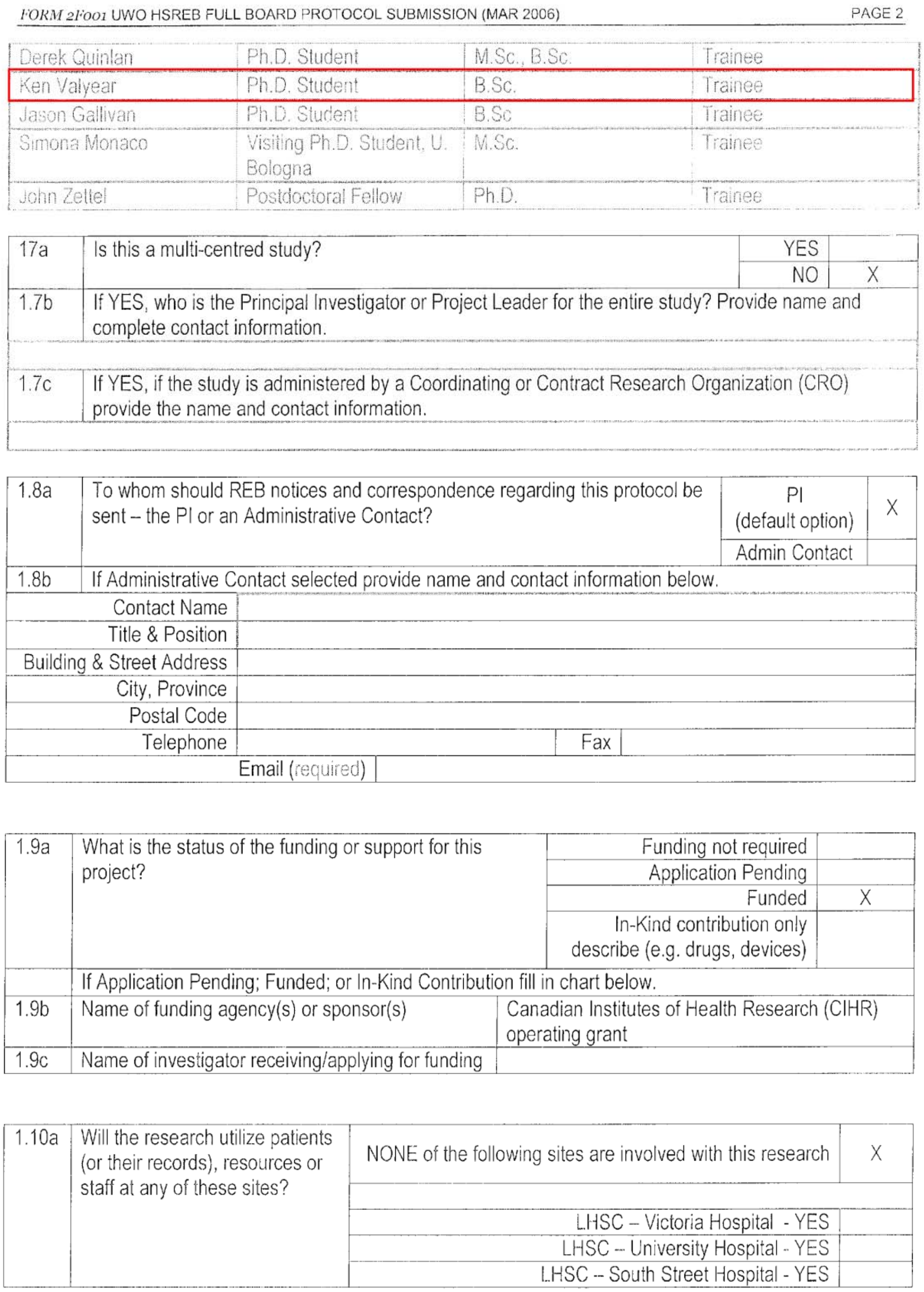
1.4	**Principal or Lead Investigator at this site.**
Name	Jody Culham
Title & Position	Associate Professor
Degrees	Ph.D., A.M., B.Sc.(Hon)
Departmental Affiliation	Department of Psychology
Mailing Address: Building & Street Address	Social Science Centre
Mailing Address: City, Province	London, ON
Mailing Address: Postal Code	N6A 3W8
Telephone	[redacted]
Email (required)	[redacted]

1.5	-- **Signature of Local Principal Investigator attesting that:**	Date:________________________

a) all co-investigators have reviewed the protocol contents and are in agreement with the protocol as submitted;
b) all investigators have read the Tri-Council Policy Statement: Ethical Conduct in Research Involving Humans and the UWO Guidelines on Health Sciences Research Involving Human Subjects and agree to abide by the guidelines therein;
c) the investigator(s) will adhere to the Protocol and Consent Form as approved by the REB;
d) the Principal Investigator will notify the REB of any changes or adverse events/experiences in a timely manner;
e) the study will not start until the contract/ agreement has been approved by the appropriate university, hospital or research institute official;
f) if the study is funded by Industry the investigators will adhere to the conditions described in Section 3.2: and
g) if external regulatory approval is required, the investigators will not start the study until all approvals are in place.

1.6 List all local co-investigators and collaborators. Include research personnel only if they have a significant role in the conduct of the study.

Name	Title/Position	Degrees	Role
Teresa McAdam	Research Technician	B.Sc.(Hon), B.P.H.E., MSc	Research Assistant



FORM 2F001 UWO HSREB FULL BOARD PROTOCOL SUBMISSION (MAR 2006) PAGE 2

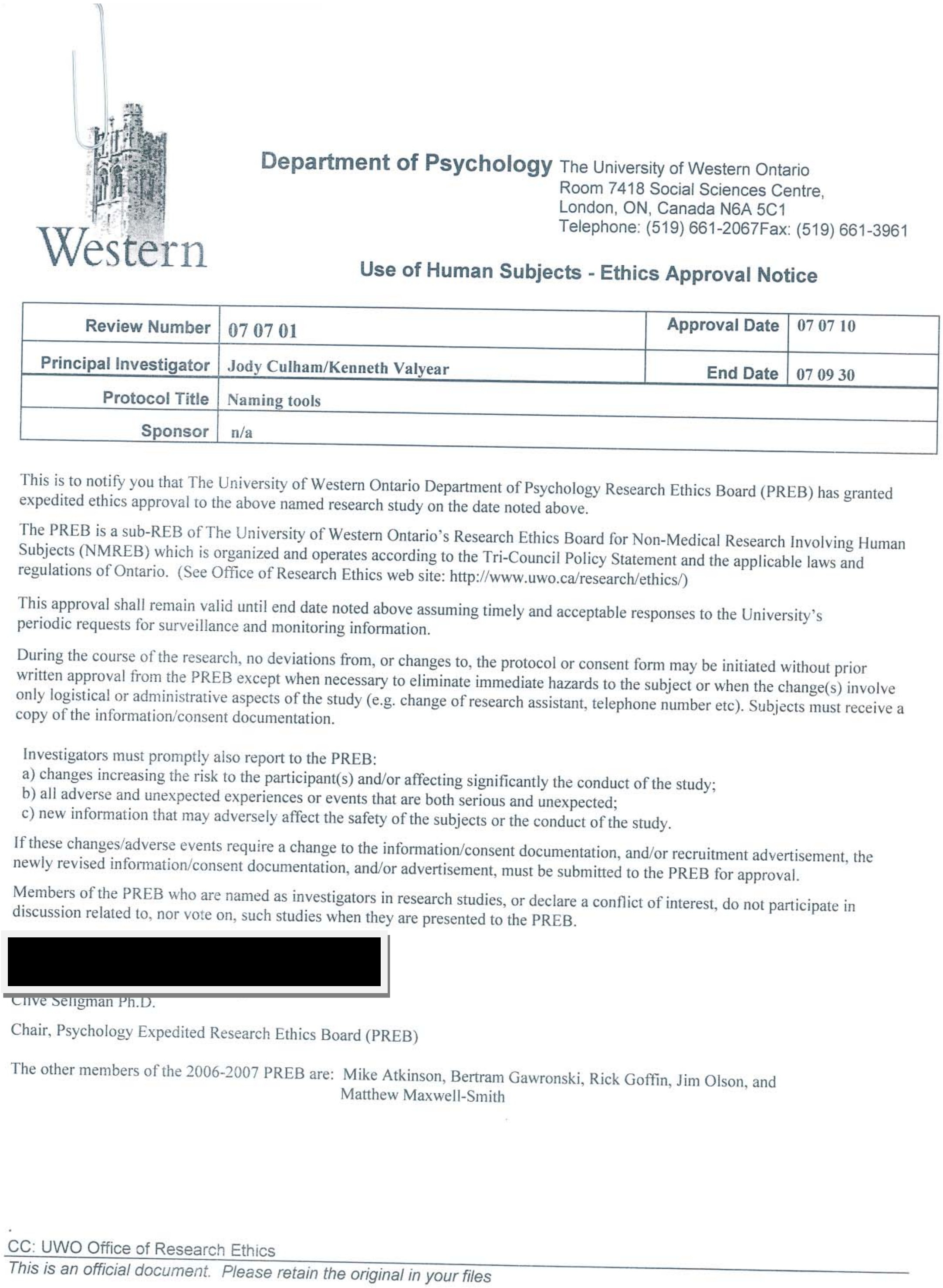
Derek Quinlan	Ph.D. Student	M.Sc., B.Sc.	Trainee
Ken Valyear	Ph.D. Student	B.Sc.	Trainee
Jason Gallivan	Ph.D. Student	B.Sc	Trainee
Simona Monaco	Visiting Ph.D. Student, U. Bologna	M.Sc.	Trainee
John Zettel	Postdoctoral Fellow	Ph.D.	Trainee

17a	Is this a multi-centred study?	YES	
		NO	X
1.7b	If YES, who is the Principal Investigator or Project Leader for the entire study? Provide name and complete contact information.		
1.7c	If YES, if the study is administered by a Coordinating or Contract Research Organization (CRO) provide the name and contact information.		

1.8a	To whom should REB notices and correspondence regarding this protocol be sent – the PI or an Administrative Contact?	PI (default option)	X
		Admin Contact	
1.8b	If Administrative Contact selected provide name and contact information below.		
Contact Name			
Title & Position			
Building & Street Address			
City, Province			
Postal Code			
Telephone		Fax	
Email (required)			

1.9a	What is the status of the funding or support for this project?	Funding not required	
		Application Pending	
		Funded	X
		In-Kind contribution only describe (e.g. drugs, devices)	
	If Application Pending; Funded; or In-Kind Contribution fill in chart below.		
1.9b	Name of funding agency(s) or sponsor(s)	Canadian Institutes of Health Research (CIHR) operating grant	
1.9c	Name of investigator receiving/applying for funding		

1.10a	Will the research utilize patients (or their records), resources or staff at any of these sites?	NONE of the following sites are involved with this research	X
		LHSC – Victoria Hospital - YES	
		LHSC – University Hospital - YES	
		LHSC – South Street Hospital - YES	



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Room 7418 Social Sciences Centre,
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Use of Human Subjects - Ethics Approval Notice

Review Number	07 07 01	**Approval Date**	07 07 10
Principal Investigator	Jody Culham/Kenneth Valyear	**End Date**	07 09 30
Protocol Title	Naming tools		
Sponsor	n/a		

This is to notify you that The University of Western Ontario Department of Psychology Research Ethics Board (PREB) has granted expedited ethics approval to the above named research study on the date noted above.

The PREB is a sub-REB of The University of Western Ontario's Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement and the applicable laws and regulations of Ontario. (See Office of Research Ethics web site: http://www.uwo.ca/research/ethics/)

This approval shall remain valid until end date noted above assuming timely and acceptable responses to the University's periodic requests for surveillance and monitoring information.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the PREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of research assistant, telephone number etc). Subjects must receive a copy of the information/consent documentation.

Investigators must promptly also report to the PREB:
a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to the PREB for approval.

Members of the PREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the PREB.

[redacted]

Clive Seligman Ph.D.

Chair, Psychology Expedited Research Ethics Board (PREB)

The other members of the 2006-2007 PREB are: Mike Atkinson, Bertram Gawronski, Rick Goffin, Jim Olson, and Matthew Maxwell-Smith

CC: UWO Office of Research Ethics

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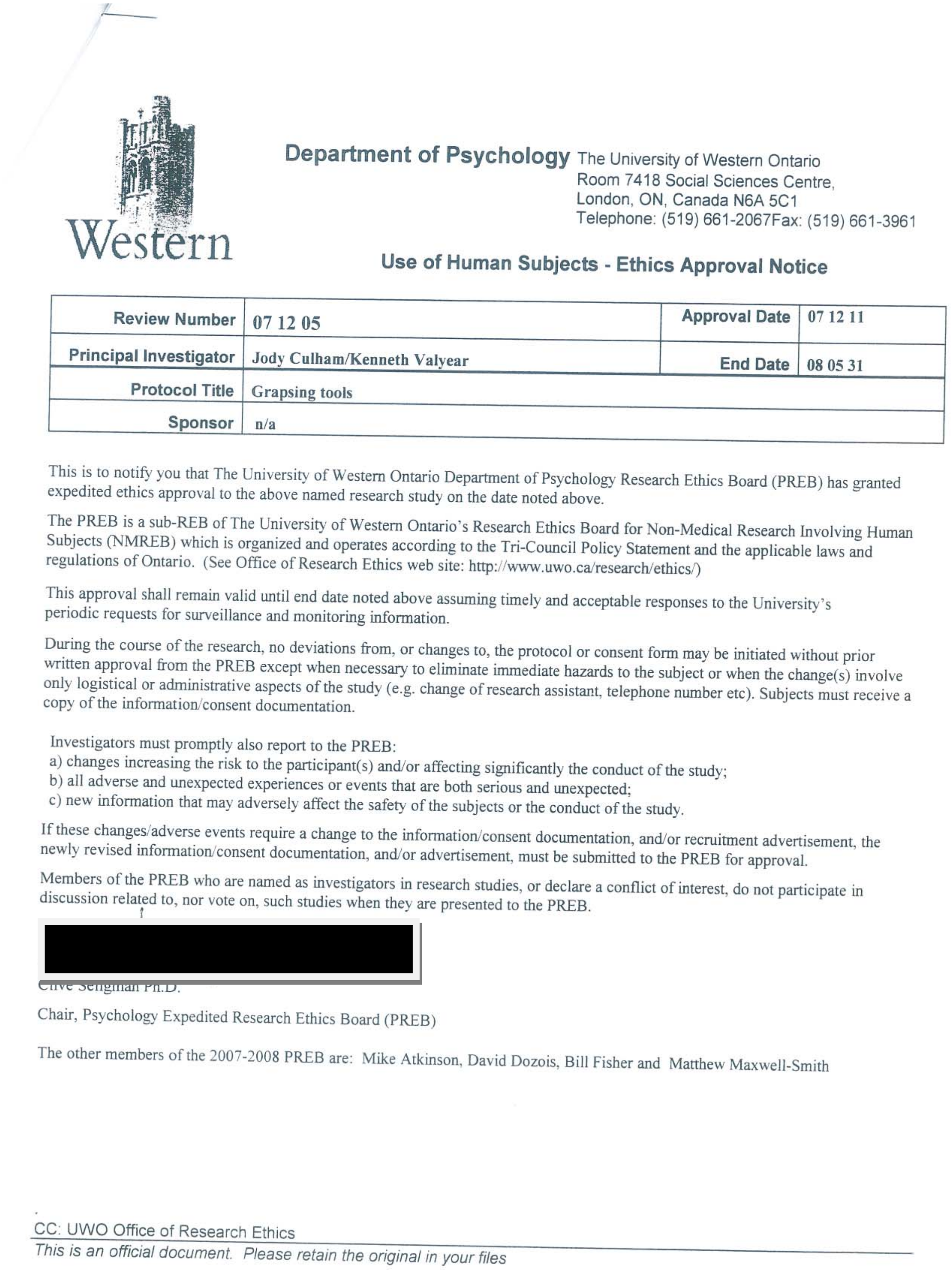

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Use of Human Subjects - Ethics Approval Notice

Review Number	07 12 05	**Approval Date**	07 12 11
Principal Investigator	Jody Culham/Kenneth Valyear	**End Date**	08 05 31
Protocol Title	Grapsing tools		
Sponsor	n/a		

This is to notify you that The University of Western Ontario Department of Psychology Research Ethics Board (PREB) has granted expedited ethics approval to the above named research study on the date noted above.

The PREB is a sub-REB of The University of Western Ontario's Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement and the applicable laws and regulations of Ontario. (See Office of Research Ethics web site: http://www.uwo.ca/research/ethics/)

This approval shall remain valid until end date noted above assuming timely and acceptable responses to the University's periodic requests for surveillance and monitoring information.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the PREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of research assistant, telephone number etc). Subjects must receive a copy of the information/consent documentation.

Investigators must promptly also report to the PREB:
a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to the PREB for approval.

Members of the PREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the PREB.

[redacted]

Chair, Psychology Expedited Research Ethics Board (PREB)

The other members of the 2007-2008 PREB are: Mike Atkinson, David Dozois, Bill Fisher and Matthew Maxwell-Smith

CC: UWO Office of Research Ethics

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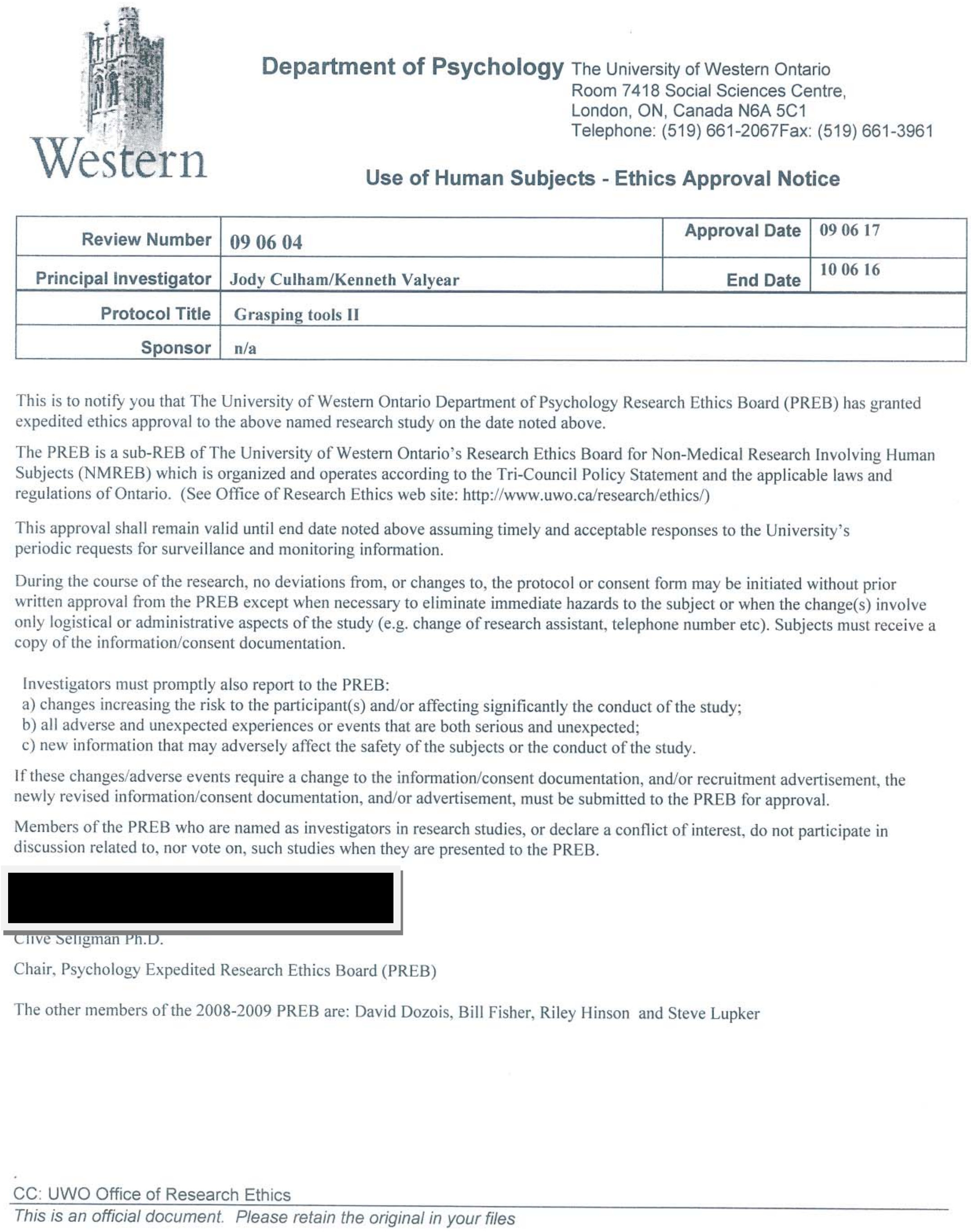

Western

Department of Psychology The University of Western Ontario
Room 7418 Social Sciences Centre,
London, ON, Canada N6A 5C1
Telephone: (519) 661-2067Fax: (519) 661-3961

Use of Human Subjects - Ethics Approval Notice

Review Number	09 06 04	**Approval Date**	09 06 17
Principal Investigator	Jody Culham/Kenneth Valyear	**End Date**	10 06 16
Protocol Title	Grasping tools II		
Sponsor	n/a		

This is to notify you that The University of Western Ontario Department of Psychology Research Ethics Board (PREB) has granted expedited ethics approval to the above named research study on the date noted above.

The PREB is a sub-REB of The University of Western Ontario's Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement and the applicable laws and regulations of Ontario. (See Office of Research Ethics web site: http://www.uwo.ca/research/ethics/)

This approval shall remain valid until end date noted above assuming timely and acceptable responses to the University's periodic requests for surveillance and monitoring information.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the PREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of research assistant, telephone number etc). Subjects must receive a copy of the information/consent documentation.

Investigators must promptly also report to the PREB:
a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to the PREB for approval.

Members of the PREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the PREB.

[redacted]

Clive Seligman Ph.D.

Chair, Psychology Expedited Research Ethics Board (PREB)

The other members of the 2008-2009 PREB are: David Dozois, Bill Fisher, Riley Hinson and Steve Lupker

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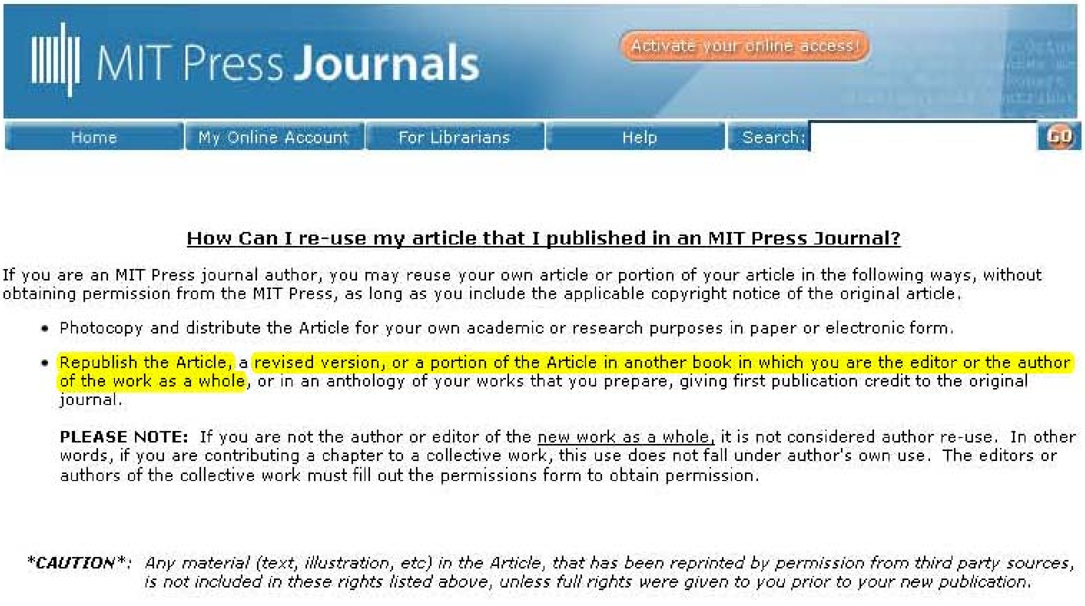
Appendix B



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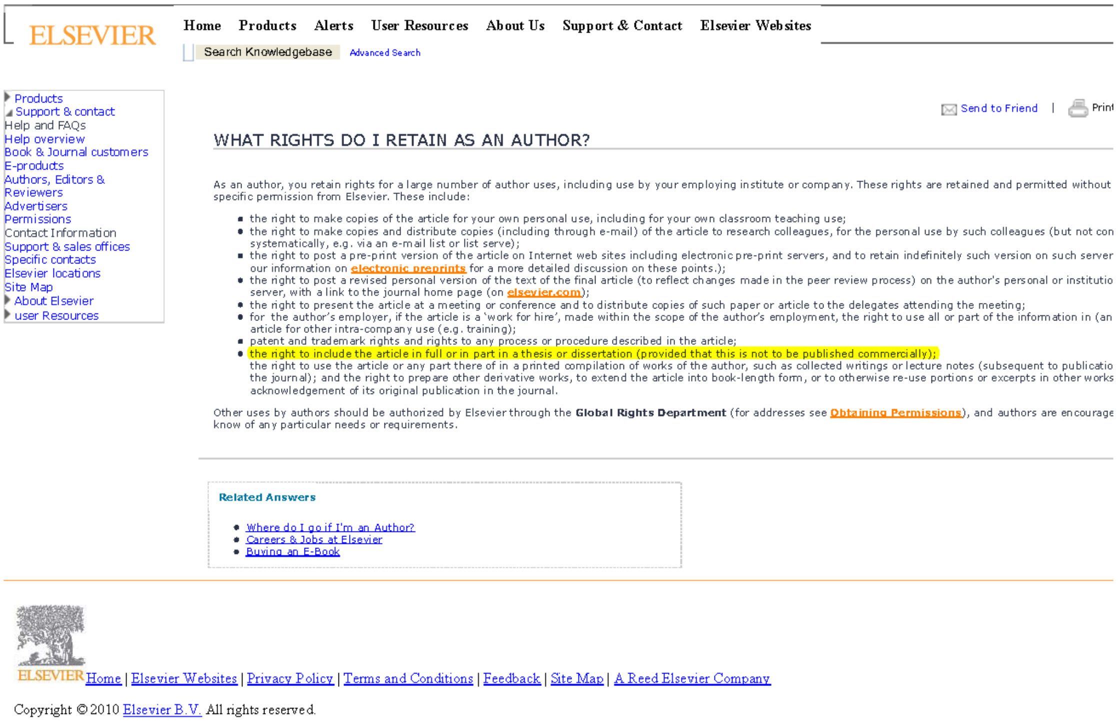

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CURRICULUM VITAE

KENNETH F VALYEAR

Ph.D. Candidate
Neuroscience Graduate Program
University of Western Ontario
London, Ontario CANADA N6A 5C2

Lab:
Fax:
Home:

E-mail:
WEB:

Date of Birth	November 28, 1978 (the Pas, Manitoba, Canada)
Citizenship:	Canadian

Research Interests: Cognitive neuroscience, fMRI, tool use, apraxia, action planning and control, action priming, motor affordances, parietal cortex, dorsal and ventral stream pathways

Publications (14): 12 empirical papers (3 first authorships); 1 review paper; 1 encyclopedia entry (detailed below).

Publication Impact:

Citation Count: 308 (October 2010, Web of Science, Valyear)
Average Citations per Item: 20.53
h-index: 9

Awards

Natural Sciences and Engineering Research Council (Canada), Canadian Postdoctoral Fellowship
University of Oregon, January 2011 – 2013
C$40000 per annum

Nellie Farthing Research Fellowship in the Medical Sciences, Schulich School of Medicine and Dentistry
University of Western Ontario, May 2009 – May 2010
C$3000 per annum

Natural Sciences and Engineering Research Council (Canada), Canadian Graduate Scholarship, Doctoral level
University of Western Ontario, May 2007 – May 2010
C$35000 per annum

Graduate Thesis Research Awards Fund, Western Internal Grants Competitions
University of Western Ontario, November 2008 – November 2009
C$500 per annum

G. Keith Humphrey Memorial Award
University of Western Ontario, May 2007 – May 2008
C$500 per annum

Natural Sciences and Engineering Research Council (Canada), Canadian Graduate Scholarship, Master's level
University of Western Ontario, May 2006 - May 2007
C$17500 per annum

Publications (14)

Valyear, K.F., and Culham, J.C. (2010). Observing learned object-specific functional grasps preferentially activates the ventral stream. *Journal of Cognitive Neuroscience*, **22/5**, 970-984. [Journal impact factor: 4.9; Citations: 3]

Malfait, N., **Valyear**, K.F., Culham, J.C., Anton, J., and Gribble, P.L. (2010). fMRI activation during observation of others' reach errors. *Journal of Cognitive Neuroscience*, 22/7, 1493-1503. [Journal impact factor: 4.9; Citations: 1]

Culham, J.C., and **Valyear**, K.F. (2009). Tool use. In B. Goldstein (Ed.) *Encyclopedia of Perception.* Thousand Oaks, CA: Sage.

Valyear, K.F., Cavina-Pratesi, C., Stiglick, A.J, and Culham, J.C. (2007). Does tool-related fMRI activity within the intraparietal sulcus reflect the plan to grasp? *NeuroImage*, **36**, T94 - T108. [Journal impact factor: 5.7; Citations: 16]

Rice, N.J., **Valyear**, K.F., Goodale, M.A., Milner, D.A., and Culham, J.C. (2007). Orientation sensitivity to graspable objects: An fMR adaptation study. *NeuroImage*, **36**, T87 - T93. [Journal impact factor: 5.7; Citations: 13]

Culham, J.C., and **Valyear**, K.F. (2006). Human parietal cortex in action. *Current Opinion in Neurobiology*, **16/2**, 205-212. [Journal impact factor: 8.1; Citations: 82]

Ganel, T., Gonzalez, C.L.R., **Valyear**, K.F., Culham, J.C., Goodale, M.A., and Köhler, S. (2006). The relationship between fMRI adaptation and repetition priming. *NeuroImage*, **32/3**, 1432-1440. [Journal impact factor: 5.7; Citations: 19]

Cavina-Pratesi, C., **Valyear**, K.F., Culham, J.C., Köhler, S., Obhi, S.S., Marzi, C.A., and Goodale, M.A. (2006). Dissociating arbitrary stimulus-response mapping from movement planning during preparatory period: Evidence from event-related fMRI. *Journal of Neuroscience*, **26/10**, 2704-2713. [Journal impact factor: 7.5; Citations: 32]

Steeves, J.K., Culham, J.C., Duchaine, B.C., Pratesi, C.C., **Valyear**, K.F., Schindler, I., Humphrey, G.K., Milner, A.D., and Goodale, M.A. (2006). The fusiform face area is not sufficient for face recognition: Evidence from a patient with dense prosopagnosia and no occipital face area. *Neuropsychologia*, **44/4**, 594-609. [Journal impact factor: 4.1; Citations: 40]

Valyear, K.F., Culham, J.C., Sharif, N., Westwood, D.A., and Goodale, M.A. (2006). A double dissociation between sensitivity to changes in object identity and orientation in the ventral and dorsal visual streams: A human fMRI study. *Neuropsychologia*, **44/2**, 218-228. [Journal impact factor: 4.1; Citations: 44]

Singhal, A., Kaufman, L., **Valyear**, K., and Culham J.C. (2006). fMRI reactivation of the human lateral occipital complex during delayed actions to remembered objects. *Visual Cognition*, **14(1)**, 122-125. [Journal impact factor: 1.5; Citations: 8]

Ganel, T., **Valyear**, K.F., Goshen-Gottstein, Y., and Goodale, M.A. (2005). The involvement of the “fusiform face area” in processing facial expression. *Neuropsychologia*, **43/11**, 1646-1654. [Journal impact factor: 4.1; Citations: 31]

Cant, J.S., Westwood, D.A., **Valyear,** K.F., and Goodale, M.A. (2005). No evidence for visuomotor priming in a visually guided action task. *Neuropsychologia*, **43/2**, 216-226. [Journal impact factor: 4.1; Citations: 14]

MacDougall-Shackleton, S.A., Hernandez, A.M., **Valyear**, K.F., and Clark, A.P. (2003). Photostimulation induces rapid growth of song-control brain regions in male and female chickadees (*Poecile atricapilla*). *Neuroscience Letters*, **340/3**, 165-168. [Journal impact factor: 2.2; Citations: 5]

Works Submitted/Under Revision (2)

Valyear, K.F., Chapman, C.S., Gallivan, J.P., Mark, R.S., and Culham, J.C. To use or to move: Goal set modulates priming when grasping real tools. Under review, October 2010.

Gallivan, J. P**.,** McLean, D.A., **Valyear**, K.F., Pettypiece, C., and Culham, J.C. Decoding action intentions from human preparatory brain activity. Submitted October 2010.

Academic and Research Training

January 2007 – present

Ph.D. in Neuroscience
Neuroscience Graduate Program,
University of Western Ontario

May 2006 – September 2006

Research Assistant
Motor Control Laboratory,
University of Western Ontario
Dr. Paul L. Gribble, Department of Psychology

August 2002 – December 2005

Functional Magnetic Resonance Imaging Research Technician
CIHR Group on Action and Perception,
University of Western Ontario
Drs. Jody C. Culham and Melvyn A. Goodale, Department of Psychology

May 2002 – August 2002

Research Assistant
Avian Biochemical Laboratory,
University of Western Ontario
Dr. Scott MacDougall-Shackleton, Department of Psychology

September 1998 – May 2002

Bachelor of Science in Physiology and Psychology, with High Distinction,
University of Western Ontario

Invited Talks (1)

Valyear, K.F. (July 2010). Priming of tool use, from kinematics to BOLD. Invited talk at Durham University, UK.

Conference Presentations (25)

Valyear, K. F., Gallivan, J.P., McLean, A., Chapman, C.S., Culham, J.C. (November 2010). Neural priming of tool use. Poster to be given at the annual meeting of the *Society for Neuroscience*, San Diego, California.

Gallivan, J.P., McLean, A., **Valyear**, K. F., Chapman, C.S., Culham, J.C. (November 2010). Decoding movement intentions from preparatory activity in human parietal and premotor cortex. Talk to be given at the annual meeting of the *Society for Neuroscience*, San Diego, California.

Valyear, K. F., Chapman, C.S., Gallivan, J.P., Culham, J.C. (October 2009). Tool identity can prime grasping, but only when the goal is to use. Talk given at the annual meeting of the *Society for Neuroscience*, Chicago, IL.

Culham, J. C., & **Valyear**, K. F. (July 2008). Neuroimaging investigations of tool-selective regions in the human dorsal and ventral streams. Talk given at the *Asia Pacific Conference on Vision*, Brisbane, Australia.

Culham, J.C., Witt, J.K., **Valyear**, K.F., Dutton, G.N., and Goodale, M.A. (May 2008). Preserved processing of motion and dorsal stream functions in a patient with large bilateral lesions of occipito-temporal cortex. Talk given at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Valyear, K.F., Witt, J.K., Goodale, M.A., and Culham, J.C. (November 2008). Activation for viewing meaningful and meaningless tool actions in a patient with large bilateral lesions of occipito-temporal cortex. Poster presented at the annual meeting of the *Society for Neuroscience*, Washington, DC.

Malfait, N., **Valyear**, K.F., Culham, J.C., Brown, L.E., Anton, J-L, and Gribble, P.L. (November 2008). fMRI activation during observation of others' reach errors. Poster presented at the annual meeting of the *Society for Neuroscience*, Washington, DC.

Valyear, K.F., and Culham, J.C. (May 2007). Grasping the function of tools: fMRI suggests that the ventral but not the dorsal stream codes the functional significance of objects. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Valyear, K.F., and Culham, J.C. (May 2007). Grasping the function of tools: fMRI suggests that the ventral but not the dorsal stream codes the functional significance of objects. Poster presented at the annual meeting of the *Canadian Association for Neuroscience*, Toronto, Ontario.

Valyear, K.F., Cavina-Pratesi, C., Stiglick, A.J, and Culham, J.C. (May 2006). Tool-related activity in parietal cortex does not reflect the plan to grasp. Poster presented at the *Symposium on Cortical Control of Higher Motor Cognition*, Lubeck, Germany.

Chang, E.C., Hampson, E., **Valyear**, K.F., and Goodale, M.A. (May 2006). Sex differences in the neural substrates of manual praxis. Poster presented at the *Symposium on Cortical Control of Higher Motor Cognition*, Lubeck, Germany.

Steeves, J.K., Cant, J.S., **Valyear**, K.F., Démonet, J.F., Kentridge, B., Heywood, C., and Goodale, M.A. (May 2006). Seeing the forest but not the trees: Spared categorization and functional activation for scenes in patients with object agnosia. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Singhal, A., **Valyear**, K. F., and Culham, J. C. (June 2005). Distinguishing between delayed actions and the termination of action preparation. Poster presented at the annual *Organization for Human Brain Mapping*, Toronto, Ontario.

Singhal, A., Kaufman, L., **Valyear**, K.F., and Culham, J.C. (November 2005). fMRI reactivation of the human lateral occipital complex during delayed actions to remembered objects. Talk given at the *Annual Workshop on Object Perception and Memory*, Toronto, Ontario.

Ganel, T., **Valyear**, K.F., Goshen-Gottstein, Y., and Goodale, M.A. (August 2004). The involvement of the "fusiform face area" in processing facial expression. Poster presented at the *27th Annual Meeting of the European Conference on Visual Perception (ECVP)*, Budapest, Hungary.

Valyear, K.F., Westwood, D.A., Sharif, N., Cant, J.S., and Goodale, M.A. (May 2004). Differential fMRI adaptation for object identity and orientation in the ventral and dorsal streams. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Culham, J.C., **Valyear**, K.F., and Stiglick, A.J. (May 2004). fMRI activation in grasp-related regions during naming of tools and other graspable objects. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Cant, J.S., **Valyear**, K.F., and Goodale, M.A. (May 2004). ‘Stuff’ versus ‘things’: Neural processing of the material properties and geometric form of objects in human visual pathways. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Ganel, T., **Valyear**, K.F., Goshen-Goshen, Y., and Goodale, M.A. (May 2004). Greater fMRI activation in the “fusiform face area” for the processing of expression than the processing of identity: Implications for face-recognition models. Talk given at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Cant, J.S., **Valyear**, K.F., and Goodale, M.A. (April 2004). ‘Stuff’ versus ‘things’: Neural processing of the material properties and geometric form of objects in human visual pathways. Talk given at *Epilepsy Research Day* workshop, University of Western Ontario, London, Ontario.

Valyear, K.F., Culham, J.C., and Goodale, M.A. (April 2004). The use of fMRI adaptation to dissociate visual processing of object orientation and form in the dorsal and ventral pathways. Poster presented at *Computational Neuroimaging: Adaptation & Priming* conference, University of Minnesota, Minneapolis, Minnesota.

Pratesi, C.C., **Valyear**, K.F., Obhi, S.S., Brown, M., Marzi, C.A., and Goodale, M.A. (October 2004). Neural correlates of preparatory set: Response selection versus movement planning. Poster presented at the annual meeting of the *Society for Neuroscience*, San Diego, California.

Cant, J.S., Westwood, D.A, **Valyear**, K.F., and Goodale, M.A. (May 2003). No evidence for visuomotor priming in a visually guided action task. Poster presented at the annual meeting of the *Vision Sciences Society*, Sarasota, Florida.

Cant, J.S., Westwood, D.A., **Valyear**, K.F., and Goodale, M.A. (April 2003). No evidence for visuomotor priming in a visually guided action task. Poster presented at the *Southern Ontario Neuroscience Association*, University of Western Ontario, London, Ontario.

Cant, J.S., **Valyear**, K.F., and Goodale, M.A. (March 2003). The role of early visual processing in the control and execution of arm and hand movements. Invited research talk given at *'Metaphysics of Mind and Language'* Graduate Conference in Philosophy of Mind, University of Western Ontario, London, Ontario.

Teaching

Teaching Assistant – **Neuroimaging of Cognition**. Graduate level psychology course, University of Western Ontario (January 1 – April 30, 2007).

fMRI Brian Imaging Data Analysis and Design Concepts Workshop. Dalhousie University, Halifax, CANADA. (May 26-27, 2005).

Reviewer Contributions

Ad hoc reviewer of submitted manuscripts: *Advances in Cognitive Psychology* (1); *Brain and Cognition* (1); *Cerebral Cortex* (1); *Experimental Brain Research* (1); *Journal of Experimental Psychology: Human Perception and Performance* (1); *NeuroImage* (5); *Neuropsychologia* (1)

Ad hoc co-reviewer of submitted manuscripts: *Journal of Cognitive Neuroscience* (1); *Journal of Neuroscience* (2); *Nature* (1); *Nature Neuroscience* (1); *NeuroImage* (1)

Professional Affiliations

Member of the Society for Neuroscience
Member of the Vision Sciences Society
Member of the Organization for Human Brain Mapping

Youth Outreach and Community Service

Canadian Medical Hall of Fame/TD Discovery Day in Health Science (http://www.cdnmedhall.org/discoverydays/) – Co-supervised a hands-on workshop, entitled "correspondence between visual and motor systems in the control of visually-guided action", held May, 8, 2009.

London Ontario Brain Bee (http://www.uwomeds.com/ncog/main.php), in association with the Canadian Institutes of Health Research Canadian National Brain Bee (**http://www.science.mcmaster.ca/brainbee/**) – I led a demonstration on the basics of functional magnetic resonance imaging, held February 28, 2009.