CORTEX 56 (2014) 85–98

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Research report

# Structural network underlying visuospatial imagery in humans

Kevin Whittingstall [a,b,*], Michael Bernier [a,b], Jean-Christophe Houde [c], David Fortin [d] and Maxime Descoteaux [c]

[a] Department of Diagnostic Radiology, Faculty of Medicine and Health Science, Université de Sherbrooke, 12e Avenue Nord, Sherbrooke, QC, Canada J1H 5N4

[b] Sherbrooke Molecular Imaging Center, Department of Nuclear Medicine and Radiobiology, Faculty of Medicine and Health Science, Université de Sherbrooke, 12e Avenue Nord, Sherbrooke, QC, Canada J1H 5N4

[c] Computer Science department, Faculty of Science, Université de Sherbrooke, 2500 Boulevard Université, Sherbrooke, QC, Canada J1K 2R1

[d] Division of Neurosurgery and Neuro-Oncology, Faculty of Medicine and Health Science, Université de Sherbrooke, 12e Avenue Nord, Sherbrooke, QC, Canada, J1H 5N4

ARTICLE INFO

*Article history:*
Received 13 April 2012
Reviewed 10 August 2012
Revised 16 August 2012
Accepted 5 February 2013
Published online 17 February 2013

*Keywords:*
fMRI
Tractography
Visuospatial imagery
V1 deactivation

ABSTRACT

*Introduction:* Several neuroimaging studies have shown that visuospatial imagery is associated with a multitude of activation nodes spanning occipital, parietal, temporal and frontal brain areas. However, the anatomical connectivity profile linking these areas is not well understood. Specifically, it is unknown whether cortical areas activated during visuospatial imagery are directly connected to one another, or whether few act as hubs which facilitate indirect connections between distant sites. Addressing this is important since mental imagery tasks are commonly used in clinical settings to assess complex cognitive functions such as spatial orientation.

*Methods:* We recorded functional magnetic resonance imaging (fMRI) data while participants ($N = 18$) performed a visuospatial imagery task. In the same subjects, we acquired diffusion MRI (dMRI) and used state-of-the-art tractography robust to fiber crossings to reconstruct the white matter tracts linking the fMRI activation sites. For each pair of these sites, we then computed the fraction of subjects showing a connection between them.

*Results:* Robust fMRI activation was observed in cortical areas spanning the dorsal (extrastriate, parietal and prefrontal areas) and ventral (temporal and lingual areas) pathways, as well as moderate deactivation in striate visual cortex. In over 80% of subjects, striate cortex showed anatomical connectivity with extrastriate (medial occipital) and lingual (posterior cingulate cortex – PCC) sites with the latter showing divergent connections to ventral (parahippocampus) and dorsal (BA7) activation areas.

*Conclusion:* Our results demonstrate that posterior cingulate cortex is not only activated by visuospatial imagery, but also serves as an anatomical hub linking activity in occipital,

* *Corresponding author*. Université de Sherbrooke, Radiologie diagnostique, Faculté de médecine et des sciences de la santé, 3001, 12e Avenue Nord, Sherbrooke, Québec, Canada J1H 5N4.
E-mail address: kevin.whittingstall@usherbrooke.ca (K. Whittingstall).

http://dx.doi.org/10.1016/j.cortex.2013.02.004

parietal and temporal areas. This finding adds to the growing body of evidence pointing to PCC as a connector hub which may facilitate integration across widespread cortical areas.



## 1. Introduction

The brain is composed of anatomically distinct areas which are highly-interconnected via dense white matter (WM) tracts that form large-scale patterns of anatomical connectivity. This enables communication between neurons at widely separated locations, and thus directly relates to neurocognitive function (Catani and Ffytche, 2005). Therefore, interpreting function without structure is difficult, a fact that was quickly acknowledged by Brodmann, who stated in 1909: "*One thing must be stressed quite firmly: henceforth functional localization of the cerebral cortex without the lead of anatomy is utterly impossible in man as in animals… so, first anatomy, and then physiology; but if first physiology, then not without anatomy*" (Brodmann, 1909). Knowledge about how anatomical connectivity is related to function is essential to our understanding of information processing pathways, and how they may be modified in neurological disorders.

Until recently, information on brain function and structure was limited to studies in animal models. Developments in the field of magnetic resonance imaging (MRI) have now made it possible to non-invasively map the structural and functional organization of the human brain in-vivo. With functional MRI (fMRI), one can obtain high-resolution whole-brain images that represent the changes in cortical blood flow, volume and oxygen metabolism (so-called Blood-Oxygenation-Level-Dependent or BOLD signal) associated with 'active' brain tissue (Bandettini et al., 1993; Buxton, 2002; Kwong et al., 1992; Menon and Kim, 1999; Turner, 1992). Diffusion MRI (dMRI) captures the average diffusion of water molecules, which probes the structure of the biological tissues. The diffusion of water molecules is Brownian under normal unhindered conditions, but in fibrous structures such as WM, water molecules tend to diffuse along fibers rather than across them, reflecting the average orientation of neural tissue at the imaging voxel level (Descoteaux and Poupon, 2012). Hence, anisotropic diffusion is observed and can be reconstructed at every imaging voxel using diffusion tensor imaging (DTI) (Basser et al., 1994; Basser and Pierpaoli, 1996; Pierpaoli and Basser, 1996). However, DTI-based tractography cannot recover fiber crossing configurations due to modeling limitations of the diffusion tensor. Recent advances in high angular resolution diffusion imaging (HARDI) and corresponding improvements in local modeling techniques for HARDI (Descoteaux and Poupon, 2012; Seunarine and Alexander, 2009; Tournier et al., 2012) allow for robust estimation of the fiber crossing phenomenon in imaging voxels with complex fiber configurations, thus overcoming the limitations of DTI and allowing for more accurate tractography (Descoteaux et al., 2009; Tournier et al., 2012). Moreover, while traditional approaches performed fiber tracking from a limited number of regions in the brain, recent *connectomics* developments in dMRI tractography allows mapping of anatomical connections patterns between gray matter (GM) areas of multiple brain regions (Gong et al., 2009; Hagmann et al., 2007; Honey et al., 2007; Johansen-Berg and Behrens, 2006).

Combining fMRI with dMRI thus provides a unique approach for investigating the structural architecture linking areas which are functionally active during cognitive processing. The use of fMRI-guided dMRI is advantageous since regions of interests (ROIs) can be directly derived from activation maps in individual subjects as opposed to using an anatomical atlas which may not take into account the structural variability from individual to individual. For example, several neuroimaging studies have demonstrated that mental imagery (perception in the absence of retinal input) evokes activity in widespread cortical areas spanning occipital, temporal, parietal and frontal lobes [see Sack and Schuhmann (2012) and references therein]. However, the anatomical network which inter-connects these activation sites is unknown. That is, do sites in visual cortex make direct connections with the rest of the brain, or are some sites indirectly linked? A better understanding of the anatomical structure which facilitates mental imagery is important since such tasks are often used for communicating with patients who are conscious yet non-responsive (Owen et al., 2006). Indeed, it has been suggested that measures of WM alone may help in better classifying such patients (Fernández-Espejo et al., 2011), and thus may complement responses observed with traditional fMRI. Moreover, mental imagery tasks are commonly used to assess associative parietal cortical functions in patients with a pathological process (e.g., lesion) in the posterolateral area of the right hemisphere.

In this study, 18 healthy subjects performed a visuospatial imagery task that evoked strong BOLD activity in the lingual gyrus (retrosplenial cortex) and areas along the dorsal (extrastriate, parietal) and ventral (parahippocampal gyrus) pathways. From this extensive functional network, we used state-of-the-art HARDI tractography to resolve fiber crossings and accurately reconstruct the WM pathways between activated areas. To our knowledge, we are the first to perform an fMRI–dMRI analysis of the brain sites activated during mental imagery. Rather than using dMRI metrics such as fractional anisotropy (FA) and other DTI metrics, we investigate reliability and reproducibility across 18 subjects to highlight the connectivity hubs of mental imagery. Hence, we concentrated on the fiber bundles which were most reproducible across subjects (>80%) and found that fMRI sites in the occipital lobe were indirectly linked to the ventral and dorsal stream via the posterior cingulate cortex (PCC). This highlights how PCC may act as a connector hub for linking the different visual processing pathways. Finally, we also investigate WM connectivity of deactivation patterns for the first time in the literature.