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Metacognitive ability correlates with hippocampal and prefrontal microstructure

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ABSTRACT

The ability to introspectively evaluate our experiences to form accurate metacognitive beliefs, or insight, is an essential component of decision-making. Previous research suggests individuals vary substantially in their level of insight, and that this variation is related to brain volume and function, particularly in the anterior prefrontal cortex (aPFC). However, the neurobiological mechanisms underlying these effects are unclear, as qualitative, macroscopic measures such as brain volume can be related to a variety of microstructural features. Here we leverage a high-resolution (800 μm isotropic) multi-parameter mapping technique in 48 healthy individuals to delineate quantitative markers of *in vivo* histological features underlying metacognitive ability. Specifically, we examined how neuroimaging markers of local grey matter myelination and iron content relate to insight as measured by a signal-theoretic model of subjective confidence. Our results revealed a pattern of microstructural correlates of perceptual metacognition in the aPFC, precuneus, hippocampus, and visual cortices. In particular, we extend previous volumetric findings to show that right aPFC myeloarchitecture positively relates to metacognitive insight. In contrast, decreased myelination in the left hippocampus correlated with better metacognitive insight. These results highlight the ability of quantitative neuroimaging to reveal novel brain-behaviour correlates and may motivate future research on their environmental and developmental underpinnings.

Introduction

The metacognitive capacity for self-monitoring is at the core of learning and decision-making (Flavell, 1979). As a general capacity, metacognition is thought to enable the flexible monitoring and control of perception, memory, and other cognitive processes (Fernandez-Duque et al., 2000). An efficient approach to quantifying this ability lies in the application of signal-detection theory to estimate the sensitivity of self-reported confidence to objective discrimination performance (Fleming and Lau, 2014). Individual differences in metacognitive sensitivity thus quantified are related to the morphology, function, and connectivity of the anterior prefrontal cortex (aPFC), precuneus, and other cortical areas (Fleming and Dolan, 2012). Here, we expand on these findings using a recently developed multi-parameter mapping (MPM) and voxel-based quantification (VBQ) technique to better elucidate the neurobiological mechanisms underpinning these effects.

The volume and function of the anterior prefrontal cortex (aPFC) and precuneus have repeatedly been related to metacognitive ability (Fleming et al., 2014, 2012, 2010a; McCurdy et al., 2013; Sinanaj et al., 2015). Notably, several studies found a positive relationship between right aPFC volume and metacognition (Fleming et al., 2010a; McCurdy et al., 2013; Sinanaj et al., 2015). While convergent evidence from anatomical, lesion-based, and functional connectivity studies suggest that the right aPFC is specific to perceptual metacognition, metacognition for memory has instead been related to midline cortical (e.g., mPFC and PCC/precuneus) and hippocampal structures (Baird et al., 2013; Fleming et al., 2014, 2012; McCurdy et al., 2013). Although these studies suggest that the ability to introspect on perception and memory depends on the development of a neural mechanism involving both domain-specific and general aspects, the underlying neurobiology driving the relationship between

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neuroanatomy and metacognition remains unclear.

One important source of uncertainty is the inherent lack of specificity offered by volumetric measures of brain structure, which are fundamentally qualitative in nature. Indeed, voxel-based morphometry (VBM) yields measures in arbitrary units which can be driven by a variety of macroscopic factors such as cortical thickness and variability in cortical folding, owing to a non-specific variety of microstructural features (Ashburner, 2009). It has recently been shown that microstructural properties of brain tissue, such as myelination levels and iron content can lead to the detection of spurious morphological changes (Lorio et al., 2016, 2014). As volumetric measures are highly dependent on acquisition parameters which can vary widely across scanners, field strengths, and other variables, they are difficult to directly replicate across studies (Boekel et al., 2015).

The emerging field of *in vivo* histology aims to address these issues by combining maps of specific MRI parameters measured via quantitative imaging (qMRI) with biophysical models and voxel-based quantification (VBQ) techniques to provide direct indicators of the microstructural mechanisms driving morphological findings. This approach quantifies biologically relevant metrics such as myelination and iron concentrations, oligodendrocyte distributions, and the g-ratio of fibre pathways (Mohammadi et al., 2015; Weiskopf et al., 2015). As these measures are quantitative in nature, they are largely invariant to specific scanner protocols and offer improved neurobiological specificity, thus facilitating our understanding of brain-behaviour mechanisms, improving reproducibility, and identifying novel biomarkers for clinical research.

In the present study, we used qMRI to map a number of key contrast parameters with differential sensitivity to underlying biological metrics, in order to better understand the microstructural correlates of metacognitive ability. To do so, we acquired high-resolution (800 μm isotropic) data using the Multi-Parametric Mapping (MPM) qMRI protocol (Weiskopf et al., 2013). We then conducted voxel-based quantification (VBQ) analysis (Draganski et al., 2011) in 48 healthy participants to relate these microstructural markers to individual differences in metacognitive sensitivity during an adaptive visual motion discrimination task. Our results revealed that right aPFC markers of myeloarchitecture (increased R_1 & MT) positively correlate with metacognitive ability, whereas the dentate gyrus of the left hippocampus showed effects consistent with decreased myelination (reduced MT). Cortical iron markers in the precuneus (increased R_2*) and visual cortex (decreased R_2*) also covaried with metacognitive ability. These results extend our understanding of the microstructural neuroanatomy of metacognition and provide novel targets for future clinical research.

Methods

Participants

48 healthy participants (29 female) were recruited from University College London and the surrounding community. As age is a strong determinant of brain microstructure (Callaghan et al., 2014), we restricted our inclusion criteria to 20–40 years, resulting in a mean age of 24 (SD = 5). All participants were right handed, and were mentally and physically healthy with no history of neurological disorders and with normal (or corrected-to normal) vision and hearing. Participants were recruited from a local participant database using broadcast emails. All participants gave informed written consent to all procedures. In accordance with the Declaration of Helsinki, the University College London Research Ethics Committee approved all procedures.

Study design

Participants completed the experiment in two sessions, consisting of a 2-h appointment at the Wellcome Trust Centre for Neuroimaging to acquire all imaging data, and a separate 1-h appointment to complete the metacognition task, a brief non-verbal auditory memory measure (Harrison et al., 2016; Müllensiefen et al., 2014), a tonotopy functional scan, and other auditory and behavioural measures as part of a study on individual differences in the auditory cortex (data not reported here). The neuroimaging session involved 30 min of multi-parameter mapping (MPM) while subjects silently viewed a muted nature documentary to maintain wakefulness (and hence limit motion). During the behavioural session, participants completed an adaptive psychophysical visual metacognition task (see *Behaviour*, below) lasting 30 min.

Behaviour – Metacognition Global Motion Task

To measure participants' metacognitive ability, we employed a global dot motion discrimination task comprising a forced-choice motion judgement with retrospective confidence ratings on every trial. As part of another investigation, in which we were investigating noise-induced confidence bias (Spence et al., 2016; Allen et al., 2016), we used a dual-staircase approach with two conditions in which either mean direction or standard deviation across dot directions was continuously adapted to stabilize discrimination performance. Thus, to control sensory noise independently of task difficulty, in two randomly interleaved conditions we presented either a stimulus with a fixed 15-degree mean angle of motion from vertical and a variable (adaptive) standard deviation (SD), or a variable (adaptive) mean angle from vertical at a fixed 30° SD. In either case, the mean (μ-staircase condition, μ*S*) or standard deviation (σ-staircase condition, σ*S*) of motion was continuously adjusted according to a 2-up-1 down staircase, which converges on 71% performance. On each trial the motion signal was thus constructed using the formula:

$$DotDirections = (Left \mid Right) \times MeanOrientation + (GaussianNoise \times SD)$$

In which the condition-specific staircase determined either mean orientation or SD. Each trial consisted of a 500 ms fixation, followed by a 250 ms central presentation of the motion stimulus, which was then replaced by a central letter display “L R”. Participants then had 800 ms to make their response to indicate whether the mean motion direction was to the left or right of vertical. After this, a confidence rating scale marked by 4 equal vertical lines appeared. Each line was labelled, from left to right “no confidence, low, moderate, high confidence”. Participants’ heads were fixed with a chin and forehead rest 72 cm from the screen. Motion stimuli consisted of a central array of 1100 dots presented over a central fixation dot, within a circular aperture of radius 9.5° visual angle (DVA), with dots advancing 0.02 DVA per frame. To ensure participants attended the global rather than the local motion direction, dot lifetimes were randomized and limited to a maximum of 93% stimulus duration.

Participants were instructed that the goal of the task was to measure their perceptual and metacognitive ability. Metacognitive ability was defined as a participant's insight into the correctness of their motion judgements, i.e. how well their confidence reports reflected their discrimination accuracy. Participants completed a short practice block of 56 trials, in which they performed the motion discrimination without confidence ratings, with choice accuracy feedback provided by changing the colour of the fixation to green or red. All participants achieved better than 70% accuracy and indicated full understanding of the task before continuing. Participants completed 320 trials divided evenly between the two staircase conditions. Trials were divided into 10 blocks each with 40 trials, randomly interleaved across conditions within each block. 14 participants did not complete the last two blocks of the task due to a technical error, however all participants had at least 100 trials per condition (Fleming and Lau, 2014). See Fig.1 for an graphical summary of our task.