

Diffusion property and functional connectivity of superior longitudinal fasciculus underpin human metacognition

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ABSTRACT

Metacognition as the capacity of monitoring one's own cognition operates across domains. Here, we addressed whether metacognition in different cognitive domains rely on common or distinct neural substrates with combined diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI) techniques. After acquiring DTI and resting-state fMRI data, we asked participants to perform a temporal-order memory task and a perceptual discrimination task, followed by trial-specific confidence judgments. DTI analysis revealed that the structural integrity (indexed by fractional anisotropy) in the anterior portion of right superior longitudinal fasciculus (SLF) was associated with both perceptual and mnemonic metacognitive abilities. Using perturbed mnemonic metacognitive scores produced by inhibiting the precuneus using TMS, the mnemonic metacognition scores did not correlate with individuals' SLF structural integrity anymore, revealing the relevance of this tract in memory metacognition. To further verify the involvement of several cortical regions connected by SLF, we took the TMS-targeted precuneus region as a seed in a functional connectivity analysis and found the functional connectivity between precuneus and two SLF-connected regions (inferior parietal cortex and precentral gyrus) mediated mnemonic metacognition performance. These results illustrate the importance of SLF and a putative white-matter grey-matter circuitry that supports human metacognition.

1. Introduction

The capacity of reflecting on one's own cognitive process is known as metacognition (Flavell, 1979; Fleming and Dolan, 2012; Yeung and Summerfield, 2012). Given that metacognition has been considered as one of the most crucial functions emerged during evolution (Heyes, 2016), researchers have endeavored to understand how a metacognitive judgment is computed (Fleming and Daw, 2017; Kepecs et al., 2008; Zylberberg et al., 2016), how it is disrupted in psychiatric disorders (Hauser et al., 2017a; Rouault et al., 2018a), and how its accuracy can be improved (Carpenter et al., 2019). Metacognition is an umbrella term

for the higher-level cognition about the lower-level cognition in various domains (e.g., perception and memory). An interesting and important question is whether the neural circuit supporting metacognition is the same or distinct across different cognitive domains (Rouault et al., 2018b).

A large body of functional magnetic resonance imaging (fMRI) work have demonstrated a nuanced picture for this domain-general issue of metacognition. For example, the dorsolateral prefrontal cortex (DLPFC) might be involved in accessing to the evidence supporting primary decision-making and using it for computing both perceptual and mnemonic metacognitive judgments (Chua and Ahmed, 2016; Fleming and

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Dolan, 2012; Kwok et al., 2019; Rounis et al., 2010). Morales et al. (2018) reported that the dorsal anterior cingulate cortex (dACC) was active during metacognitive evaluation in both memory and perception tasks but also found the activation patterns decoded from a perception task in the posterior medial frontal cortex and ventral medial prefrontal cortex predict metacognitive judgements in a memory task. In contrast to these domain-general components, other evidence also indicates domain-specific mechanisms. For example, accurate perceptual metacognition is dependent on the accessibility of performance-monitoring information coded in the dACC to the anterior PFC (Allen et al., 2017; Fleming et al., 2010, 2014; McCurdy et al., 2013), whereas accurate memorial metacognition is dependent on memory-mediated regions such as the medial PFC, mid/posterior cingulate cortex, inferior parietal lobule (IPL) and precuneus (Baird et al., 2013; Chua and Ahmed, 2016; McCurdy et al., 2013; Simons et al., 2010; Ye et al., 2018).

Although much progress has been made on how cortical networks support metacognition in different domains, less is known about how white matter pathways, through which inter-regional information communicates, contribute to supporting these cognitive processes. Fleming et al. (2010) reported that metacognitive ability on perception domain was positively correlated with the diffusion anisotropy in the genu of corpus callosum (the callosum forceps minor) which links the anterior PFC. To our knowledge, Baird et al. (2015) was the only study to date directly compared the white matter microstructure related to perceptual and mnemonic metacognitive ability. They found that accurate metacognitive evaluation on a perception task positively correlated with the diffusion anisotropy underlying the anterior cingulate cortex (ACC), whereas accurate metacognitive evaluation on a memory task positively correlated with the diffusion anisotropy of the white matter underlying the inferior parietal lobule (IPL), indicating metacognition in different cognitive domains might rely on distinct neural substrates. Nevertheless, Baird and colleagues did not control for the local task properties (visual stimuli vs verbal words) nor the metrics quantifying the perceptual and mnemonic metacognitive ability (2-AFC vs Y/N responses), which can bias the comparison across domains (Lee et al., 2018; Rouault et al., 2018b). They also did not characterize the diffusion property at specific, finely-defined locations along white matter tracts and their relationship with metacognitive abilities, so that the actual extent to which white matter tracts contributes to metacognition in each cognitive domain might be underestimated (Teubner-Rhodes et al., 2016).

Therefore, the present investigation sought to elucidate the neurobiological mechanisms underpinning metacognition across two different domains in relation to the white-matter diffusion property. We used a diffusion tensor imaging (DTI) tractography technique, named as automated fibre quantification (AFQ; Yeatman et al., 2012, 2014), to perform intra-tract analysis of tissue features along the neuronal fibre tracts. This method gives sensitive measures of white matter structural integrity and allows us to examine its relationship with metacognitive ability in different domains. Given the known neural substrates of metacognition, we selected the following five white matter tracts (two bilateral and one unilateral): The bilateral superior longitudinal fasciculus (SLF), which links the domain-general DLPFC to the precentral gyrus and inferior parietal cortex (Hecht et al., 2015); the bilateral cingulum bundle (CB), which connects the domain-general ACC to the posterior parietal regions (Heilbronner and Haber, 2014); and the callosum forceps minor (CFM), which connects the perceptual metacognition related regions such as the left and right anterior PFC (Fleming et al., 2010; Park et al., 2008).

In addition, making use of our published behavioral data (Ye et al., 2018), we verified the relevance of mnemonic metacognition-related white matter tracts using a set of perturbed mnemonic metacognition scores following TMS to the precuneus. We observed that the FA of the right SLF was significantly correlated with both perceptual and mnemonic metacognitive ability measured in the TMS control condition. However, with altered metacognitive scores induced by precuneus-TMS,

the relationship of SLF FA with mnemonic metacognition disappeared, while the one with perceptual metacognition was preserved.

Finally, to fully elucidate how the afferent and efferent between precuneus and brain regions connected by the right SLF exclusively supports mnemonic metacognition, we ran a resting-state functional connectivity (rs-FC) analysis with the TMS-targeted precuneus site as the seed. The precuneus-right precentral gyrus and precuneus-right IPL rs-FCs were found to be correlated with intact mnemonic metacognitive ability (but not the perturbed one); while these frontal-parietal network rs-FCs were not correlated with the perceptual metacognitive ability. Taken together, the current results indicate that the superior longitudinal fasciculus assumes an important anatomical function to support human metacognition.

2. Materials and methods

2.1. Participants

Eighteen university students (7 females, aged 19–24 years) from East China Normal University participated in this study. All participants had normal or corrected-to-normal vision, reported no history of psychiatric and neurological diseases, and no other contraindications for MRI. All participants gave written informed consent, and were financially compensated for their participation. The study was approved by University Committee on Human Research Protection of East China Normal University. To guarantee the quality of metacognition estimation, we followed previous investigations (Allen et al., 2017; Morales et al., 2018; Rouault et al., 2018a), and excluded one participant whose first-order performance in the memory task was at chance level ($d = -0.04$) and one participant who missed 10% of the trials in total ($>3SD$ from the average missed trials, which was $2.6\% \pm 2.2\%$). For each participant, we discarded trials of which the first-order decision and confidence response time was faster than 100 ms or slower than three standard deviations from per-subject mean (2.1% of trials were discarded).

2.2. Study design

We combined diffusion tensor imaging tractography (automated fibre quantification; Yeatman et al., 2012, 2014) and a seed-based resting-state functional connectivity (rs-FC) method with established metacognition measurements in healthy normal subjects to investigate the importance of white matter tract diffusion properties to metacognitive processes. The former examines intra-tract tissue features along the neuronal fibre tracts and the latter clarifies the afferent and efferent connectivity properties of our target tracts. Human metacognition in two cognitive domains is measured by an established protocol and is quantified by a hierarchical Bayesian Meta-d' model (Fleming, 2017) as metacognitive efficiency (meta-d'/d'). The experimental protocols are described as follows.

2.3. Behavioral tasks and stimuli

All participants completed a memory (temporal order judgment; TOJ) task and a perception (visual discrimination) task (Fig. 1A). Each cognitive task contained two testing sessions. Prior to each testing session, participants received 20-min repetitive TMS that targeted at the precuneus or the vertex (as control site) in a counterbalanced order (Fig. 1B, see section *Repetitive TMS: procedure, protocol, and sites* below). The two sessions of each cognitive task were carried out on different days, and the memory task was conducted first. For safety reason and to avoid carryover effects of rTMS across sessions, experimental Sessions 1 and 2 were conducted on 2 separate days for both tasks (memory: mean interval = 8 d; perceptual: mean interval = 3.9 d). There were 480 trials for each cognitive task (2 sessions \times 4 blocks \times 60 trials per block), and thus 960 trials in total for each participant.

A two-alternative forced choice (2-AFC) design was used for both

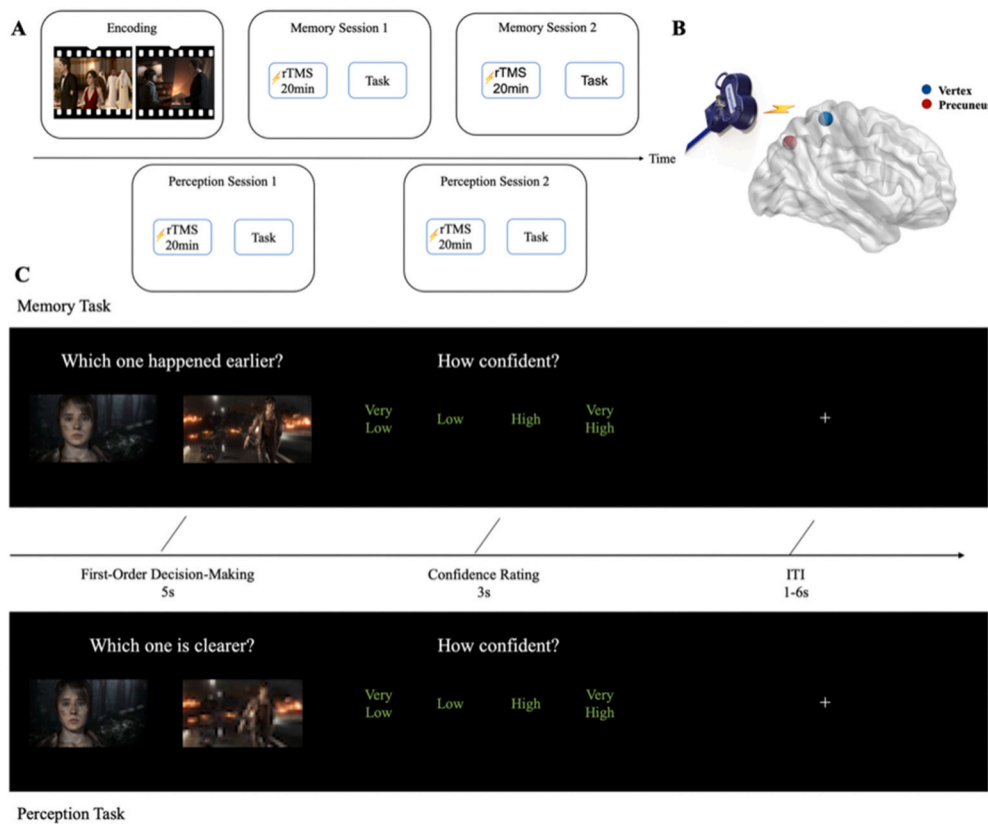


Fig. 1. Study overview. **A**, Experiment design. Each participant completed two cognitive tasks crossing with TMS stimulations. **B**, TMS locations. Precuneus stimulation was set at (MNI $x, y, z = 6, -70, 44$) whereas vertex stimulation was set as a control site. **C**, Trial structure. In the memory task, participants chose the image that occurred earlier in the video game; in the perceptual task, participants were required to identify which image was clearer (or blurrier; counterbalanced across participants). In both tasks, after each first-order judgement, participants rated their confidence for the current trial on a scale of 4 levels.

tasks and the experiment-related parameters (i.e., number of trials; dimension, position and sequence of the presented stimulus; time limits for responses; and the inter-trial intervals) were set identical in both (Fig. 1C). For each memory testing session, 24 h before the testing period, participants played seven chapters of a first-person perspective action-adventure video game *Beyond: Two Souls* with Sony PlayStation as the memory encoding period. The game play was recorded. We performed the image-extraction at the end of each encoding session and prepared the images immediately afterwards so that the images would be ready for use on the following day. The impetus was to provide each participant a personally-unique experience for their source memory. In each trial of the TOJ memory task, participants were presented with two images extracted from the personalised recording, and were required to choose the one that occurred earlier. Images were presented for 5 s, followed by a 3-s confidence rating period where participants needed to report their confidence in the TOJ judgement in four scale (i.e., “Very Low”, “Low”, “High”, or “Very High”). The decision confidence reflects the subjective probability of making a correct response, and requires participants to think about their primary decision-making process. Therefore, in line with previous research (Fleming and Dolan, 2012), confidence is used as an operational definition of metacognition here (see also 2.4 Quantification of metacognition). Participants were encouraged to make use of the whole confidence scale. After the confidence rating, participants entered the inter-trial interval with a variable duration from 1 to 6 s.

The perception task carried a similar procedure with the memory task. The same sets of paired images in each memory task session were presented in each perception task session in an identical order, but with manipulation on the image resolutions. In each trial, we manipulated resolution differences between the images, and asked participants to report which one was clearer (or blurrier) and their associated confidence level. We used Python Imaging Library to reduce the resolution of one of the two images (i.e., resizing the image to change the pixel per inch [PPI]). The higher the PPI, the smaller the difference would be in

the resolution between the resized and original images, thus the harder for participants to discriminate the clearer one. For example, if we reduced the PPI of one of the paired images to 30%, the image resolution difference would be 0.7; while if the PPI of one image was reduced to 0.9, the resolution difference would be 0.1. The range of the resolution difference for all image pairs was from 0.05 to 0.65. We used an n -down/1-up adaptive staircase procedure to adjust the image resolution online and converge on $\sim 71\%$ performance.

All the visual stimuli were presented with E-prime software (Psychology Software Tools), and the presentation order of the paired images were counterbalanced throughout the experiment.

2.4. Quantification of metacognition

Type-1 memory and perceptual performance were quantified as a signal detection theoretic measure of type-I sensitivity (d'). Type-2 metacognitive sensitivity was estimated by meta- d' , which is expressed in the same scale as d' and indicates the extent to which a participant could discriminate correct responses from incorrect ones by confidence. Individuals who accumulated more evidence to make accurate primary (or first-order) decision might have more evidence to guide accurate metacognitive evaluations. Therefore, we applied a hierarchical Bayesian Meta- d' model (Fleming, 2017) to calculate meta- d' . This meta- d' is then considered as a ratio together with the subject's primary task performance (d'), as meta- d'/d' (or $Mratio$), to reflect her metacognitive efficiency that takes consideration of first-order performance.

2.5. MR image acquisition

High-resolution structural, DTI, and resting-state fMRI data were acquired on a separate day prior to the first session. All MR images were acquired using a 3.0 T S Trio MRI scanner with a 32-channel head coil. High-resolution T1-weighted images were acquired using Magnetization

Prepared Rapid Gradient Recalled Echo (MPRAGE) sequence with the following parameters: repetition time (TR) = 2530 ms, echo time (TE) = 2.34 ms, inversion time = 1100 ms, flip angle = 7°, field of view (FOV) = 256 mm, slice number = 192, voxel size = $1 \times 1 \times 1 \text{ mm}^3$, slice thickness = 1.0 mm.

Seventy transverse DWI (diffusion-weighted imaging) slices were acquired with the parameters: TR = 11,000 ms, TE = 98 ms, FOV = 256 mm, voxel size = $2 \times 2 \times 2 \text{ mm}^3$, acquisition matrix = 128×128 , phase encoding direction: anterior to posterior (A > P), 60 gradient directions ($b = 1000 \text{ s/mm}^2$) and 2 non-diffusion images were obtained. The fMRI images were collected with the following parameters: TR = 2000 ms, TE = 30 ms, FOV = 230 mm, flip angle = 70°, voxel size = $3.6 \times 3.6 \times 4 \text{ mm}^3$, slice number = 33, parallel to the AC-PC plane. For each subject, 220 whole-brain volumes were acquired.

2.6. MR image processing

2.6.1. Tract-based analysis for DTI data

For tract-based analysis, we performed DTI image preprocessing using VISTASOFT package (<http://web.stanford.edu/group/vista/cgi-bin/wiki/index.php/Software>). After the correction of head motion and eddy-current distortion, the DWI images were registered to the averaged non-diffusion weighted images. After that, the DWI images were registered to the T1-weighted image and the corresponding fractional anisotropy (FA) maps were obtained. A higher FA value implies a stronger structural connectivity between the brain regions (Greicius et al., 2009).

Fiber tracking was performed using Automating Fiber-Tract Quantification (AFQ, <https://github.com/jyeatman/AFQ>; Yeatman et al., 2012). First, a deterministic streamline tracking algorithm (Basser et al., 2000; Mori et al., 1999) was employed for whole-brain tractography. The tracking was performed within the white matter mask, seeded at the voxels with FA > 0.3 and terminated if the voxelwise FA value was below 0.2 or the minimum angle between last path segment and next step direction was larger than 30° (Yeatman et al., 2012). Second, we performed fiber tract segmentation using waypoint regions of interest (ROIs). The fiber was included in the fiber tract if it passes through two ROIs that define the trajectory of the fiber tract. The ROIs defined in Montreal Neurological Institute (MNI) space were registered to each participant's native structural space through nonlinear transformation (Dougherty et al., 2007; Wakana et al., 2007). Finally, the candidate fibers were removed if passing through the white matter regions unlikely the parts in fiber tract probability map (Hua et al., 2008) or the three-dimensional Gaussian covariance of the sample points are larger than 5 s.d. from the mean (Yeatman et al., 2012). The obtained tract was centered in all the corresponding tract fibers. A curve was created by defining 100 evenly spaced sample points along each fiber and calculating the mean position of each sample point in the curve accordingly. For each node along the streamline, the FA profile was calculated as a weighted sum of FAs of all streamlines at each node. The weight of each fiber was determined by its corresponding Mahalanobis distance, which corresponds to its probability following the Gaussian distribution (Yeatman et al., 2012). Five frontal-parietal white matter tracts (i.e., right/left superior longitudinal fasciculus, SLF; right/left cingulum bundle, CB; the callosus forceps minor, CFM) were selected for further analysis.

2.6.2. Functional connectivity analysis

For the FC calculation, the fMRI image processing was performed using Data Processing Assistant for Resting-State fMRI (DPARSF, <http://www.nitrc.org/projects/dparsf/>), which is based on Statistical Parametric Mapping 8 (SPM8, <http://www.fil.ion.ucl.ac.uk/spm/>) and Resting-State fMRI Data Analysis Toolkit (REST v1.8, <http://www.restfmri.net>). The first 10 vol were discarded for machine stabilization and participants' adaption to the environment. The remaining 210 vol were subsequently preprocessed by the following steps: slice-timing,

head motion correction, normalization to the MNI space with voxel size resampled to $3 \times 3 \times 3 \text{ mm}^3$, spatial smoothing using an isotropic Gaussian filter kernel with 6 mm full-width at half maximum (FWHM), linear detrending, nuisance signal regression and temporal band-pass filtering (0.01–0.10 Hz). No participant was excluded by the criterion that the head motion was above 3 mm or 3°. Nuisance regressors included Friston-24 head motion parameters (Friston et al., 1996), white matter and CSF signals and the global signal. The FC map was generated by computing the averaged time series within the 8-mm-radius sphere centered at the precuneus (MNI coordinate: $x = 6, y = -70, z = 44$; Kwok et al., 2012) and correlating them with the time series of all other grey matter voxels in the whole brain using Pearson's correlation analyses. The FC map was transformed to Z-score map by Fisher's Z transformation for statistical analysis.

2.6.3. MRI data statistical analysis

Pearson correlation analysis was performed between FCs or DTI metrics and cognitive scores (i.e., first-order performance, mean confidence level, and metacognitive efficiency) for all the subjects using IBM SPSS 20. For FCs, the correlations were corrected for multiple comparisons using AlphaSim ($M = 1000, p < 0.001$, cluster size = 13 voxels). The correlations between DTI metrics and cognitive scores were calculated using Pearson correlation analysis. For each tract, we performed correlation analyses between FA and behavioral measures at each of the 100 nodes. The results were then corrected for multiple comparisons of all the 100 nodes along a single tract using false discovery rate (FDR) correction at $p < 0.05$. Each correction was performed for each fasciculus individually. Moreover, a cluster correction was performed using nonparametric permutation tests (1000 permutations) to obtain the minimum number of continuous nodes reaching the significance. For example, for the correlation between the perceptual metacognition before TMS and the FA of SLF, the corresponding corrected cluster size was 25.

2.7. TMS: procedure, protocol, and sites

To verify the functional relevance of white-matter tracts and their functional connectivity in support of metacognition, we utilized our previously published behavioral data (Ye et al., 2018) for the DTI and functional connectivity analyses here. In that study, we used repetitive TMS (rTMS) to alter subjects' metacognitive scores. rTMS was applied using a Magstim Rapid² magnetic stimulator connected to a 70 mm double air film coil (The Magstim Company, Ltd., Whitland, UK). To localize the target brain regions,Brainsight2.0 (Rogue Research Inc., Montreal, Canada) was used for the subject-specific structural T1-weighted images. Participants' brains were normalised by transforming to the Montreal Neurological Institute (MNI) template. To prepare the subject-image registration and promote online processing of the neuronavigation system, four location information of each subject's head were obtained manually by touching the tip of the nose, the nasion, and the inter-tragal notch of each ear using an infra-red pointer. In each session, rTMS was delivered to either the precuneus or vertex before the main task. TMS was applied at 1 Hz frequency for a continuous duration of 20 min (1200 pulses in total) at 110% of active motor threshold. The order of stimulation sites was counterbalanced across sessions. The coil was held to the scalp of the participant with a custom coil holder and the subject's head was propped a comfortable position. Coil orientation was parallel to the midline with the handle pointing downward. The stimulation sites are in the precuneus with MNI coordinates $x = 6, y = -70, z = 44$ (Kwok et al., 2012) and in a control area on the vertex (Jung et al., 2016) (Fig. 1B).

3. Results

3.1. Diffusion tensor imaging results

The individual-level metacognitive efficiency scores in both memory and perception tasks in both TMS conditions are illustrated in Fig. 2 (Mean \pm Standard Deviation: Memory-Vortex, 1.89 ± 0.50 ; Perception-Vortex, 1.31 ± 0.33 ; Memory-Precuneus, 1.68 ± 0.64 ; Perception-Precuneus 1.29 ± 0.20). These subject-level scores, including the ones in precuneus TMS conditions, were used in the DTI and functional connectivity analyses.

Neurally, we report how FA in the white matter tracts might be correlated with participants' metacognitive scores. First and foremost, we found a significant positive correlation between the FA in the anterior portion of right SLF and memory metacognition (nodes 1–53, FA: $r_{14} = [0.56, 0.77]$, $p_{FDR} < 0.05$) as well as a significant positive correlation with their perceptual metacognition (nodes 1–40, FA: $r_{14} = [0.59, 0.76]$, $p_{FDR} < 0.05$) in the TMS-vertex condition (Fig. 3B and C, top panel). With TMS applied to the precuneus, the correlation between right SLF FA and perceptual metacognition are preserved (nodes 6–43, FA: $r_{14} = [0.58, 0.74]$, $p_{FDR} < 0.05$; Fig. 3C, bottom panel) whereas correlation between the SLF FA and memory metacognition did not survive FDR correction (Fig. 3B, bottom panel).

This finding indicated that the right SLF play a domain-general role in supporting metacognition. To further examine this possibility, we modelled together both perceptual and mnemonic metacognitive efficiency scores when testing against the right SLF FA to see how the intact metacognitive ability in each domain (i.e., measured in the vertex TMS condition) might be uniquely correlated with the SLF structural integrity. A multiple linear regression analysis revealed that, after controlling for covariance between the intact mnemonic and perceptual metacognitive efficiency scores, neither of them significantly related to the FA of right SLF nodes ($p_{FDR} > 0.05$). This confirmed the importance of the right SLF in explaining the correlation between mnemonic and perceptual metacognition, suggesting domain-generality of metacognition.

In order to provide further support for our claim that SLF FA is associated specifically with metacognition but not with other first-order processes, we ran the same analyses, now separately using either participants' primary task accuracy (d') or mean confidence ratings. We did not find any nodes along SLF that showed the diffusion properties significantly correlated with subjects' first-order performance, nor with confidence ratings, in either of the cognitive tasks. These control tests

indicate that the FA results cannot be explained by first-order performance or confidence, thus providing evidence that the putative effects are indeed metacognition-specific.

In contrast to the SLF, neither the FA of the callosus forceps minor (Mnemonic: nodes 9–13, 20–23, 92–95, FA: $r_{14} = [0.50, 0.58]$, $p_{unc} < 0.05$), nor that of the cingulum bundle portion (Mnemonic: nodes 28–34, 42–44, 86–92, FA: $r_{14} = [0.51, 0.56]$, $p_{unc} < 0.05$; Perceptual: nodes 27–32, FA: $r_{14} = [0.52, 0.64]$, $p_{unc} < 0.05$) reached full FDR corrected significance. We accordingly did not consider them further in the functional connectivity analyses.

3.2. Functional connectivity MRI (fc-MRI) results

The precuneus is known to mediate human memory metacognition (Ye et al., 2018, 2019) and given the aforementioned results that the perturbed mnemonic metacognitive efficiency after precuneus-stimulation did not correlate with the SLF FA any more, we selected the precuneus as an anatomical seed and calculated its resting-state functional connectivity (rs-FC) with each voxel in the whole brain. This aimed to examine how the rs-FC might be associated with metacognitive abilities. For the memory domain, under the control TMS condition, the rs-FC between precuneus and two SLF-crossed clusters, the right caudal ventrolateral precentral gyrus (PrG; peak voxel MNI location, [42, -18, 3]) and the right IPL (peak voxel MNI location, [42, 27, 39]), were found to be significantly correlated with mnemonic metacognitive efficiency ($ps < .001$, Fig. 4A). Notably, with precuneus-TMS disrupted mnemonic metacognitive efficiency scores, the relationships between these two rs-FCs and mnemonic metacognition diminished significantly and did not reach statistical significance any more (not shown). In contrast, as expected and in line with our domain-specificity hypothesis, no cluster survived correction when we repeated the same set of analyses when taking perceptual metacognitive efficiency into account in both TMS conditions. These FC results demonstrated the specificity of the information transmission between precuneus and right SLF-connected regions in supporting the mnemonic metacognitive ability alone, and highlight the importance of the right SLF structural profile in mediating mnemonic metacognition. As control analyses, instead of metacognitive efficiency scores, we entered individual subjects' first-order task performance and confidence ratings to repeat the same sets of FC analyses. Under the TMS-vertex condition, the correlation between first-order memory performance and the PrG-IPL resting-state functional connectivity was not significant.

Interestingly, in terms of confidence rating, the precuneus/right IPL

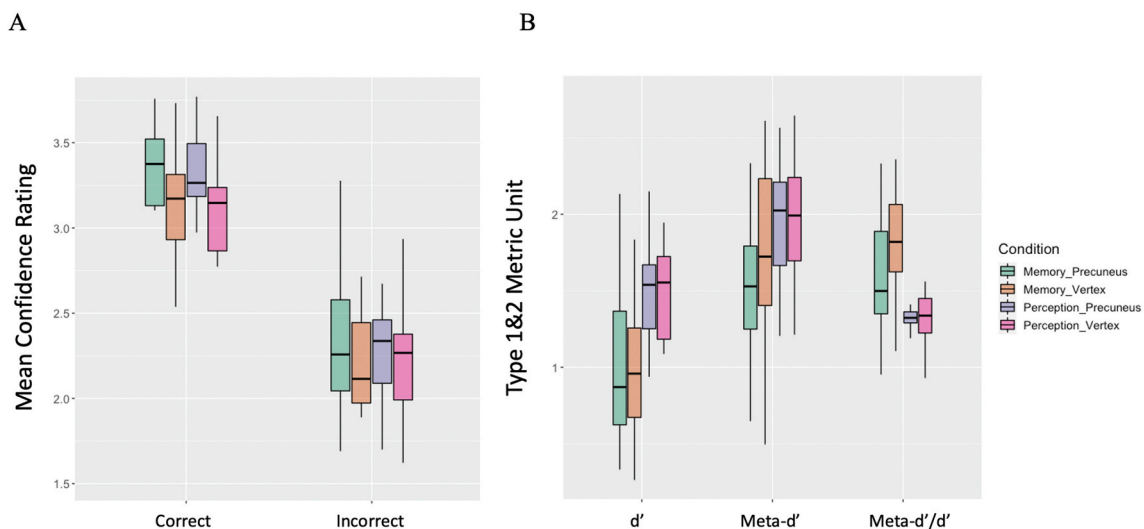


Fig. 2. Descriptive behavioral results. Participants' confidence in correct and incorrect trials in each condition (A) and first-order performance (d'), metacognitive sensitivity (i.e., meta- d'), metacognitive efficiency (meta- d'/d' , also referred as Mratio; B) across two tasks by TMS conditions.

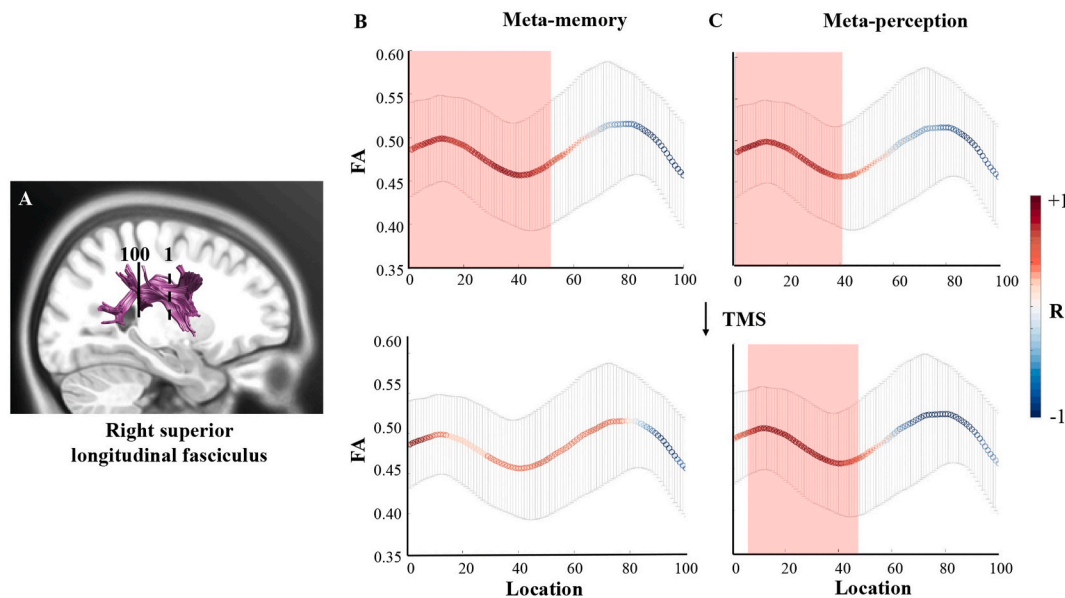


Fig. 3. DTI results. The FAs of the nodes along the right anterior SLF had positive correlations with both perceptual and mnemonic metacognitive efficiency. **A**, the portion of SLF that was tracked and evenly divided into 100 nodes by the AFQ method. The dash line represents the location of the starting point (marked by numeral 1) and the solid line represents the location of the ending point (marked by numeral 100). **B** and **C** respectively illustrates the correlation between the FA value of each SLF node and mnemonic or perceptual metacognitive efficiency (Top two panels: without TMS to precuneus; bottom two panels: TMS to precuneus). With perturbed mnemonic metacognitive scores, the correlation between right SLF FA and memory metacognition disappeared. The x-axis is the individual node alongside the SLF, and its corresponding FA value is shown on y-axis. The colour of the curved lines illustrates the correlation between the FA of a SLF node and metacognitive efficiency scores. Those nodes that had significant correlation with metacognitive efficiency scores are marked by a red rectangular. The error bars denote standard error of the means over participants. Note: DTI, diffusion tensor imaging; FA, fractional anisotropy; AFQ, Automating Fiber-Tract Quantification; SLF, superior longitudinal fasciculus; TMS, transcranial magnetic stimulation. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

rs-FC positively correlated with the confidence in the memory task (peak voxel MNI location, [36, -57, 54], $p < 0.001$), whereas the precuneus/right PrG rs-FC negatively correlated with the confidence in the task (peak voxel MNI location, [57, 0, 39], $p < 0.001$; Fig. 4B). In TMS-precuneus condition, no significant correlations were observed in any of these tests. The opposite directions shown in the correlations for precuneus/right PrG with metacognitive efficiency versus trial-confidence (positive trend for meta-d'/d' in Fig. 4A but negative trend for confidence in Fig. 4B) indicate the mechanisms underpinning confidence computation and overall metacognitive ability might not fully correspond in this memory task.

4. Discussion

Whether the computation of metacognition relies on the same mechanism across cognitive domains has been a controversial issue. In the present study, we addressed this domain-generality/specificity issue at the white matter structural integrity and grey matter functional connectivity level. Supported by DTI and resting-state fMRI techniques, we found metacognitive performance in perception and memory tasks are related to the superior longitudinal fasciculus and its connected regions.

We observed that the right SLF serves a domain-general role on metacognition. The structural integrity of the anterior portion of this tract correlates significantly with metacognitive efficiency in both perception and memory tasks, but not with primary decision-making performance or confidence rating level. This specific portion of the right SLF underlies the precentral gyrus and links the right DLPFC to the right IPL (Hecht et al., 2015). Additionally, it lies within the frontal lobe, which is not mixed by the temporal fibres in the arcuate fasciculus (Wakana et al., 2007) and is indicative of the DLPFC – IPL communication (Yeatman et al., 2012). Anatomically, on the one end, the SLF connects with the right DLPFC, which is involved in both perceptual and

mnemonic metacognition in both humans and monkeys, and suggested as accessing to the evidence related to the primary decision-making and computing metacognitive judgements (Fleming and Dolan, 2012; Kwok et al., 2019; Morales et al., 2018; Shekhar and Rahnev, 2018). On the other end, it connects with the right IPL, which has been identified as crucial in mnemonic metacognition (Berryhill et al., 2007; Davidson et al., 2008; Simons et al., 2010). The right IPL has been reported as the “output gating” of working memory for information selection (Baddeley, 2000; Vilberg and Rugg, 2008; Wallis et al., 2015). Some studies reported that individuals would selectively ignore evidence favouring the unchosen alternatives during metacognitive evaluation (Aitchison et al., 2015; Samaha et al., 2016; Zylberberg et al., 2012), which implies the importance of such working-memory gating mechanism in metacognition. Thus, given the functional and anatomical meaning of white-matter structural integrity, we propose that, in a metacognitive process, the right IPL select what information regarding the previous decision-making should be used and convey it to the right DLPFC through SLF for further computation. The better structural integrity of the right SLF is, the lower noise will be added during the information transmission, allowing the right DLPFC to more precisely utilise the first-order decision-making related information to compute metacognitive evaluations.

The involvement of the right SLF to metacognition was further confirmed with a set of cognitive scores following TMS modulation on the precuneus. Applying TMS on the precuneus, we disrupted participants' mnemonic metacognitive ability, and observed that the SLF FA – mnemonic metacognition relationship did not exist anymore (while the SLF FA – perceptual metacognition remained). To investigate how the precuneus communicates with SLF-connected regions to support metacognition, we chose the targeted precuneus region as seed and examined how its resting-state functional connectivity correlated with the metacognitive efficiency scores (Hampson et al., 2006; Seeley et al., 2007). A frontal-parietal network (precuneus – IPL and precuneus – PrG) was

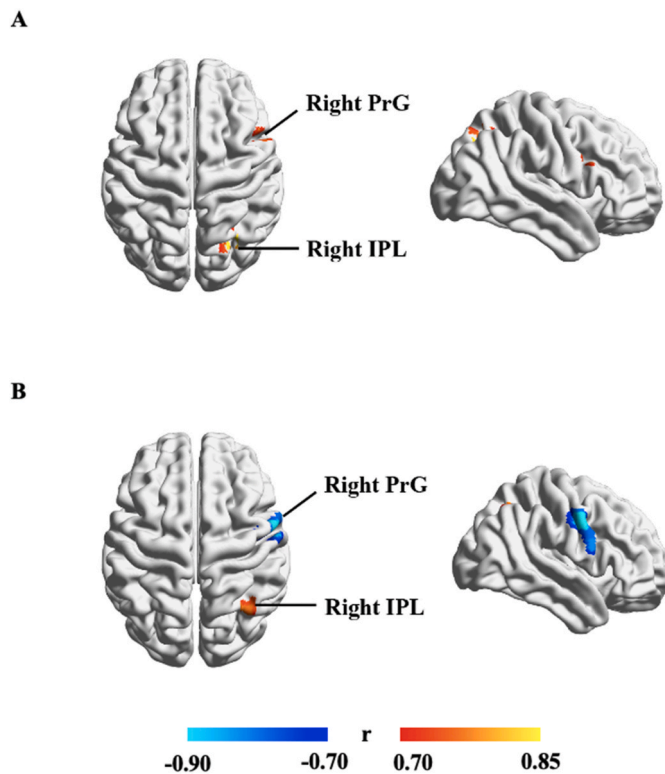


Fig. 4. Functional connectivity results. Choosing the precuneus (8-mm-radius sphere centering at [6, -70, 44]) as seed, **A**, the precuneus/right PrG FC and the precuneus/right IPL FC positively correlated with mnemonic metacognitive efficiency. **B**, the precuneus/right PrG FC negatively correlated with the overall confidence in the memory task, whereas the precuneus/right IPL FC positively correlated with the overall confidence. PrG = caudal ventrolateral precentral gyrus; IPL = inferior parietal lobule.

found exclusively related to the mnemonic metacognition under the TMS control condition. The functional relevance of this network disappeared when we used cognitive scores obtained after TMS was applied at the precuneus. This result demonstrated that, while the structural integrity of right SLF supports both perceptual and mnemonic metacognition, the information afferent and efferent along the SLF are domain-specific.

Several recent investigations have identified certain white-matter tracts, including the uncinate fasciculus, SLF and CFM, are related to the source memory performance (Davis et al., 2018; Lockhart et al., 2012; Metzler-Baddeley et al., 2011). Our observed correlation between SLF FA and metacognition on a source memory task (i.e., TOJ) shows that mnemonic metacognition processes here might be related to source memories (Ye et al., 2019). Furthermore, this hypothesis was also supported by the follow-up resetting-state functional connectivity analysis. Taking the precuneus as a seed, we observed that mnemonic metacognition is supported by the precuneus/right IPL and precuneus/right PrG communication. The precuneus has been linked to generating mental images to aid detailed episodic memory retrieval (Fletcher et al., 1995; Hebscher et al., 2020; Koch et al., 2018; Richter et al., 2016), as well as realizing temporal organization of episodic details (Foudil et al., 2020; Hasson et al., 2015; Kwok et al., 2014). The IPL might be involved in the information sampling and selection processes (e.g., Baddeley, 2000), and thus the more first-order memory-related inputs received from the precuneus, the higher and more accurate confidence rating would be. The PrG or a broader presupplementary motor area (pre-SMA) region, which connects with the DLPFC and ACC, might be involved in cognitive control processes (Morales et al., 2018; Völker et al., 2018). The opposite pattern between confidence and metacognition in relation to the precuneus/right PrG connectivity suggests the respective processes

might differentially implicate a broader network such as a frontal-parietal network during episodic memory retrieval (Robin et al., 2015). Our findings on the relationship of the right IPL – precuneus and right PrG – precuneus rs-FCs with mnemonic metacognitive ability support the hypothesis that mnemonic metacognition relies on the read out of memory trace (Nelson and Narens, 1990). Together with the precuneus - hippocampus functional link (Ye et al., 2019) and a cortico-hippocampal network of meta-mnemonic process (McClelland et al., 1995; Wang et al., 2014; Zeidman et al., 2015), the hippocampus might be implicated in initiating the retrieval of the memory traces, which are then integrated to detailed recollections and conscious monitoring supported by the precuneus and the IPL (Richter et al., 2016).

In line with previous investigations (Allen et al., 2017; Bang et al., 2019; Fleming et al., 2014; Hauser et al., 2017b; Qiu et al., 2018; Rounis et al., 2010; Shekhar and Rahnev, 2018), the SLF FA was not related to primary TOJ performance. Our results lend support to the hierarchical model of metacognition (Fleming and Daw, 2017), which proposes that the metacognition evaluation is an inference based on primary decision-making evidence and other sources of information. The functional relevance of SLF might further provide evidence that how the domain-general hierarchical inference is implemented in the brain.

On a more speculative note, metacognition has been associated with states of consciousness (Lau and Rosenthal, 2011), and our current results help facilitate the understanding on the neurocognitive mechanisms underlying consciousness. Several studies have revealed that subjective conscious awareness is dissociated from the objective visual perception, and requires the involvement of the prefrontal and parietal cortices apart from primary sensory regions (Colás et al., 2019; Del Cul et al., 2009; Lau and Passingham, 2006; Persaud et al., 2011). It has been argued that to generate conscious experiences, a higher-level neural circuit needs to metacognitively access the primary sensory representation from the lower-level neural circuit to the working memory (Dehaene and Changeux, 2011; Lau and Rosenthal, 2011; Shea and Frith, 2019). Indeed, our results imply that, to form a conscious metacognitive evaluation, the IPL firstly represents first-order decision-making related information in the memory and then conveys it to the DLPFC via the SLF for further monitoring. Incidentally, in patients with right DLPFC lesion the structural integrity of the right SLF was significantly correlated with their subjective visual conscious experiences but not objective perception task performance (Colás et al., 2019). Moreover, the white-matter volume of the right SLF correlates with the metacognitive beliefs of schizophrenia patients (Spalletta et al., 2014). These clinical findings are in line with ours in the health, thereby reinforcing the possibility that the SLF is indeed needed for the higher-level conscious assessment of mental processes.

There are several caveats and intriguing issues for future research to consider. First, the small sample employed in the study inflated the observed correlations between metacognition and SLF-related structural and functional connectivity, and thus did not fully reflect the true effect size (Button et al., 2013). It is worthwhile for future research to recruit a larger sample size to replicate the effect we reported here. Second, the current study only concerns the two broad cognitive domains of perception and memory. Future research could test whether our “domain-general” results are applicable to other cognitive domains. Third, further research could employ the diffusion spectrum imaging (DSI) technique to better examine the structural integrity of the SLF and its functional relevance with metacognition by excluding the effects of crossing fibres. Future research could also consider using task-state fMRI together with dynamic causal modelling to draw a more comprehensive picture of the neural circuit of metacognition. Moreover, we noticed that TMS on the precuneus reduced above-average perceptual metacognitive performance but enhanced the below-average one, and resulted in a smaller variability of the perceptual metacognitive efficiency scores. The precuneus is in the default model network (DMN), and has been found in engaging in mind-wandering (Christoff et al., 2009). It could be possible

that inhibiting the mind-wandering process by the precuneus-TMS would partially improve the perceptual metacognitive function. Research in the future could target the interaction between DMN and other brain regions in supporting metacognition in different domains, and also the relationship between mind-wandering and metacognition.

In conclusion, our findings reveal how the structural integrity of the right SLF supports both perceptual and mnemonic metacognition, and how the efferent and afferent between the precuneus and the right SLF-connected regions support mnemonic metacognition. The results reveal that human metacognition relies on the superior longitudinal fasciculus to support metacognitive computation for both domain-general and domain-specific processes.

Credit author statement

Yunxuan Zheng: Conceptualization, Methodology, Formal analysis, Writing-Original Draft, Visualization; **Danni Wang:** Conceptualization, Methodology, Formal analysis, Writing-Original Draft, Visualization; **Qun Ye:** Conceptualization, Methodology, Investigation; **Futing Zou:** Conceptualization, Methodology, Investigation; **Yao Li:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Project administration, Funding Acquisition; **Sze Chai Kwok:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Project administration, Funding Acquisition.

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Declaration of competing interest

The authors declare no competing financial interests.

References

- Aitchison, L., Bang, D., Bahrami, B., Latham, P.E., 2015. Doubly Bayesian analysis of confidence in perceptual decision-making. *PLoS Comput. Biol.* 11 (10), e1004519.
- Allen, M., Glen, J.C., Müllensiefen, D., Schwarzkopf, D.S., Fardo, F., Frank, D., Callaghan, M.F., Rees, G., 2017. Metacognitive ability correlates with hippocampal and prefrontal microstructure. *Neuroimage* 149, 415–423.
- Baddeley, A., 2000. The episodic buffer: a new component of working memory? *Trends Cognit. Sci.* 4 (11), 417–423.
- Baird, B., Cieslak, M., Smallwood, J., Grafton, S.T., Schooler, J.W., 2015. Regional white matter variation associated with domain-specific metacognitive accuracy. *J. Cognit. Neurosci.* 27 (3), 440–452.
- Baird, B., Smallwood, J., Gorgolewski, K.J., Margulies, D.S., 2013. Medial and lateral networks in anterior prefrontal cortex support metacognitive ability for memory and perception. *J. Neurosci.* 33 (42), 16657–16665.
- Bang, J., Shekhar, M., Rahnev, D., 2019. Sensory noise increases metacognitive efficiency. *J. Exp. Psychol. Gen.* 148 (3), 437–452.
- Basser, P.J., Pajevic, S., Pierpaoli, C., Duda, J., Aldroubi, A., 2000. In vivo fiber tractography using DT-MRI data. *Magn. Reson. Med.* 44, 625–632.
- Berryhill, M.E., Phuong, L., Picasso, L., Cabeza, R., Olson, I.R., 2007. Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. *J. Neurosci.* 27, 14415–14423.
- Button, K.S., Ioannidis, J.P., Mokrysz, C., Nosek, B.A., Flint, J., Robinson, E.S., Munafò, M.R., 2013. Power failure: why small sample size undermines the reliability of neuroscience. *Nat. Rev. Neurosci.* 14 (5), 365–376.
- Carpenter, J., Sherman, M.T., Kievit, R.A., Seth, A.K., Lau, H., Fleming, S.M., 2019. Domain-general enhancements of metacognitive ability through adaptive training. *J. Exp. Psychol. Gen.* 148 (1), 51–64.
- Christoff, K., Gordon, A.M., Smallwood, J., Smith, R., Schooler, J.W., 2009. Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proc. Natl. Acad. Sci. U. S. A.* 106 (21), 8719–8724.
- Chua, E.F., Ahmed, R., 2016. Electrical stimulation of the dorsolateral prefrontal cortex improves memory monitoring. *Neuropsychologia* 85, 74–79.
- Colás, I., Chica, A.B., Ródenas, E., Busquier, H., Olivares, G., Triviño, M., 2019. Conscious perception in patients with prefrontal damage. *Neuropsychologia* 129, 284–293.
- Davidson, P.S., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A.S., Murphy, K.J., Troyer, A.K., Moscovitch, M., Levine, B., 2008. Does lateral parietal cortex support episodic memory? evidence from focal lesion patients. *Neuropsychologia* 46 (7), 1743–1755.
- Davis, S.W., Szymanski, A., Boms, H., Fink, T., Cabeza, R., 2018. Cooperative contributions of structural and functional connectivity to successful memory in aging. *Network Neuroscience* 3 (1), 173–194.
- Dehaene, S., Changeux, J.P., 2011. Experimental and theoretical approaches to conscious processing. *Neuron* 70 (2), 200–227.
- Del Cul, A., Dehaene, S., Reyes, P., Bravo, E., Slachevsky, A., 2009. Causal role of prefrontal cortex in the threshold for access to consciousness. *Brain* 132 (9), 2531–2540.
- Dougherty, R.F., Ben-Shachar, M., Deutsch, G.K., Hernandez, A., Fox, G.R., Wandell, B.A., 2007. Temporal-callosal pathway diffusivity predicts phonological skills in children. *Proc. Natl. Acad. Sci. U. S. A.* 104 (20), 8556–8561.
- Flavell, J., 1979. Metacognition and cognitive monitoring: a new area of cognitive-developmental inquiry. *Am. Psychol.* 34 (10), 906–911.
- Fleming, S.M., Daw, N.D., 2017. Self-evaluation of decision-making: a general Bayesian framework for metacognitive computation. *Psychol. Rev.* 124 (1), 91–114.
- Fleming, S.M., Dolan, R.J., 2012. The neural basis of metacognitive ability. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 367 (1594), 1338–1349.
- Fleming, S.M., Ryu, J., Golfinos, J.G., Blackmon, K.E., 2014. Domain-specific impairment in metacognitive accuracy following anterior prefrontal lesions. *Brain* 137 (10), 2811–2822.
- Fleming, S.M., Weil, R.S., Nagy, Z., Dolan, R.J., Rees, G., 2010. Relating introspective accuracy to individual differences in brain structure. *Science* 329 (5998), 1541–1543.
- Fleming, S.M., 2017. HMeta-d: hierarchical Bayesian estimation of metacognitive efficiency from confidence ratings. *Neurosci Conscious* 2017 (1), nix007.
- Fletcher, Paul, Frith, Chris, Suzanne, Baker, Tim, Shallice, Frackowiak, Richard, Dolan, Raymond, 1995. The mind's eye—precuneus activation in memory-related imagery. *Neuroimage* 2 (3), 195–200.
- Foudil, S.A., Kwok, S.C., Macaluso, E., 2020. Context-dependent coding of temporal distance between cinematic events in the human precuneus. *J. Neurosci.* 40 (10), 2129–2138.
- Friston, K.J., Williams, S., Howard, R., Frackowiak, R.S., Turner, R., 1996. Movement-related effects in fMRI time-series. *Magn. Reson. Med.* 35 (3), 346–355.
- Greicius, M.D., Supekar, K., Menon, V., Dougherty, R.F., 2009. Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cerebr. Cortex* 19 (1), 72–78.
- Hampson, M., Driesen, N.R., Skudlarski, P., Gore, J.C., Constable, R.T., 2006. Brain connectivity related to working memory performance. *J. Neurosci.* 26 (51), 13338–13343.
- Hasson, U., Chen, J., Honey, C.J., 2015. Hierarchical process memory: memory as an integral component of information processing. *Trends Cognit. Sci.* 19, 304–313.
- Hauser, T.U., Allen, M., Consortium, N.S.P.N., Rees, G., Dolan, R.J., 2017a. Metacognitive impairments extend perceptual decision making weaknesses in compulsivity. *Sci. Rep.* 7 (1), 1–10.
- Hauser, T.U., Allen, M., Purg, N., Moutoussis, M., Rees, G., Dolan, R.J., 2017b. Noradrenaline blockade specifically enhances metacognitive performance. *Elife* 6, e24901.
- Hebscher, M., Ibrahim, C., Gilboa, A., 2020. Precuneus stimulation alters the neural dynamics of autobiographical memory retrieval. *Neuroimage*, 116575.
- Hecht, E.E., Gutman, D.A., Bradley, B.A., Preuss, T.M., Stout, D., 2015. Virtual dissection and comparative connectivity of the superior longitudinal fasciculus in chimpanzees and humans. *Neuroimage* 108, 124–137.
- Heilbronner, S.R., Haber, S.N., 2014. Frontal cortical and subcortical projections provide a basis for segmenting the cingulum bundle: implications for neuroimaging and psychiatric disorders. *J. Neurosci.* 34 (30), 10041–10054.
- Heyes, C., 2016. Who knows? Metacognitive social learning strategies. *Trends Cognit. Sci.* 20 (3), 204–213.
- Jung, J., Bungert, A., Bowtell, R., Jackson, S.R., 2016. Vertex stimulation as a control site for transcranial magnetic stimulation: a concurrent TMS/fMRI study. *Brain Stimulation* 9 (1), 58–64.
- Kepecs, A., Uchida, N., Zariwala, H.A., Mainen, Z.F., 2008. Neural correlates, computation and behavioural impact of decision confidence. *Nature* 455 (7210), 227–231.
- Koch, G., Bonni, S., Pellicciari, M.C., Casula, E.P., Mancini, M., Esposito, R., Ponzo, V., Picazio, S., Di Lorenzo, F., Serra, L., et al., 2018. Transcranial magnetic stimulation of the precuneus enhances memory and neural activity in prodromal Alzheimer's disease. *Neuroimage* 169, 302–311.
- Kwok, S.C., Cai, Y., Buckley, M.J., 2019. Mnemonic introspection in macaques is dependent on superior dorsolateral prefrontal cortex but not orbitofrontal cortex. *J. Neurosci.* 39 (30), 5922–5934.
- Kwok, S.C., Shallice, T., Macaluso, E., 2012. Functional anatomy of temporal organisation and domain-specificity of episodic memory retrieval. *Neuropsychologia* 50 (12), 2943–2955.
- Kwok, S.C., Shallice, T., Macaluso, E., 2014. Set-relevance determines the impact of distractors on episodic memory retrieval. *J. Cognit. Neurosci.* 26, 2070–2086.
- Lau, H., Rosenthal, D., 2011. Empirical support for higher-order theories of conscious awareness. *Trends Cognit. Sci.* 15 (8), 365–373.
- Lau, H.C., Passingham, R.E., 2006. Relative blindsight in normal observers and the neural correlate of visual consciousness. *Proc. Natl. Acad. Sci. U. S. A.* 103 (49), 18763–18768.

- Lee, Alan, Ruby, Eugene, Giles, Nathan, Lau, Hakwan, 2018. Cross-domain association in metacognitive efficiency depends on first-order task types. *Front. Psychol.* 9, 2464.
- Lockhart, S.N., Mayda, A.B., Roach, A.E., Fletcher, E., Carmichael, O., Maillard, P., et al., 2012. Episodic memory function is associated with multiple measures of white matter integrity in cognitive aging. *Front. Hum. Neurosci.* 6, 56.
- McClelland, J.L., McNaughton, B.L., O'Reilly, R.C., 1995. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* 102, 419–457.
- McCurdy, L.Y., Maniscalco, B., Metcalfe, J., Liu, K.Y., De Lange, F.P., Lau, H., 2013. Anatomical coupling between distinct metacognitive systems for memory and visual perception. *J. Neurosci.* 33 (5), 1897–1906.
- Metzler-Baddeley, C., Jones, D.K., Belaroussi, B., Aggleton, J.P., O'Sullivan, M.J., 2011. Frontotemporal connections in episodic memory and aging: a diffusion MRI tractography study. *J. Neurosci.* 31 (37), 13236–13245.
- Morales, J., Lau, H., Fleming, S.M., 2018. Domain-general and domain-specific patterns of activity support metacognition in human prefrontal cortex. *J. Neurosci.* 38 (14), 3534–3546.
- Mori, S., Crain, B.J., Chacko, V.P., van Zijl, P.C., 1999. Three-dimensional tracking of axonal projections in the brain by magnetic resonance imaging. *Ann. Neurol.* 45, 265–269.
- Nelson, T.O., Narens, L., 1990. Metamemory: a theoretical framework and new findings. *Psychol. Learn. Motiv.* 26, 125–141.
- Park, H.J., Kim, J.J., Lee, S.K., Seok, J.H., Chun, J., Kim, D.I., Lee, J.D., 2008. Corpus callosal connection mapping using cortical gray matter parcellation and DT-MRI. *Hum. Brain Mapp.* 29 (5), 503–516.
- Persaud, Navindra, Davidson, Matthew, Maniscalco, Brian, Mobbs, Dean, Passingham, Richard, Cowey, Alan, Lau, Hakwan, 2011. Awareness-related activity in prefrontal and parietal cortices in blindsight reflects more than superior visual performance. *NeuroImage* 58 (2), 605–611.
- Qiu, L., Su, J., Ni, Y., Bai, Y., Zhang, X., Li, X., Wan, X., 2018. The neural system of metacognition accompanying decision-making in the prefrontal cortex. *PLoS Biol.* 16 (4), e2004037.
- Richter, F.R., Cooper, R.A., Bays, P.M., Simons, J.S., 2016. Distinct neural mechanisms underlie the success, precision, and vividness of episodic memory. *Elife* 5, e18260.
- Robin, J., Hirshhorn, M., Rosenbaum, R.S., Winocur, G., Moscovitch, M., Grady, C.L., 2015. Functional connectivity of hippocampal and prefrontal networks during episodic and spatial memory based on real-world environments. *Hippocampus* 25 (1), 81–93.
- Rouault, M., McWilliams, A., Allen, M.G., Fleming, S.M., 2018b. Human metacognition across domains: insights from individual differences and neuroimaging. *Personal Neurosci.* 1.
- Rouault, M., Seow, T., Gillan, C.M., Fleming, S.M., 2018a. Psychiatric symptom dimensions are associated with dissociable shifts in metacognition but not task performance. *Biol. Psychiatr.* 84 (6), 443–451.
- Rounis, E., Maniscalco, B., Rothwell, J.C., Passingham, R.E., Lau, H., 2010. Theta-burst transcranial magnetic stimulation to the prefrontal cortex impairs metacognitive visual awareness. *Cognit. Neurosci.* 1 (3), 165–175.
- Samaha, J., Barrett, J.J., Sheldon, A.D., LaRocque, J.J., Postle, B.R., 2016. Dissociating perceptual confidence from discrimination accuracy reveals no influence of metacognitive awareness on working memory. *Front. Psychol.* 7, 851.
- Seeley, W.W., Menon, V., Schatzberg, A.F., Keller, J., Glover, G.H., Kenna, H., Reiss, A.L., Greicius, M.D., 2007. Dissociable intrinsic connectivity networks for salience processing and executive control. *J. Neurosci.* 27 (9), 2349–2356.
- Shea, N., Frith, C.D., 2019. The global workspace needs metacognition. *Trends Cognit. Sci.* 23 (7), 560–571.
- Shekhar, M., Rahnev, D., 2018. Distinguishing the roles of dorsolateral and anterior PFC in visual metacognition. *J. Neurosci.* 38 (22), 5078–5087.
- Simons, J.S., Peers, P.V., Mazuz, Y.S., Berryhill, M.E., Olson, I.R., 2010. Dissociation between memory accuracy and memory confidence following bilateral parietal lesions. *Cerebr. Cortex* 20 (2), 479–485.
- Spalletta, G., Piras, F., Piras, F., Caltagirone, C., Orfei, M.D., 2014. The structural neuroanatomy of metacognitive insight in schizophrenia and its psychopathological and neuropsychological correlates. *Hum. Brain Mapp.* 35 (9), 4729–4740.
- Teubner-Rhodes, S., Vaden, K.I., Cute, S.L., Yeatman, J.D., Dougherty, R.F., Eckert, M.A., 2016. Aging-resilient associations between the arcuate fasciculus and vocabulary knowledge: microstructure or morphology? *J. Neurosci.* 36 (27), 7210–7222.
- Völker, M., Hammer, J., Schirmeister, R.T., Behncke, J., Fiederer, L.D., Schulze-Bonhage, A., Marusić, P., Burgard, W., Ball, T., 2018. Intracranial Error Detection via Deep Learning.
- Vilberg, K.L., Rugg, M.D., 2008. Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. *Neuropsychologia* 46, 1787–1799.
- Wakana, S., Caprihan, A., Panzenboeck, M.M., Fallon, J.H., Perry, M., Gollub, R.L., Hua, K., Zhang, J., Jiang, H., Dubey, P., et al., 2007. Reproducibility of quantitative tractography methods applied to cerebral white matter. *Neuroimage* 36 (3), 630–644.
- Wallis, G., Stokes, M., Cousijn, H., Woolrich, M., Nobre, A.C., 2015. Frontoparietal and cingulo-opercular networks play dissociable roles in control of working memory. *J. Cognit. Neurosci.* 27 (10), 2019–2034.
- Wang, J.X., Rogers, L.M., Gross, E.Z., Ryals, A.J., Dokucu, M.E., Brandstatt, K.L., Hermiller, M.S., Voss, J.L., 2014. Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science* 345, 1054–1057.
- Ye, Q., Zou, F., Dayan, M., Lau, H., Hu, Y., Kwok, S.C., 2019. Individual susceptibility to TMS affirms the precuneal role in meta-memory upon recollection. *Brain Struct. Funct.* 224 (7), 2407–2419.
- Ye, Q., Zou, F., Lau, H., Hu, Y., Kwok, S.C., 2018. Causal evidence for mnemonic metacognition in human precuneus. *J. Neurosci.* 38 (28), 6379–6387.
- Yeatman, J.D., Dougherty, R.F., Myall, N.J., Wandell, B.A., Feldman, H.M., 2012. Tract profiles of white matter properties: automating fiber-tract quantification. *PLoS One* 7 (11), e49790.
- Yeatman, J.D., Wandell, B.A., Mezer, A.A., 2014. Lifespan maturation and degeneration of human brain white matter. *Nat. Commun.* 5 (1), 1–12.
- Yeung, N., Summerfield, C., 2012. Metacognition in human decision-making: confidence and error monitoring. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 367 (1594), 1310–1321.
- Zeidman, P., Mullally, S.L., Maguire, E.A., 2015. Constructing, perceiving, and maintaining scenes: hippocampal activity and connectivity. *Cerebr. Cortex* 25, 3836–3855.
- Zylberberg, A., Barttfeld, P., Sigman, M., 2012. The construction of confidence in a perceptual decision. *Front. Integr. Neurosci.* 6, 79.
- Zylberberg, A., Fetsch, C.R., Shadlen, M.N., 2016. The influence of evidence volatility on choice, reaction time and confidence in a perceptual decision. *Elife* 5, e17688.