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Research Report

Regulation of action selection based on metacognition in humans via a ventral and dorsal medial prefrontal cortical network

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ABSTRACT

Metacognition is defined as cognition about one's own cognitive state; it enables us to estimate our own performance during goal-directed actions and to select a suitable strategy based on that estimation. Identifying the neural mechanisms that underlie this process will contribute to our understanding of how we realize adaptive self-control in daily life. Here, we focused on the neural substrates that allow us to voluntarily utilize prospective metacognition to carry out such action selection. Participants were asked to bet on their recall of sound stimuli presented at an earlier time in a delayed match-to-sample task of rapidly changing sound stimuli. During the task, brain activity was measured using functional magnetic resonance imaging. We found that the brain network composed of the ventral and dorsal parts of the medial prefrontal cortex and the medial precuneus regulated the strategic selection of risk/return profiles based on metacognition. In particular, increments in functional connectivity between the ventral and dorsal medial prefrontal cortices during high-risk/return bets correlated with the adaptiveness of the bet (as measured by the correspondence between choosing high risk/return bets and high accuracy of task performance). This index is considered to reflect the degree of voluntary use of metacognition to bet. These findings suggest that the strong connectivity within the network involving the ventral and dorsal medial prefrontal cortices enables us to utilize metacognition to select actions for achieving a goal efficiently.

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1. Introduction

Metacognition is broadly defined as "knowledge and cognition about cognitive phenomena" (Flavell, 1979, p. 906), and it enables us to adaptively select reasonable behaviors to accomplish desired goals (Efklides, 2008; Fernandez-Duque, Baird, & Posner, 2000; Gourgey, 1998; Nelson & Narens, 1990; Smith, Shields, & Washburn, 2003). One of the core functions of metacognition is to increase the flexibility and effectiveness of behavioral adaptation (Fernandez-Duque et al., 2000; Gourgey, 1998).

Prospective and voluntary action selection is a typical example of behavioral adaptation based on metacognition, and it can help prevent future problems. For example, when we withdraw cash from an ATM, the number of times we try to type the password is based on our confidence about our memory of the password. If we are confident, we may decide to try more times than if we realize we do not remember the password. This is something we decide internally before actually typing. In doing so, we prevent being locked out of our bank account from entering the wrong password too many times. Revealing the neural mechanisms that underlie this action selection based on prospective metacognition about memory will contribute to our understanding of how we realize adaptive self-control in daily life situations.

Previous neuroimaging studies have suggested that activation of the prefrontal and posterior parietal/cingulate cortices is involved in metacognition of the confidence about memory, and that each region plays a different role (see Chua, Pergolizzi, & Weintraub, 2014, pp. 267–291). These studies asked participants to self-report on their metacognition of their prediction or postdiction for performance in a cognitive task (as summarized in Chua et al., 2014, pp. 267–291), and the task was designed so that self-reporting did not affect the performance of the cognitive task (Fleming, Dolan, & Frith, 2012). The paradigm effectively isolated the neural correlates underlying metacognitive monitoring and thus contributed to the advancement of neurophysiological research on metacognition. However, the neural basis for action selection via metacognition is still unclear, and we address this in our study. Moreover, in previous studies, it is possible that neural correlates for self-report itself overlap with those associated with metacognition.

Therefore, by not including self-report in our paradigm, the present study in a novel way investigates the neural mechanism that allows us to carry out action selection based on metacognition about memory to efficiently accomplish a cognitive task. To select the best of several possible actions, information gained by metacognition must be integrated and reflected into the selection. Hence, the multiple regions reported for metacognition (i.e., prefrontal and posterior parietal/cingulate cortices) should be activated, and these activations could be intercorrelated during the action selection based on metacognition. We assume that functional integration between regions is reflected in the functional connectivity (Friston et al., 1997; Van Den Heuvel & Pol, 2010). Thus, we hypothesize that the action selection based on metacognition is reflected in the brain as changes in activations of, and in functional connectivity between, the regions distributed among the prefrontal and posterior parietal/cingulate cortices.

As exemplified above, people can adaptively select actions based on metacognition without verbal instruction to do so or the requirement to provide self-reports about their own metacognition in daily-life situations. To fully reveal the neural mechanism underlying such behavioral adaption and to exclude possible confounds of self-reports, the present study avoided using explicit verbal instructions or self-reporting by applying a behavioral paradigm that has been used for studying metacognition in infants as well as animals (Basile & Hampton, 2014; Fujita, 2010; Goupil, Romand-Monnier, & Kouider, 2016; Hampton, 2009; Smith et al., 2003; Tanaka & Funahashi, 2007). The behavioral task used in our study consisted of an auditory memory task and a risk/return choice (high or low risk/return) and was designed to induce reliance on metacognition to adaptively choose a betting option. We particularly focused on the relationship between the degree of reliance on metacognition and actual task performance to investigate how participants executed the action selection based on metacognition. Brain activity during this task was measured using functional magnetic resonance imaging (fMRI), and the consistency of our results with previous reports was evaluated using a meta-analysis. Then, we assessed the change in functional connectivity between the activated regions in relation to action selectability based on metacognition, using a psychophysiological interaction (PPI) analysis (Friston et al., 1997).

To assess individual differences, we further calculated a behavioral measure that reflected individual difference in the degree of reliance on metacognition for action selection. The measure was the difference in performance in two different situations where metacognition was either available (selectable condition) or not available (forced condition). In the available condition, only metacognition is an effective cue for selecting the high risk/return option. Improvements in performance induced by voluntary high risk/return bets can be regarded as having more reliance on metacognition about memory. This measure is identical to the behavioral index of metacognition used in previous animal studies (Hampton, 2001) and suitable to aseess the degree of reliance on metacognition for action selection. To confirm whether our index appropriately reflects individual differences in the degree of reliance on metacognition, we tested the consistency between the index in our task and self-assessed reliance on prospective metacognition in daily life through a questionnaire.

2. Materials and methods

2.1. Participants

Forty-two participants (20 females, 18–23 years old, mean ± SD: 19.4 ± 1 years) participated in this study. Participants had normal or corrected-to-normal vision and normal hearing, and were right-handed [laterality quotient (Oldfield, 1971): .83 ± .15]. We recruited only participants who stated that they did not have a history of neurological disease or absolute pitch. The participants that had absolute pitch were excluded because tone sequences are presented in the

experiments. Written informed consent was obtained from all participants before starting the experiments. All experimental protocols were performed in accordance with relevant guidelines and regulations, and were approved by the institutional ethics committee at the University of Tokyo (No. 386).

2.2. Tasks

There were two tasks for participants in this study: a "Metacog" task and a "Detect" task. The Metacog task was based on a delayed match-to-sample paradigm requiring participants to perform a risk selection. Each trial consisted of a *sample* (.5 sec), *delay* (3.0 sec), *bet* (2.0 sec), *match* (1.1 sec), and *answer* (1.0 sec) phase (Fig. 1A). Participants were asked to decide whether a sound stimulus presented in the *match* phase was the same as or different from that presented in the *sample* phase by pressing the left or right response buttons in the *answer* phase. In half of the trials, they had to choose high or low risk/returns in the *betting* phase based on their confidence level (see explanations below in detail) prior to the answer phase; two white squares were presented vertically to show the bet options and participants indicated their choice by pressing the upper or lower response buttons (*selectable* condition). Because the bet had to be selected before listening to the matching stimulus, the only effective cue that participants could rely on to predict their success or failure in each trial was their confidence in their memory of the sample stimulus. Thus, the selectable condition of the Metacog task was expected to strongly elicit action selection based on metacognition. In the other half of the trials, the participants had only one option in the *betting* phase and were forced to press that button as indicated by a single white square on the screen (*forced* condition). The forced condition was employed to assess the baseline accuracy in both risk/return trials for each task, excluding the effect of confidence or selection itself. Comparing brain activations in the *betting* phase between these two selectability conditions in the Metacog task can isolate activations related to the action selection based on metacognition.

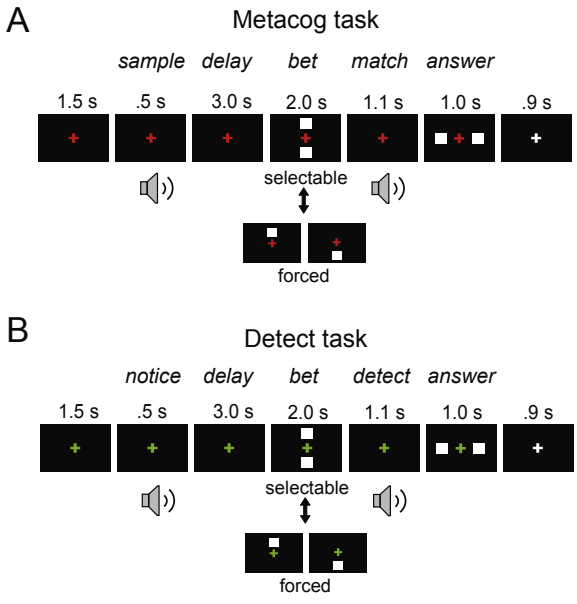

Fig. 1 – Schematic drawings of the experimental tasks. (A, B) Time sequence of the Metacog (A) and Detect (B) trials during fMRI imaging. The color of the fixation cross informed participants of the upcoming task (red: Metacog; green: Detect). Participants had to select one of two betting options, high or low risk/return, in the "*betting*" phase before performing the matching or the detection task. In the Metacog task, the second sound had to be matched ("*match*" phase) to the first sound stimulus ("*sample*" phase). In the Detect task, participants had to detect a target sound stimulus ("*detect*" phase) in background masking noise; the loudness of the sound was indicated in the "*notice*" phase.

The Detect task was introduced in the experiment as a control for non-metacognitive factors, which possibly influence participant's action selection. This task required participants to detect a target stimulus embedded in background noise. Each trial of the Detect task also consisted of five phases with the same temporal sequence as the Metacog task: *notice*, *delay*, *bet*, *detect*, and *answer* phases (Fig. 1B). Participants were asked to judge if the target stimulus was presented in the *detect* phase, and responses were given by a right/left key press in the *answer* phase. We created two levels of task difficulty by manipulating the loudness level of the background noise in the *detect* phase. A short excerpt of the background noise was presented in the "notice" phase so that participants could predict the task difficulty from the loudness of noise before performing the detection. The actions required in the Detect task were identical to those in the Metacog task, but metacognition about memory was not an effective cue to choose a bet option in the Detect task because participants did not need to memorize the sound presented in the *notice* phase. They simply needed to take notice of the noise level to predict the difficulty of the task. Thus, we expected action selection in the selectable condition of the Detect task to be based on non-metacognitive factors such as perceptual information and task motivation. Half of the trials were in the *selectable* condition, and participants bet either high or low risk/return options by pressing the upper or lower response button in the *betting* phase. The other half of the trials were in the *forced* condition where the participants were required to choose a single betting option indicated as a single white square on the screen. Comparing brain activations in the *betting* phase between the two selectability conditions in the Detect task should isolate activations related to action selection mainly based on non-metacognitive factors.

To notify participants about whether the upcoming trial was a Metacog or a Detect task, the color of the fixation cross was initially white and changed to either red (Metacog) or green (Detect) 1.5 sec before presenting the first sound. This color reverted to white at the end of the trial. In both tasks, a distractor sound was also presented in the *delay* phase to maintain task difficulty.

In each trial, participants gained or lost points according to whether or not their response was correct, and the goal was to maximize the total score per session. For correct answers, the score increased by two points (high risk/return) or by one

point (low risk/return). Participants lost one point when they responded incorrectly after a high risk/return bet, but lost no points when they responded incorrectly after a low risk/return bet. Trials in which they failed to press a button properly within the *betting* and/or *answer* phase (3.6% out of all trials) were excluded from the final score calculation. The high risk/return condition was presented if the participant failed to press a button within the *betting* phase, to prevent intentional trial avoidance. Additionally, participants were instructed not to persist with only one risk/return option during each session in order to avoid a selection bias. We randomly allocated the correct side (left or right) in the *answer* phases of both tasks, based on the Gellermann sequence (Gellermann, 1933).

2.3. Sound stimuli

Three types of sound stimuli were used in these experiments: a tone sequence, a distractor, and background noise. The eight-tone sequence (duration: 62.5 msec per a tone with a 10-ms rise/decay, 500 msec total) was the target sound that participants had to memorize and detect during the experiment. Each tone had six harmonic components (−6 dB/oct.) with a fundamental frequency (F0) at 440.0, 493.9, 554.4, 622.3, 698.5, 784.0, 880.0, 987.8, or 1108.7 Hz (which corresponds to a whole-tone scale from A_4 to $D^{\#}_6$ in music notation). The F0 of the first and last tone was fixed at 698.5 Hz (F_5), and those of the other six tones were randomly selected from the nine frequencies. In the *match* and *detect* phases, the tone sequence was presented after a .3-sec inter-stimulus-interval (ISI). After the presentation, the same .3-sec ISI was inserted. To control for memorability of sounds, sequences that had more than three consecutive change directions in F0 (three ups or three downs) were excluded. In each session, similarity among sequences was moderate (absolute correlation $\leq$ .6). Each sequence was presented only once to each participant. A "false" stimulus was also included in the *match* phase of the Metacog task; this stimulus was designed to have the same change directions in the F0 for the last three tones as the target stimulus presented in the *sample* phase (absolute correlation $\leq$ .2). To remove a possible effect of stimulus order, we randomized stimulus presentation across participants according to the Latin squares of order 10.

The distractor sound was a sound sequence that consisted of 63 tones with the same frequency pattern as the tone sequence, but its duration was 2500 msec total (39.7 msec for each tone). The background noise was a tone cluster with the same spectral range as the tone sequence. We created the cluster by randomly mixing up eight different distractor sounds using random time jittering. The amplitude level was set to −9 and −3 dB for the signal-to-noise ratio compared to the tone sequence, for the low and high-risk conditions, respectively. We truncated the tone cluster to yield durations of 500 msec and 1100 msec, and used these for the *notice* and the *detect* phases in the Detect task, respectively. The distractor sound was presented continuously in the *detect* phase.

All sound stimuli were created digitally at a 16-kHz sampling rate using MATLAB software (R2014b; MathWorks Inc., Natick, MA, USA). Sound amplitudes were adjusted to be a comfortable level for each participant. Presentation software (ver.18.1; Neurobehavioral Systems Inc., Albany, CA, USA) was used for stimulus and response control during both the behavioral and the fMRI experiments.

2.4. Experimental design

The entire experiment consisted of fMRI-scanning sessions and behavioral sessions conducted outside the fMRI scanner, both of which consisted of four types of trials (Metacog/Detect tasks × forced/selectable conditions).

Each participant successively performed six fMRI sessions, and each session consisted of 24 trials (144 trials in total; 36 trials per type). In the fMRI session, four trials were successively performed with inter-trial-intervals of .9 sec (task block), and resting intervals of 11 sec (rest block) were inserted between task blocks; hence, six task blocks were performed per session. All four conditions randomly appeared in each task block. We added rest blocks at the beginning (10 sec in duration) and end (28 sec) of each session to measure baseline activity. After each session, the total score was presented at the center of the display for 10 sec. The total number of high risk/return options in the forced condition was adjusted to have the same number as in the selectable condition for each task by copying the participant's response in the last task block. In the first task block, in which there was no previous participant data, the forced options (high or low risk/return) were randomly determined. This procedure was conducted to remove possible bias in the number of selected options between selectable and forced conditions, which could affect brain activity. The frequency of the high risk/return option in the Metacog task during the scan was 63.1 ± 11.8% for the selectable condition and 60.9 ± 11% for the forced condition. In the Detect task, this was 50.9 ± 10.9% and 51.3 ± 9.8% for the selectable and forced conditions, respectively. Additionally, two practice sessions were provided inside the scanner just before starting the imaging.

One or two days before the fMRI sessions, participants completed six non-imaging behavioral sessions without laying in the fMRI scanner, in order to become familiarized with the tasks. The behavioral sessions were modified from the fMRI sessions as follows: all forced trials were fixed to the high risk/return option, and we inserted a rating phase after each trial (2 sec) in which participants rated their confidence in the correctness of their response on a scale of 1–5. The rest blocks between the task blocks lasted 3 sec. After each session, the total score was presented at the center of the display. Immediately before the behavioral sessions, handedness (Oldfield, 1971) and musical experience were assessed using questionnaires, and working memory was assessed using a two-back test (Kirchner, 1958) using five Japanese vowel sounds. Results of handedness and musical experience were reported in the Participants section. Working memory was not analyzed or reported.

2.5. Adaptiveness index and behavioral data analysis

Performance accuracy (i.e., the rate of correct response) was calculated for each condition. In the Metacog task, only the metacognition on sample stimulus memory is an effective cue for selecting the high risk/return option. If the level of risk choice was based on metacognition, participants should only

choose high risk/returns in high-confidence trials. Thus, the difference in accuracy between forced high risk/return trials and selected high risk/return trials in the Metacog task is considered to reflect the degree of voluntary use of metacognition to bet. Note that the same calculation (difference in accuracy between the conditions) could be performed on the Detect task data, though the result would not reflect the degree of voluntary use of metacognition for betting because participants do not rely on metacognition for the Detect task. We calculated the difference in accuracy between the two conditions (selectable and forced) and defined this as the"-adaptiveness index" (see Fig. 4A) for both tasks. This index can be considered as the correspondence between high risk/return bets and high accuracy. To obtain stable results, we averaged the calculated indices for fMRI and behavioral sessions. We excluded the data from the first two behavioral sessions to avoid the potential effect of unfamiliarity.

2.6. Metacognition questionnaire

Participants completed the Japanese edition of the Metacognitive Awareness Inventory (Abe & Ida, 2010; Schraw & Dennison, 1994) to measure subjective awareness on the voluntary use of metacognition for learning in daily life. This questionnaire assesses eight factors related to metacognition, such as information management strategies, monitoring, and planning; however, we only focused on the score related to planning, since the task employed in this study required use of prospective metacognition to select actions. We tested the relationship between the score for planning in the questionnaire and the adaptiveness index calculated from the Metacog and Detect tasks.

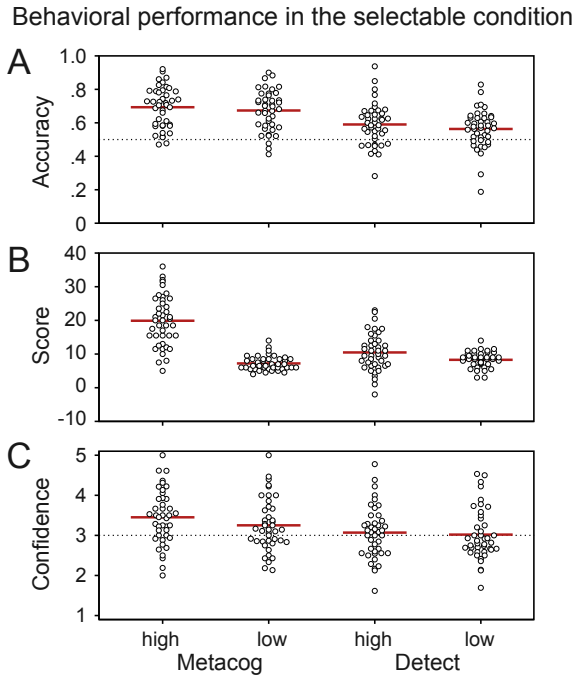

Fig. 2 – Distribution of individual behavioral performance in the selectable condition. Distribution of (A) performance accuracy, (B) total score, and (C) averaged confidence level of participants for the selected high and low risk/return trials in the Metacog and Detect tasks. Each circle represents a participant, and red bars show the mean value.

2.7. Equipment

The behavioral experiment was conducted in a soundproof room. A computer display was set up in front of the participant, at a visual angle of 16°. Sound stimuli were presented via headphones (ATH-T22, Audio-Technica, Japan). Additionally, we continuously presented acoustical noise from the fMRI scanner (EPI noise) via headphones, to imitate the environment during the fMRI experiment. We used a computer keyboard instead of response pads to detect participants' responses.

For the fMRI experiment, auditory stimuli were delivered via MRI-compatible headphones (Serene sound system, Resonance Technology Inc., Northridge, CA, USA). Visual stimuli were presented on an MRI-compatible flat-panel LCD display (NNL-LCD, NordicNeuroLab, Bergen, Norway). Subjects viewed stimuli on the display through an oblique mirror mounted on the head coil. The display had a resolution of 1920 × 1080 pixels and a refresh rate of 60-frames/s. The viewing distance was 212 cm, and the size of the display was 70.0 × 39.5 cm^2, so that all visual stimuli were presented within 16° of visual angle. To detect responses, two response pads with two buttons each were used (HHSC-1x2-BY and HHSC-1x2-GR, Current Designs, Philadelphia, PA, USA). Subjects held one pad vertically in the left hand (high and low risk/return options) and another pad horizontally in the right hand ("same"/"detect" and "different"/"undetected" responses). Participants were instructed to look at a fixation cross (.22°) and keep their eyes on the cross whenever possible.

2.8. fMRI scanning

Brain data acquisition was performed with a 3.0 T MRI scanner (MAGNETOM Prisma; Siemens, Erlangen, Germany) at the University of Tokyo, Tokyo, Japan. We used a 20-ch head coil. Functional data were derived as T2*-weighted images using an echo planar imaging (EPI) scanning sequence [voxel size: 3.0 × 3.0 × 3.2 mm^3; 35 slices of 3.2 mm thickness with a .8-mm gap; repetition time (TR): 2000 msec; echo time (TE): 30.0 msec; field of view (FOV) = 192 × 192 mm^2; flip angle (FA) = 90°; interleaved scanning order; phase overlapping: 0%]. The scanning plane was tilted 30° upwards from the AC-PC line in the direction of the forehead. The first four scans were discarded due to T1-relaxation instability. Brain anatomical data were obtained as 3D T1-weighted images using a Magnetization Prepared Rapid Acquisition Gradient Echo (MPRAGE) sequence [voxel size: 1.0× 1.0 × 1.0 mm^3, TR: 2000 msec, TE: 2.9 msec, 176 slices, FOV = 256 × 256 mm^2, FA = 9°].

2.9. Preprocessing and statistical analysis of imaging data

Spatial preprocessing and statistical analysis of imaging data were performed using SPM8 (The Wellcome Trust Centre for Neuroimaging, University College London, UK). All functional

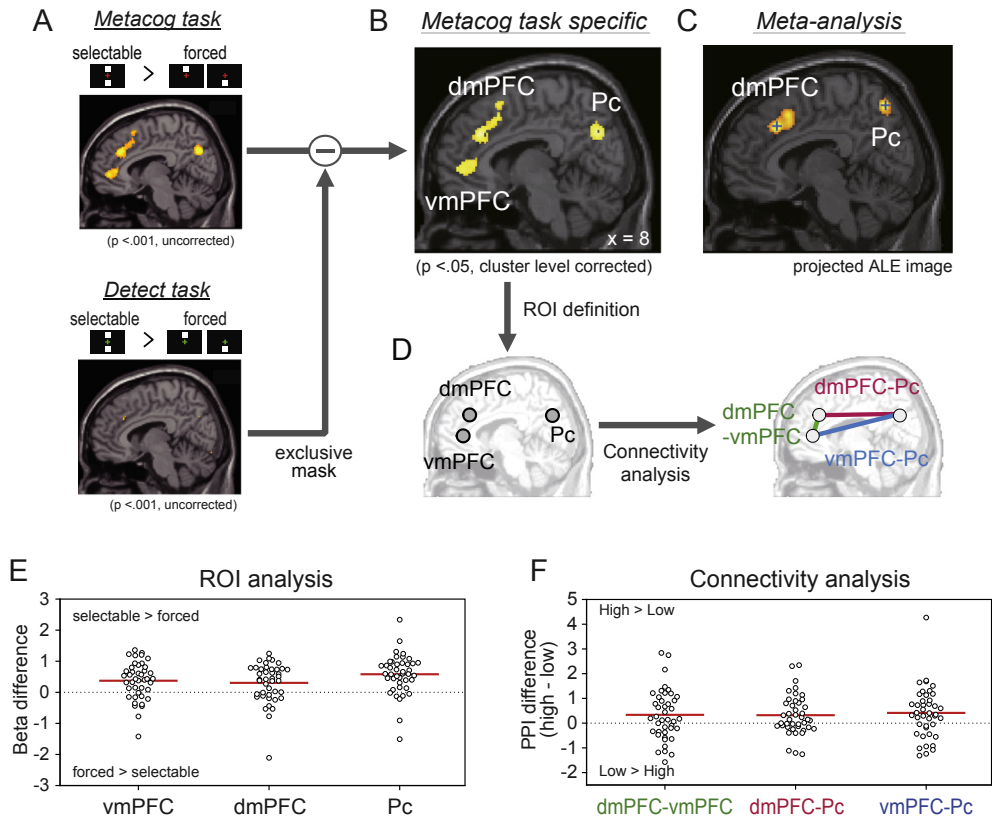

Fig. 3 – (A) Schematic representation for the process to identify brain regions related to action selection based on metacognition. Full details are in the Methods section. (B) Significant activations related to action selection based on metacognition were found in the ventral and dorsal medial prefrontal cortices (dmPFC and vmPFC), as well as in the medial precuneus region (Pc). (C) Accumulated activation patterns from a meta-analysis of previous reports on metacognition. Here, we only show the significant clusters that have the peak coordinates in the medial regions ($-16 \leqq x \leqq 16$). The ALE image was projected onto the y-z plane by calculating the maximum values, and they are corresponding to the dmPFC and Pc clusters in Table 3. The blue crosses show the peak of the reported clusters. Statistical significance was tested at $p < .05$ (FWE corrected at cluster level, and cluster-defining threshold was $p < .001$ in voxel level) for the activation contrast (B), and at uncorrected $p < .001$ voxel level for the meta-analysis (C). (D) Three regions of interest used for the connectivity analysis: ventromedial prefrontal cortex (vmPFC), dorsomedial prefrontal cortex (dmPFC), and posterior cingulate/precuneus region (Pc). These ROIs were defined based on the peak coordinates of metacognition-related clusters. We focused on functional connectivity among these three regions since we hypothesized that action selection based on metacognition is facilitated by the integration of information across regions related to action selection based on metacognition. (E) Individual effect differences between the selectable and the forced conditions in the Metacog task obtained within the three regions of interest (ROIs), which were spheres centered at the dmPFC, the vmPFC, and the Pc with a radius of 8 mm. Each circle represents a participant. (F) Differences in connectivity indices between high and low risk/return choice in the selectable condition of the Metacog task for each area combination. Each circle represents a participant, and red bars show the mean value.

images were realigned to the first image and re-sliced. Realigned images were co-registered to a segmented T1 image, normalized to the MNI template image, and smoothed using an 8-mm full-width-at-half-maximum Gaussian kernel.

Statistical processing at the individual level was performed by a general linear model analysis. To construct a design matrix, we divided each trial into three epochs corresponding to the *betting* phase and before and after the *betting* phase. In addition, we divided each epoch into 4 regressors corresponding to all combinations: two tasks × two selectability conditions. Thus, 12 regressors were included in the general linear model (two tasks: Metacog, Detect × two selectability conditions: selectable, forced × three epochs for each session). These regressors were composed of the canonical hemodynamic response function convolved with boxcar functions for the epochs.

The short but fixed intervals in our task design could potentially lead to high correlations among regressors, and this could increase the variability of the parameter estimates. Since the mean of multiple estimates from independent subjects will converge on the true mean estimate at the group level (Mumford, Poline, & Poldrack, 2015), high correlations among regressors can be problematic in individual-level statistics. Thus, we assessed a potential risk of collinearity among regressors at the individual level statistics in the fMRI analysis. We calculated the variance inflation factor (VIF) to

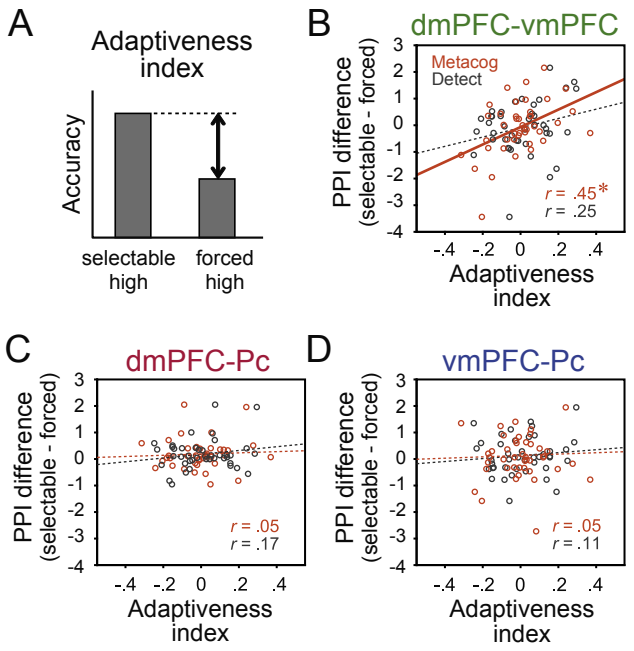

Fig. 4 – Behavioral index for adaptiveness of bet choice and its correlation with functional connectivity among the metacognition-related brain regions (A) The adaptiveness index was calculated as the difference in accuracy for the high risk/return option between the selectable and forced conditions. (B–D) Correlation between increased connectivity in selected high risk/return bet trials compared to forced high risk/return bet trials and individual adaptiveness in the three region combinations for the Metacog (orange) and Detect (grey) tasks: dmPFC-vmPFC (B), dmPFC-Pc (C), and vmPFC-Pc (D). *statistically significant with $p < .01$. p values were corrected for multiple comparisons using the Bonferroni method.

quantify the collinearity among regressors of our data (Mumford et al., 2015). This analysis judges the statistical model as containing problematic collinearity when the VIF value exceeds a predefined threshold, which is usually set to 5 (Mumford et al., 2015). We calculated the VIF value from 12 regressors (2 tasks x 2 conditions x 3 phases) for the first-level design matrices after AR filter and whitening, excluding constant terms per sessions. The maximum VIF was 4.6 (less than 5). Thus, collinearity was not taken into account in any further analyses.

The group-level analysis was conducted using a flexible factorial design including estimated effects (beta values) for the four regressors of the *betting* phase. To reduce possible effects related to differences in task difficulty, we also included individual performance accuracies (four values for each participant) into the model as covariates. Sessions where inter-scan head motion exceeded 1 mm in any of the x, y, or z directions were excluded from the analysis.

Using an exclusive masking technique, we identified the regions related to the process that leads metacognition to action selection (as shown in Fig. 3A). We examined regions which showed significantly greater activation for the selectable condition than for the forced condition in the Metacog task (family-wise error-corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level; Fig. 3A), while excluding regions that showed significantly stronger activation for the selectable than for the forced condition in the Detect task ($p < .001$; voxel level, uncorrected; Fig. 3B). This exclusive masking did not affect the statistics of the group-level analysis and allowed us to isolate the brain regions related to the process that leads metacognition to action selection by excluding any regions related to action selection itself. For this reason, we uniformly excluded the voxels that showed significantly greater activation for the selectable condition than for the forced condition during betting in the Detect task, even if the voxel had more sensitivity to action selectability in the Metacog task than the Detect task. The statistical threshold for the whole-brain analysis at the group level after exclusive masking was set at $p < .05$ (family-wise error-corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level).

Additionally, we assessed possible activations shared between selectable and forced conditions of both tasks by conjunction analyses (Friston, Holmes, Price, Büchel, & Worsley, 1999) with the statistical threshold set at $p < .05$ (FWE corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level) to isolate the activation related to risk selectability itself regardless of the task. Moreover, to exclude the possibility that differences in the task (i.e., task difficulty, presented sound stimuli, and so on) affected the results of the above-mentioned analyses, we also identified the regions related to task difference by directly comparing activations for the Metacog and Detect tasks ($p < .05$, FWE corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level).

2.10. *Meta-analysis*

To know how the brain regions involved in betting during the Metacog task overlapped with previously reported metacognition-related regions, we performed a coordinate-based meta-analysis (Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012; Eickhoff et al., 2009; Turkeltaub et al., 2012) on stereotaxic coordinates of activation peaks reported in previous studies that focused on metacognition about memory. First, we surveyed an online database for biomedical research (PubMed; https://www.ncbi.nlm.nih.gov/pubmed/) using combinations of search keywords related to metacognition about memory (e.g., metacognition, feeling of knowing, memory confidence) and brain imaging (e.g., functional MRI, neural correlates, brain activity) to create a list of relevant literature (as of March 25, 2017). We also listed a research paper that was introduced in a review paper on brain activity for metacognition about memory (Chua et al., 2014, pp. 267–291) but was not registered on PubMed. We then narrowed the list down to non-pathological reports on fMRI experiments in healthy participants that included a group-level whole-brain analysis.

We excluded activation peaks that did not belong in either of the following categories: significantly activated/deactivated in situations where a response based on metacognition about memory was required (i.e., a task requiring behavioral regulation rather than passive viewing of stimuli; Category 1), or significantly altered by the degree of self-report about

metacognition about memory (Category 2). We chose the most relevant contrast if the paper contained multiple contrasts, and selected only the maximum peak when the paper reported several peaks for one cluster (the list of literature is available as supplementary material). We then performed a coordinate-based meta-analysis on the list of extracted coordinates using GingerALE ver. 2.3 (www.brainmap.org/ale/), and obtained the ALE image with a statistical threshold of $p < .05$, cluster level, FWE-corrected (cluster-defining threshold was $p < .001$ in voxel level).

To quantify the overlap between the results of our whole brain analysis and the meta-analysis, we calculated the co-occurrence probability between them using Mango software (v 4.0.1; http://ric.uthscsa.edu/mango/mango.html) for the dorsomedial prefrontal cortex, ventromedial prefrontal cortex, and precuneus clusters of our whole brain analysis by the following formula:

$$probability\ for\ each\ cluster = \frac{\#voxels\ of\ meta-analysis\ result\ included\ in\ the\ cluster}{\#voxels\ of\ the\ cluster}$$

Please note that this meta-analysis used only the peak coordinates and number of participants and did not take into account other information such as size or shape of the original clusters or the statistics for each coordinate such as t-value. Thus, voxels obtained in the meta-analysis need not exactly match common activation patterns seen in previous studies. Despite the above limitations, we compared the results of our whole brain analysis and that of the meta-analysis to provide a comprehensive analysis on the consistency between them.

2.11. ROI definition and functional connectivity analysis

Three regions of interest (ROIs) were defined as spheres centered at the dmPFC (8, 34, 32), the vmPFC (−2, 42, 6), and the Pc (−4, −70, 34), with a radius of 8 mm (see Fig. 3D, left). These center coordinates are defined according to the peaks in activation clusters that showed significantly greater activation for the selectable condition than for the forced condition in the Metacog task (Fig. 3B). We extracted estimated effects (beta values) in the ROIs using MarsBaR (ver.0.44; http://marsbar.sourceforge.net) from the individual level of the whole-brain analysis, and obtained individual differences in the effects between the selectable and the forced conditions in the Metacog task (as shown in Fig. 3E).

Further, we performed a PPI analysis using the generalized PPI toolbox (gPPI; McLaren, Ries, Xu, & Johnson, 2012) implemented in SPM8, in order to analyze functional connectivity among activated regions. We copied the regressors from the individual level of the whole-brain analysis, but concatenated sessions into one long sequence using the "concatR" option of gPPI. Moreover, we divided the regressors corresponding to the *betting* phase into two categories, according to the high or low risk/return option. Eight patterns of regressors corresponding to the *betting* phase (two tasks × two conditions × two risk/return options) were included in the functional connectivity calculation. We also calculated VIF for this design matrix, and we included 16 regressors (2 tasks x 2 conditions for before/after the *betting* phase, and 2 tasks x 2 conditions x 2 selected risk/return bets only for the *betting* phase). The maximum VIF was 3.7 (less than 5). Thus, we did not take the collinearity effect into account in this analysis.

Functional connectivity between the vmPFC and the Pc, as well as that between dmPFC and the Pc, was assessed by using a Pc ROI as the seed region (as shown in Fig. 3D, right), and the estimated value was extracted in vmPFC and dmPFC ROIs using MarsBaR. Within the mPFCs, we used the same dmPFC ROI as the seed region and extracted the estimated value of the vmPFC ROI.

The correlation test between the adaptiveness index and increments n connectivity for selected versus forced high risk/return bet trials was performed for each functional connection (dmPFC-Pc, vmPFC-Pc, and dmPFC-vmPFC); p values were corrected for multiple comparisons using the Bonferroni method.

3. Results

3.1. Task performance

To assess neural activations involved in action selection based on metacognition, participants performed the *Metacog* task (Fig. 1A), which requires risk/return betting just before the *matching* phase in a delayed match-to-sample paradigm. The main focus of this study was examining the brain regions involved in the process leading to action selection from metacognition rather than the regions related to action selection itself. Therefore, participants also performed the *Detect* task (Fig. 1B) as a control task. The Detect task was used to exclude brain activations related to action selection based on non-metacognitive factors. In both tasks, we presented not only a risk-selectable condition but also a forced condition in which participants were forced to choose either a high or low risk/return option. The experiment was performed twice, before and during an fMRI scan, and the behavioral results were averaged across these two rounds to reveal the general trends.

3.1.1. Accuracy

The average accuracy of the selectable condition was 68.3 ± 10.0% (mean ± SD) for the Metacog task, and 57.8 ± 8.0% for the Detect task, respectively. In both tasks, the accuracy was significantly different from a 50% chance level [Metacog task: $t(42) = 11.91$, $p < .001$, Detect task: $t(42) = 6.27$, $p < .001$; one sample t-test]. At the individual level, 30 participants in the Metacog task and 13 participants in the Detect performed significantly better than chance in the selectable condition of both tasks (one-sided binomial test for each participant). These results suggest that the participants were attentive

when performing the task. The Detect task was significantly more difficult than the Metacog task [within-subjects two-way ANOVA for averaged accuracy in the selectable condition in relation to task (Metacog or Detect) and selection (high or low risk/return); main effect for task: $F(1,41) = 34.03$, $p < .001$]. The effect of the difference in difficulty on our main whole brain analysis was assessed in the following section.

3.1.2. Score

Average total score for the selectable and forced conditions in the Metacog task during MRI scan were 32.5 ± 8.4 points (mean ± SD) in the selectable condition, and 32.3 ± 10.0 points (mean ± SD) in the forced condition. There was no significant difference between the score [paired *t*-test, $t(42) = .13$, $p > .05$]. Score ranged from 11 to 48, and 9 to 52 for each condition, respectively. Average total scores in the Detect task during MRI scan were 21.3 ± 8.1 points (mean ± SD) for selectable condition, and 22.0 ± 8.0 points (mean ± SD) for the forced condition. There was no significant difference between the score [paired *t*-test, $t(42) = -.45$, $p > .05$]. Score ranged from 2 to 40, and 2 to 38 for each condition, respectively.

3.1.3. Correspondence between accuracy and score

The average accuracy of the selected high risk/return trials was 69.3 ± 12.2% for the Metacog task, and 59 ± 12.4% for the Detect task. The average accuracy for the selected low risk/return trials was 67.4 ± 12.0% and 56.3 ± 11.6% for the Metacog and Detect tasks, respectively. The distribution of accuracy for participants in the selected high and low risk/return trials in the Metacog and Detect tasks are shown in Fig. 2A. Similarly, the average total score for the selected high risk/return trials was 19.9 ± 7.5 points (mean ± SD) for the Metacog task, and 10.5 ± 5.6 points for the Detect task. The average total score for the selected low risk/return trials was 7.2 ± 2.1 points and 8.3 ± 2.3 points for the Metacog and Detect tasks, respectively (Fig. 2B).

3.1.4. Choice ratio of high risk/return bets

The mean and standard deviation for the choice ratio of high risk/return bets was .63 ± 10.9% for the Metacog task, and .48 ± 10.8% for the Detect task. The choice ratio of high risk/return bets was not significantly correlated between the Metacog and Detect tasks [$r = .28$, $t(40) = 1.82$, $p > .05$].

3.1.5. Confidence levels in relation to selected bets (behavioral sessions only)

Using a scale of 1–5, participants rated their confidence in the correctness of their response in the selectable condition for both tasks in all behavioral sessions. We conducted paired *t*-tests for average confidence level in relation to selected bets (high or low risk/return) for each task for the last 4 sessions. In the Metacog task, the average confidence level was significantly higher in selected high risk/return bets rather than in selected low risk/return bets [$t(41) = 3.24$, $p = .002$]. However, the average confidence level was not significantly different between bets in the Detect task [$t(41) = .68$, $p > .05$]. The distribution of average confidence levels in relation to selected bets in the Metacog and Detect tasks is shown in Fig. 2C.

3.1.6. Effect of background noise in the detect task

To determine what information participants used to choose the bet in the Detect task, we averaged the accuracy for −3 dB and −9 dB noise trials in the selectable conditions in the Detect task for all scanning sessions and the last 4 behavioral sessions. The average accuracy for −3 dB noise trials was 65.2 ± 12.9%, and the average accuracy for −9 dB noise trials was 51.1 ± 9.9%. The difference in accuracy between the −3 dB and −9 dB trials was significant [paired *t*-test; $t(41) = 5.90$, $p < .001$]. We used the same method to average the choice ratio of high risk/return bets. The average choice ratio of high risk/return bets for −3 dB noise trials was 51.3 ± 14.5%, and for −9 dB noise trials was 45.7 ± 12.5%. The difference in choice ratio of high risk/return bets between the −3 dB and−9 dB trials was significant [paired *t*-test; $t(41) = 2.16$, $p = .037$]. These results suggest that performance and bet choice were affected by the difficulty of the Detect task. Because the bet could be chosen using only perceptual information (i.e., loudness of sound), we did not consider this task to rely on metacognition.

3.1.7. Adaptiveness index

The mean and standard deviation of the adaptiveness index was −.0041 ± 13.7 for the Metacog task, and .0079 ± 14.2 for the Detect task. We calculated and tested the correlation coefficients between adaptiveness indices between both tasks, and there was no significant correlation [$r = .05$, $t(40) = .33$, $p > .05$]. These results also suggest that participants chose their bets differently in each task.

Participants successfully performed the Metacog and Detect tasks, although they chose their bets differently in the two tasks. In the Metacog task, they mainly relied on memory confidence to predict the correctness of their response. In the Detect task, they relied on the prediction of the task difficulty from the loudness of the noise that was presented in the notice phase (which had same loudness when presented in the *detect* phase and served as a cue for task difficulty). This result suggests that their bets were not only based on task-independent qualities of the participants, such as tendency for risk taking, but also on task-specific effective cues.

3.2. Task-specific activations

As a first step to assess neural mechanisms underlying action selection based on metacognition, we identified regions that showed significantly greater activation for the selectable condition than for the forced condition during betting in the Metacog task (Fig. 3A, B). We excluded regions activated during betting in the Detect task from the above regions by exclusive masking (for details, see Methods). As a result, we found significantly greater activation ($p < .05$, FWE corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level; Fig. 3B; Table 1) in the ventral and dorsal areas of the medial prefrontal cortex (dmPFC and vmPFC) and in the precuneus (Pc), which were thus regarded as the regions related to the process that leads metacognition to action selection. While we also found significantly greater activation in the visual cortex, this was likely caused by physical differences in the visual stimuli between the selectable (two squares) and forced (a single square) conditions (Fig. 1). This idea is

Table 1 – Regions related to action selection based on metacognition, showing significantly greater activation for the selectable condition than for the forced condition during betting in the Metacog task, while excluding regions showing significantly stronger activation for the selectable than for the forced condition in the Detect task.

Regions	BA	Cluster size	MNI coordinates			t value	p value
			x	y	z		
dmPFC	9/32	407	8	34	32	4.89	.004
vmPFC	24/32	345	−2	42	6	4.18	.009
Pc	7	701	−4	−70	34	5.37	<.001
Visual cortex	17/18	228	−22	−98	−2	4.90	.047

The coordinates and t values were obtained from the peaks of each activated cluster. The *p* values represent statistical significance of the cluster (corrected by FWE, cluster level). The statistical threshold was $p < .05$, cluster level, FWE-corrected (cluster-defining threshold was $p < .001$ in voxel level). BA: Brodmann area. dmPFC: dorsomedial prefrontal cortex. vmPFC: ventromedial prefrontal cortex. Pc: precuneus.

supported by the results of conjunction analyses (see below, Results section), which suggested the visual cortex as a commonly activity-changed region in the selectable condition compared to the forced condition in the Metacog and Detect tasks. We therefore excluded this region from detailed analysis and further discussion.

To assess whether there were any activation clusters that were excluded by the exclusive mask technique, we conducted conjunction analyses (Friston et al., 1999) between the contrasts of the two conditions (selectable condition minus forced condition) of both tasks (statistical threshold: $p < .05$, FWE corrected at cluster level; cluster-defining threshold was $p < .001$ in voxel level). We found significant activity only in the visual cortices (Table 2). This result suggests that the activated regions related to action selection based on metacognition were only significantly activated in the contrast of the Metacog task.

To exclude the possibility that differences in task difficulty affected the activity related to action selection based on metacognition, we searched for the regions related to task differences that showed significantly greater activation for the Metacog task than for the Detect task, or vice-versa ($p < .05$, cluster level, FWE-corrected; cluster-defining threshold was $p < .001$ in voxel level). No regions showed greater activation for the Metacog task than for the Detect task. We found that the bilateral primary auditory cortex (peaks at 52, −16, 6, and −46, −26, 8 mm in MNI coordinates) displayed significantly greater activation during the Detect task than during the Metacog task, but this region did not overlap with the activated regions related to action selection based on metacognition.

To evaluate the consistency with previous reports, we summarized regions previously reported to show significant activation related to metacognition about memory. We collected stereotaxic coordinates reported in previous papers (for details, see Methods) and found significant clusters including the dmPFC and Pc, but did not find significant clusters close to the vmPFC (Table 3; Fig. 3C). The co-occurrence probability for the dmPFC was 9.3%, and zero for the Pc. We also found significant clusters including the inferior prefrontal cortex/insula or para-hippocampal gyrus, which was dissimilar to the results from our whole brain analysis.

3.3. *Task-specific regulation of functional connectivity*

To demonstrate the functional relationship between the activated regions and participants' betting behavior based on memory confidence, we examined functional connectivity between the three regions related to action selection based on metacognition (vmPFC-dmPFC, dmPFC-Pc, and vmPFC-Pc) using the generalized form of the PPI analysis (gPPI) (McLaren et al., 2012). If this network contributes to action selection based on metacognition, the strength of connectivity should differ according to selected bets (high or low risk/return choice) in the Metacog task. Thus, we compared functional connectivity within this network between low risk/return choice (corresponding to low confidence) and high risk/return choice (high confidence) during the selectable condition in the Metacog task. The results showed that functional connectivity between the two medial prefrontal and parietal regions was significantly stronger in the high-confidence trials than in the low-confidence trials [Fig. 3F; within-subjects two-way ANOVA, main effect for confidence: $F(1,41) = 9.77$, $p = .003$]. This suggests that the functional connectivity between the two mPFCs and the Pc reflects differences in

Table 2 – Regions showing significantly greater activation for the selectable condition than for the forced condition during betting in both the Metacog and Detect tasks.

Regions	BA	Cluster size	MNI coordinates			t value	p value
			x	y	z		
Visual cortex	18/19	253	30	−88	4	5.20	.033
Visual cortex	17/18/19	312	−20	−94	6	5.86	.015

The coordinates and t values were obtained from the peaks of each activated cluster. The *p* values represent statistical significance of the cluster (corrected by FWE, cluster level). The statistical threshold was $p < .05$, cluster level, FWE-corrected (cluster-defining threshold was $p < .001$ in voxel level). BA: Brodmann area.

Table 3 – Regions suggested to have significant activation related to metacognition about memory in the meta-analysis of previous reports.

Regions	BA	Cluster size	MNI coordinates		
			x	y	z
dlPFC	9/46	353	−52	24	30
dmPFC	32	327	−4	26	38
iPFC/Insula	13/47	230	44	18	−2
PHG	28/35	164	26	−24	−14
Pc	7	130	12	−68	56
iPFC/Insula	13/47	110	−32	24	−8

The coordinates were obtained from the peaks of each cluster. The statistical threshold was $p < .05$, cluster level, FWE-corrected (cluster-defining threshold was $p < .001$ in voxel level). BA: Brodmann area; dlPFC: dorsolateral prefrontal cortex; dmPFC: dorsomedial prefrontal cortex; iPFC: inferior prefrontal cortex; PHG: Parahippocampal gyrus; Pc: precuneus.

individual participants' betting based on metacognition. We also found a significant main effect [$F(2,82) = 6.26$, $p = .003$] of area combination (vmPFC-dmPFC, dmPFC-Pc, and vmPFC-Pc). As a post-hoc analysis, multiple comparisons were conducted for each area combination. Only the difference between dmPFC-vmPFC and Pc-dmPFC was significant [$t(41) = 3.74$, $p = .002$; Bonferroni-corrected].

Further, to control for the effect of score anticipation in functional connectivity analyses, we conducted the same functional connectivity analyses using data from the forced condition in the Metacog task. This is because if score anticipation strongly affected the reported functional connectivity difference in the selected ROIs, the same results should be obtained in the forced condition of the Metacog task. We compared functional connectivity within the prefrontal-posterior network between low risk/return trials and high risk/return trials during the forced condition in the Metacog task. There was no significant difference in functional connectivity between the forced risk types [within-subjects two-way ANOVA, main effect for forced risk type: $F(1,41) = .51$, $p > .05$]. We found a significant main effect of area combination [$F(2,82) = 11.95$, $p < .001$]. As a post-hoc analysis, multiple comparisons were conducted for each area combination. Only the differences between dmPFC-vmPFC and Pc-dmPFC, and dmPFC-vmPFC and Pc-vmPFC were significant [dmPFC-vmPFC and Pc-dmPFC: $t(41) = 4.23$, $p < .001$; dmPFC-vmPFC and Pc-vmPFC: $t(41) = 2.95$, $p = .016$, Bonferroni-corrected]. Thus, we concluded that differences in the functional connectivity between the selected bets were not explained by the difference in score anticipation between the bets.

3.4. *Covariation in individual adaptiveness and functional connectivity*

In the Metacog task, the adaptiveness index (Fig. 4A; see Methods for details) is considered to reflect the degree of reliance on metacognition for bet selection. We tested whether functional connectivity reflects individual differences in the degree of reliance on metacognition, by assessing the relationship between functional connectivity and the adaptiveness index in the Metacog task. For functional connectivity, we focused on the correspondence between high risk/return bets and a high gPPI effect: increments in the effect in selected high risk/return bets compared to forced high risk/return bets. The Pearson's product–moment correlation coefficient between the functional connectivity difference and the adaptiveness index was calculated for each connection (vmPFC-dmPFC, dmPFC-Pc, and vmPFC-Pc). We found that the functional connectivity between the vmPFC and dmPFC was significantly correlated with the adaptiveness index [Fig. 4B; Pearson's $r = .45$, $t(40) = 3.18$, $p = .009$, Bonferroni correction]. In contrast, functional connectivity between the Pc and each mPFC (dmPFC-Pc and Pc-vmPFC-Pc) did not show a significant correlation with the adaptiveness index [Fig. 4C, D; dmPFC-Pc: $r = .05$, $t(40) = .34$, $p = 1.000$; vmPFC-Pc: $r = .05$, $t(40) = .31$, $p = 1.000$, Bonferroni-corrected]. As a comparison analysis, the correlation coefficient between the functional connectivity difference during the betting phase in the Metacog task and the adaptiveness index for "Detect" task was calculated for each connection (vmPFC-dmPFC, dmPFC-Pc, and vmPFC-Pc). There was no significant correlation between the functional connectivity difference and the adaptiveness index for the Detect task [Fig. 4B; vmPFC-dmPFC: $r = .25$, $t(40) = 1.62$, $p = .34$; Fig. 4C; dmPFC-Pc: $r = .17$, $t(40) = 1.12$, $p = .80$; Fig. 4D; vmPFC-Pc: $r = .11$, $t(40) = .70$, $p = 1.000$, Bonferroni-corrected]. The functional connectivity within the mPFC during the betting phase in the Metacog task was thus related to the degree of reliance on metacognition.

3.5. *Consistency with degree of reliance on prospective metacognition in daily life*

To understand how the adaptiveness index reflects individual tendencies in the degree of reliance on prospective metacognition in daily life, we asked participants to self-report about their daily tendency to rely on prospective metacognition using an inventory questionnaire (Abe & Ida, 2010; Schraw & Dennison, 1994). The questionnaire score was significantly correlated with the adaptiveness index obtained from the Metacog task [Fig. 5A; $r = .53$, $t(40) = 3.96$, $p < .001$], but not with the index obtained from the Detect task [Fig. 5B; $r = -.12$, $t(40) = -.79$, $p = .433$]. This indicates that the action selection based on metacognition observed in our task is consistent with self-control based on metacognition in daily life.

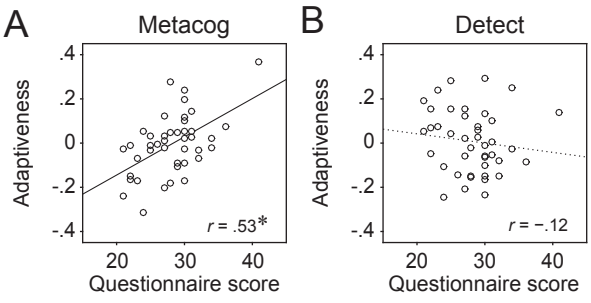

Fig. 5 – Correlation between individual scores on the use of prospective metacognition in daily planning and adaptiveness indices in the Metacog (A) and Detect (B) tasks. *$p < .01$.

4. Discussion

We found that the medial prefrontal-parietal network participates in action selection based on metacognition. This network comprises the dmPFC, the vmPFC, and the Pc, which were significantly activated for metacognition-required risk selection. There is the possibility that the significant difference in difficulty between the tasks could affect the results of whole brain analysis. However, the regions that displayed significant activity differences between the tasks did not overlap with the activated regions related to action selection based on metacognition. Moreover, we included performance accuracy for all tasks and conditions into the analysis as covariates to remove possible effects related to differences in task difficulty. Thus, above results are not explained by the difference in performance accuracy between the tasks.

Previous metacognition studies have suggested that the vmPFC, dmPFC, and Pc play different roles in metacognition. Activations in the vmPFC and the Pc are involved in the monitoring of the memory retrieval process (Chua, Schacter, Rand-Giovannetti, & Sperling, 2006; Hebscher & Gilboa, 2016; Schnyer, Nicholls, & Verfaellie, 2005), whereas activation in the dmPFC has been associated with the monitoring of conflicted feelings regarding which option to choose (Chua, Schacter, & Sperling, 2009; Maril, Simons, Weaver, & Schacter, 2005; Maril, Wagner, & Schacter, 2001). Previous studies have reported significant clusters that had peak coordinates close to the identified regions in our whole-brain analysis. For example, Kikyo & Miyashita (2004) reported a cluster that had peak coordinates (0, 30, 39) that were close to the peak coordinates of the dmPFC cluster in our whole brain analysis (8, 34, 32). Similarly, Moritz, Gläscher, Sommer, Büchel, and Braus (2006) and Risius et al. (2013) reported clusters that had peak coordinates [(9, 45, 6) and (−2, −64, 24), respectively] that were close to that of our vmPFC (−2, 42, 6), and Pc (−4, −70, 34) clusters, respectively. Our meta-analysis of previous studies (see Fig. 3C) suggested the existence of a significant cluster that had peak coordinate in the dmPFC in relation to metacognition, and this partially overlapped with the dmPFC cluster that was identified in our whole-brain analysis. However, the significant cluster that had peak coordinates in the Pc in our meta-analysis did not overlap with the Pc cluster in our whole brain analysis, and there was no significant cluster in our meta-analysis that was close to the vmPFC. Also, our meta-analysis and other studies have suggested that the lateral parts of the prefrontal and posterior regions may be involved in metacognition (Chua et al., 2009; Kim & Cabeza, 2007), although such activations were not found in our experiments. The lateral parts of prefrontal regions supposedly represent internal states that are verbalized, such as someone stating that they feel confident (Fleming & Dolan, 2012). Our task, however, did not require participants to verbalize their internal state or confidence level, which could explain this discrepancy in the results between previous studies and those of our experiments. On the one hand, our experiments and previous studies have some similarities among the activated brain regions even though there were differences in the task paradigm. On the other hand, our meta-analysis suggested there are also some differences in those activated regions. Further research is needed to clarify these similarities and differences in the brain regions that participate in metacognition.

The functional connectivity between the dmPFC, the vmPFC, and the Pc was modulated for selected risk/return to be stronger during the selection of high risk/return betting (corresponding to high confidence) compared to during low risk/return betting (corresponding to low confidence). As the increase in information exchange between regions is generally considered to correspond to an enhanced functional connectivity (O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012), the brain networks between the dmPFC, vmPFC, and Pc observed in our results should subserve the action selection based on metacognition about memory. Similarly, it has been hypothesized that networks between the medial prefrontal and parietal regions are related to metacognition-related processes (Fleming & Dolan, 2012; Shimamura, 2000, 2008). Several previous studies on metacognition have focused on connectivity between brain regions that are not limited to the prefrontal and parietal regions (Baird, Smallwood, Gorgolewski, & Margulies, 2013; De Martino, Fleming, Garrett, & Dolan, 2013; Fleming, Huijgen, & Dolan, 2012). However, these previous studies did not examine the direct correspondence between functional connectivity and action selection based on the participants' confidence in their memory. Since we successfully demonstrated that functional connectivity between the prefrontal and posterior regions did change according to participants' betting in the Metacog task, this result represents the network-level involvement of the prefrontal and posterior cortical regions in action selection based on metacognition.

In addition to the modulation based on memory confidence within individuals, stronger functional connectivity within the medial prefrontal regions (dmPFC-vmPFC) was observed in participants who exhibited a higher adaptiveness index in the Metacog task. This suggests that the network within the medial prefrontal region contributes to both the degree of confidence and the degree of adaptiveness during betting. According to the idea that the functional connectivity among brain regions reflects the integration of information which is processed locally in these regions (Friston et al., 1997; Van Den Heuvel & Pol, 2010), the increments in functional connectivity between the vmPFC and the dmPFC can be interpreted as increments in the reliance on metacognition about memory to solve the decision conflict. Since memory confidence was the only effective cue to predict answer correctness in our Metacog task, the increased reliance on memory confidence should be reflected in the adaptiveness index of betting. Moreover, individual differences in the adaptiveness index for the Metacog task was correlated with the degree of reliance on prospective metacognition in daily life, as measured by a questionnaire given to all participants. Thus, the neural basis found in our study also underlies self-control based on metacognition in daily life.

The adaptiveness index in the Metacog task successfully showed individual differences in action selection based on metacognition, combined a wide range of values (from −.31 to .37), and did not correlate with the adaptiveness index in the Detect task. The fact that the index value was negative in some participants can be explained by several reasons. Firstly, cognitive load for risk selection itself in the selectable condition (Schwartz, 2002) can reduce task performance compared

to the forced condition. In addition, since we did not directly require participants to rely on memory confidence to select their bet, it is possible that some participants also relied on non-metacognitive information, such as general risk-taking tendencies. This strategy would prevent improvement of performance in the selectable condition because metacognition about memory was designed to be the only effective cue for betting in the Metacog task. Our task provides novelty to this human neurophysiological study by allowing participants to voluntarily regulate the degree that they rely on memory confidence to select their bets. However, at the same time this is also a limitation of our paradigm because we are unable to completely eliminate the possibility that some participants also relied on non-metacognitive information in the Metacog task. This trade-off is inevitable because allowing the voluntary use of metacognition is equivalent to allowing the voluntary use of non-metacognitive information. This issue should be addressed with appropriately designed experiments in future studies. Revealing the cause of the individual differences in the degree of reliance for metacognition will contribute to our understanding of how we realize adaptive self-control in daily life.

To conclude, the present study for the first time shows the neural correlates of action selection based on metacognition in human adults, and sheds light on the mechanism of how we realize adaptive behavioral control in daily life. Moreover, our study shows that it is possible to integrate behavioral and neuroscientific studies on metacognition in animals (Smith, Couchman, & Beran, 2014), infants (Goupil et al., 2016), and human adults, because we showed that an experimental paradigm and behavioral index for animals and infants was applicable for neuroscientific studies in human adults. Integration of behavioral and neural studies across a wide range of species will contribute to revealing the core factors and evolutionary processes underlying metacognition. It should be noted that a causal relationship within the functional network is still unknown, and should be tested directly in future neurophysiological studies both in humans and in animals.

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Conflicts of interest

There are no conflicts of interest to declare.

Data availability

The data that supports the findings of this study is available upon request to the corresponding author R.O.T (only for the verification purposes and not for future studies). Concerning the raw brain imaging data, one participant did not agree to share his data, and thus data from this one participant is not available.

CRediT authorship contribution statement

Shoko Yuki: Conceptualization, Formal analysis, Investigation, Writing - original draft, Visualization, Project administration. **Hironori Nakatani:** Conceptualization, Investigation, Writing - review & editing, Writing - review & editing. **Tomoya Nakai:** Conceptualization, Investigation, Writing - review & editing, Writing - review & editing. **Kazuo Okanoya:** Supervision, Writing - review & editing. **Ryosuke O. Tachibana:** Conceptualization, Formal analysis, Writing - review & editing, Visualization, Supervision.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cortex.2019.05.001.

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