Functional and cortical morphometric basis of metacognitive introspection in Macaque

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Introduction

Metacognition refers to the ability to be aware of one's own cognition. Ample evidence indicated that metacognition in the human primates is highly dissociable from cognition[1] and specialized across domains[2]. However, such metacognitive sophistication is highly under-studied in monkeys. Here we set out to make a thorough inquiry of the complexity in macaques' metacognition by combining a challenging behavioral paradigm (temporal wagering by macaque monkeys), computational modelling (hierarchical Bayesian meta-d'), focal neuromodulation (inhibitory transcranial magnetic stimulation), and longitudinal morphometric magnetic resonance imaging (pre- vs. post- metacognitive training).

Method & Data Analysis
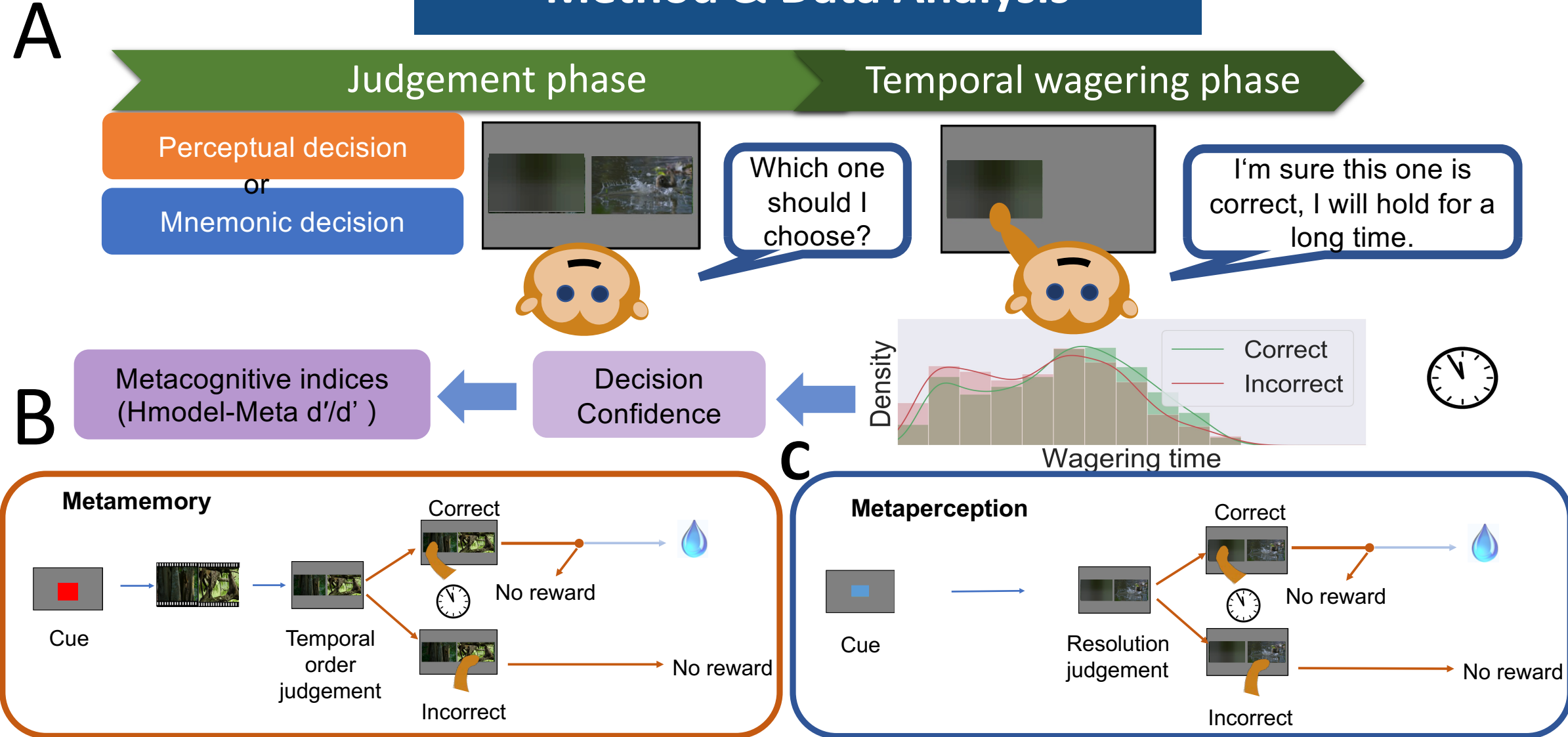
Confidence expression & temporal wagering in memory and perception task. In metamemory task (Panel B), we trained monkeys to report the sequencing of pictures by making mnemonic choices based on a learned stimulus–response rule (e.g., always choosing the picture they saw earlier in a pre-watched 4s clips). In perception task (Panel C), we trained monkeys to report the resolution of pictures by making perceptual choices based on another rule (e.g., choosing the picture with higher or lower resolution, counterbalanced in monkeys).
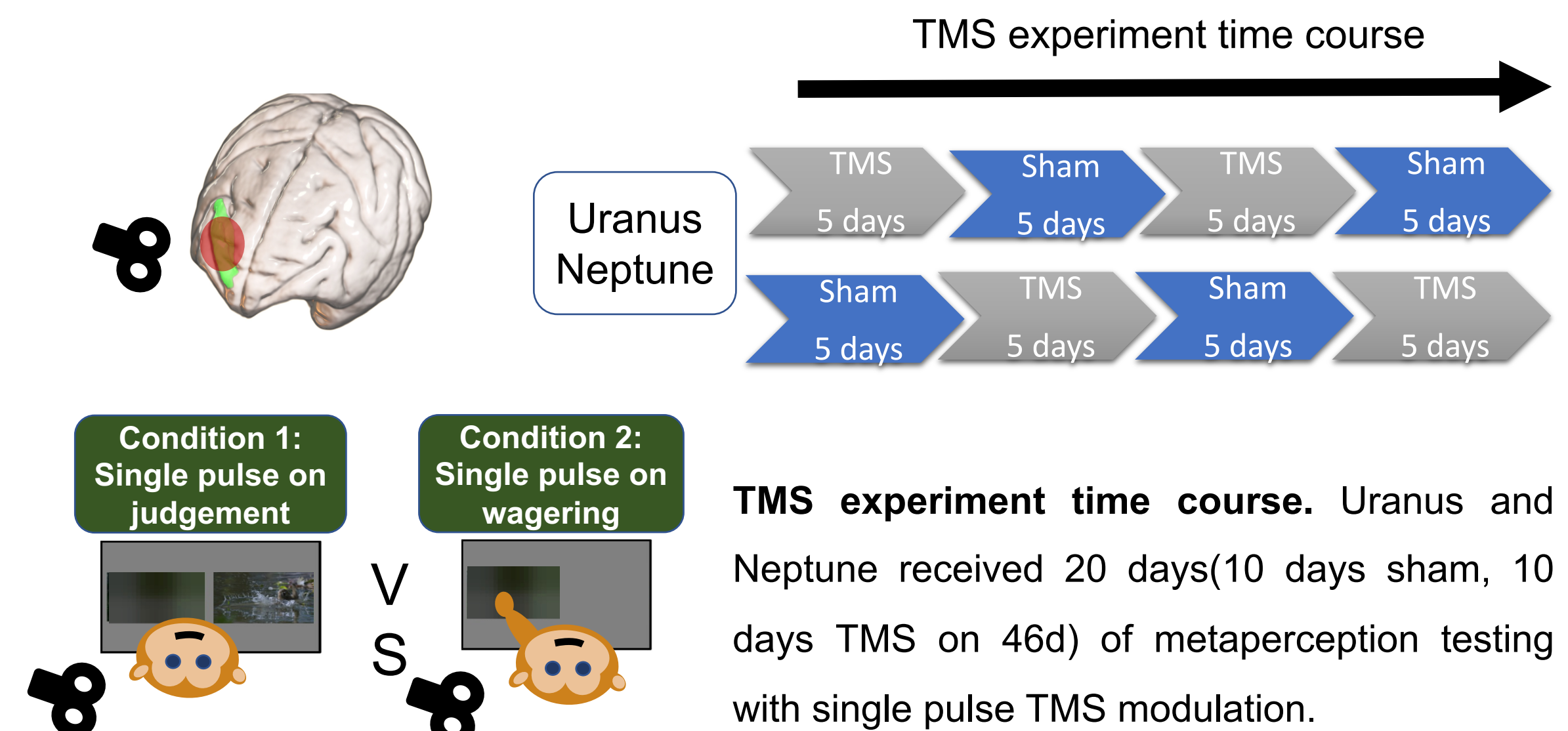
Temporal wagering: following mnemonic or perceptual judgement, macaque monkeys expressed their confidence by time-wagering: they could wait for a variable amount of time before they could receive a possible reward or initiate a new trial. This design allowed us to measure confidence on a trial-by-trial basis. We found monkeys can monitor their behaviors by distributing more time in correct trials (right bottom distribution plot in Panel A).

Meta-ability analysis: we then take wagering time and response to classify trials into four kinds: correct/high confidence (long WT), incorrect/high confidence (long WT), correct/low confidence (short WT), incorrect/low confidence (short WT), and to compute bias-free measures of metacognitive indices (Hmodel meta d'/d' : hierarchical Bayesian meta-d')[3] on memory and perception to further test the capability of metamemory and metaperception.
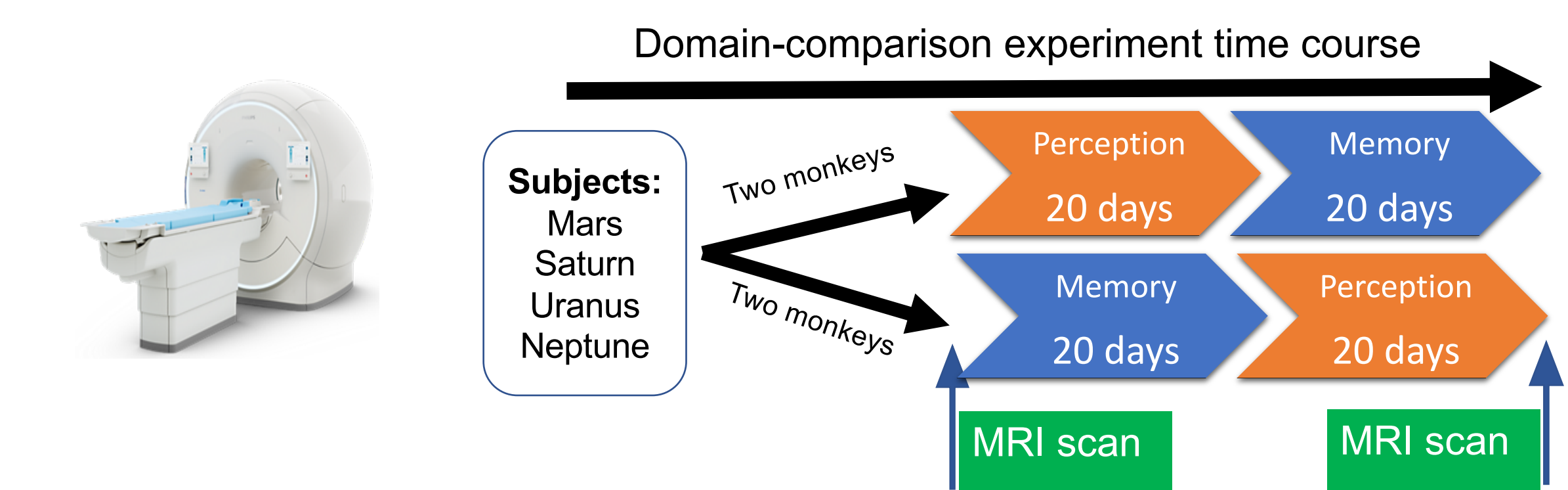

Domain-comparison experiment time course & structural MRI data acquisition. Four male adult macaque monkeys provided data to the experiment one (*Macaca Mulatta*, age: 6 yr, weight: 8.2 ± 0.4kg). Monkey received 40 days testing, (20 days metaperception, 20 days of metamemory). Mars and Saturn received MRI scanning before and after the metacognitive training. All monkeys received MRI scanning after the training.

Macaque MRI preprocessing and ROIs. We obtained the anatomical segmentation of subcortical structure by registering (affine and non-linear registration) the single-subject D99 atlas[4] to each individual monkey.

TMS experiment time course. Uranus and Neptune received 20 days(10 days sham, 10 days TMS on 46d) of metaperception testing with single pulse TMS modulation.
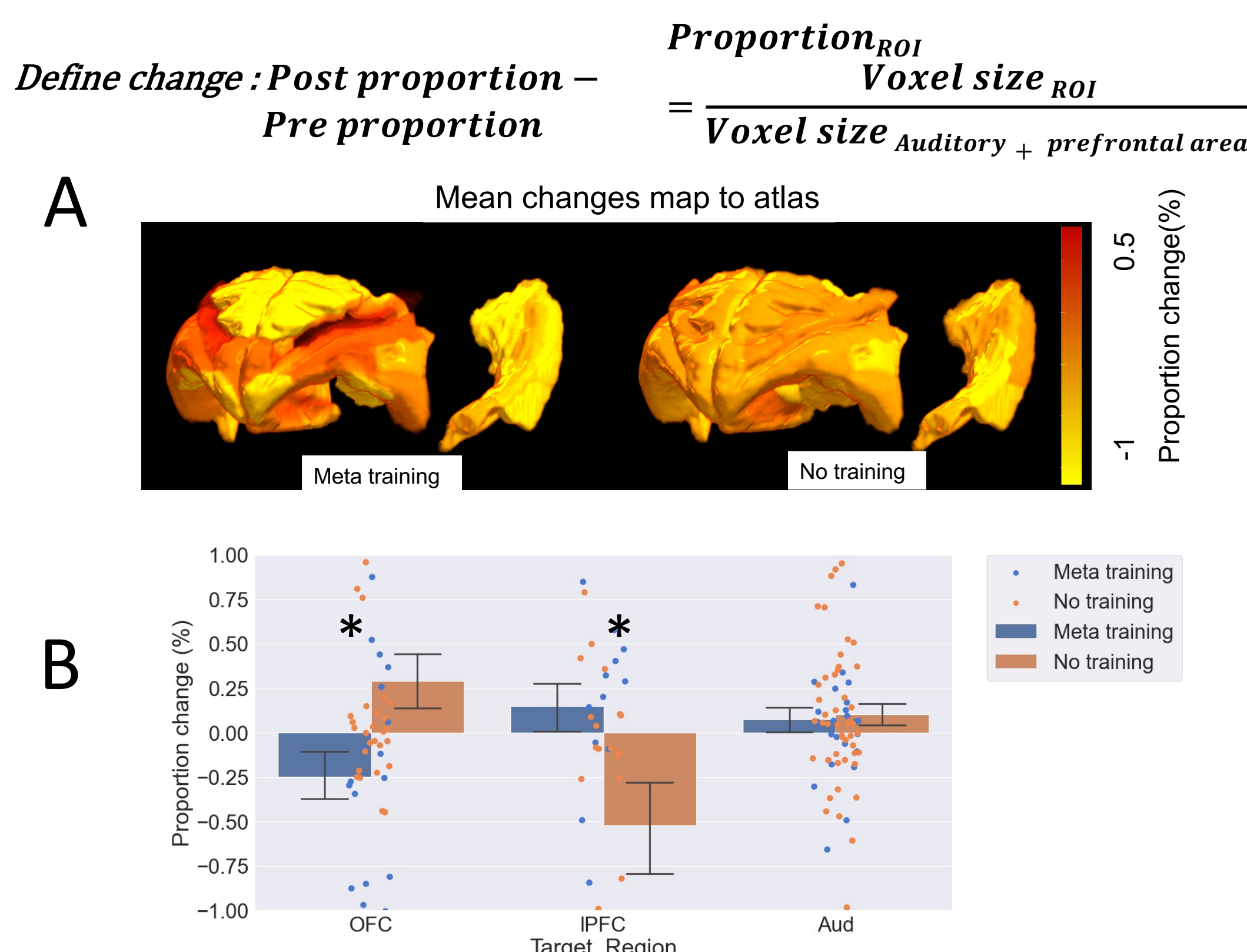
On judgement pulse vs on wagering pulse. In order to locate the timing of metacognitive computing, we also set up two blocks in each day (On_judgement: monkeys received a single pulse 100 ms after stimulus onset; On_wagering: single pulse 100 ms after they made their decision, indicating starting wagering).

Results

$$DGI(domain-generality\ index)=|M_p-M_M|$$

M = Memory task; P = Perceptual task
Monkeys = Mars and Saturn
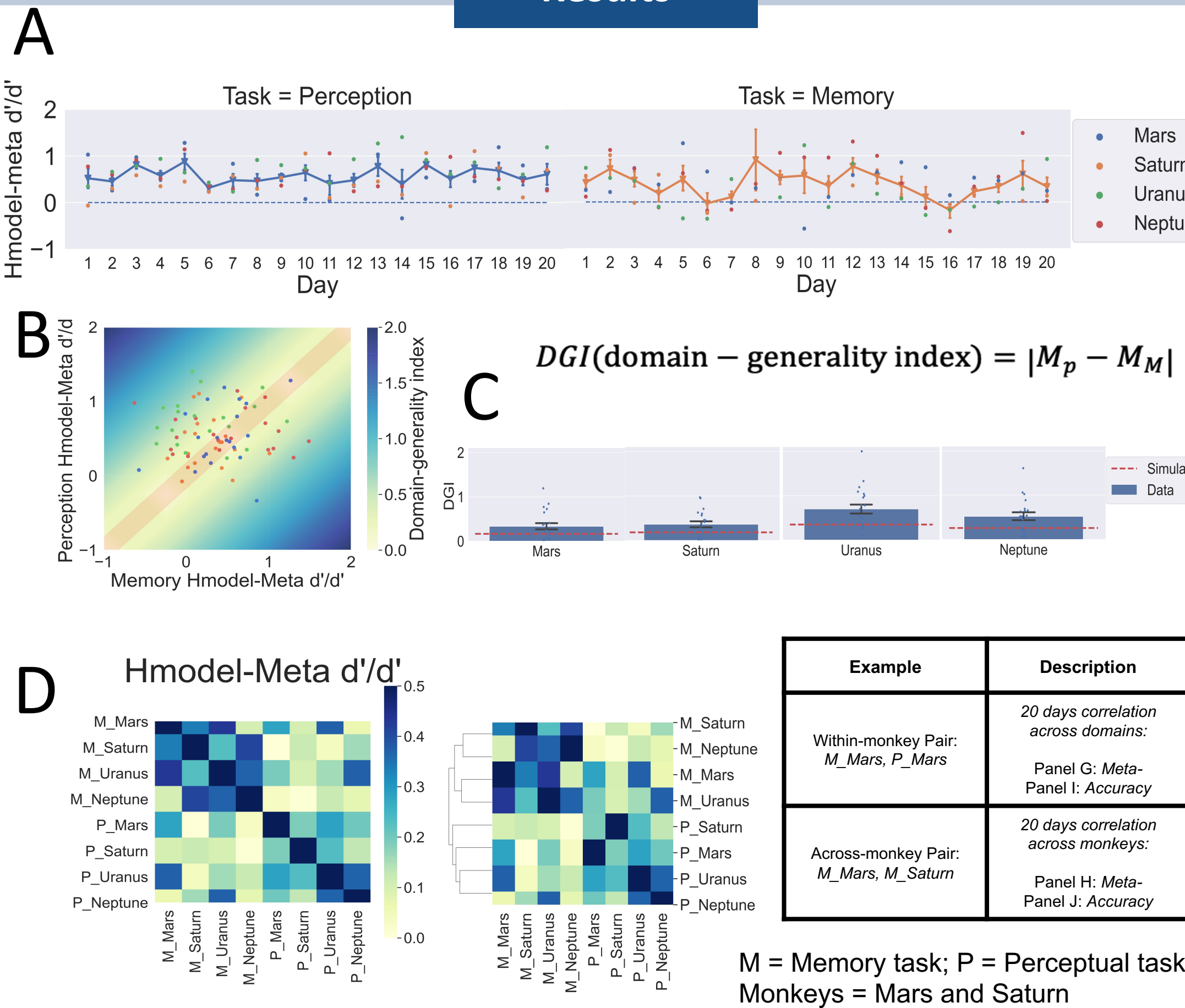
Finding one: Domain-specific metacognitive ability in monkeys. First, we showed that monkeys have above zero metaperception and metamemory ability measured by Hmodel meta d'/d' (panel A), one sample T test against zero (all p values < 0.05). Second, we found metacognition in monkeys is domain specific, we calculated for each subjects a domain-generality index (DGI) that quantifies the similarity between scores in each domain (equation in panel B, where M_P perceptual H-model *meta-d' /d'* and M_M memory H-model *meta-d' /d'*). Specifically, we randomly shuffle the task labels (memory/perception) of all 40 days (20 days' memory and 20 days' perception) within each subject. This procedure shuffled 1000 times, by this mean and we will have simulated DGI (assuming they are perfectly domain-general) for each monkey, and we found the actual monkey data is all higher than simulated data (all p values < 0.01). Also, see DGI results of color map for a clear illustration (panel B), each dot represent a daily DGI for each monkey, darker color indicates less metacognitive consistency across domains, red area indicates the random shuffled DGI (panel C). We also found the similarity within domain is even stronger than within each monkey. Specifically, we did a cluster analysis with pairwise correlation between every pair of monkey and domain and revealed two clear clusters represent the memory and perception (see example in panel D).

$$Define\ change : Post\ proportion-Pre\ proportion = \frac{Proportion_{ROI}}{Voxel\ size_{Auditory\ +\ prefrontal\ area}} \frac{Voxel\ size_{ROI}}{}$$

Finding two: Gray matter in IPFC increase with metacognitive training. We first aligned the images to the common space (D99 atlas https://afni.nimh.nih.gov/Macaque). Then, the same atlas was used to define each monkey's cortical substructure. We chose the subcortical structure in OFC and in IPFC as target region (see the proportional change for each in panel B) and auditory area as control region. Additionally, we collect data from no-training monkey (n=4). No-training monkeys didn't not receive any trainings during two scanning timepoints. To perform analysis for each monkey, we computed the voxel size for all subcortical structure in prefrontal and auditory area in each monkey. We calculated the voxel proportion for each areas (see first equation above panel A). We then compute the morphometric change between Pre-training and Post-training using the Post scanning proportion minus Pre scanning proportion for each areas (see second equation above panel A). We also mapped the mean proportional changes to the atlas (Panel A) for demonstration.

We compared the mean proportional changes between meta-training group and no-training group in OFC, IPFC and auditory region (Panel B). Voxel-wise analysis identified gray matter volume increased in IPFC and decreased in OFC in meta-training group. Disproportional gray matter changes shows the importance of IPFC in metacognitive ability and plasticity in monkeys.
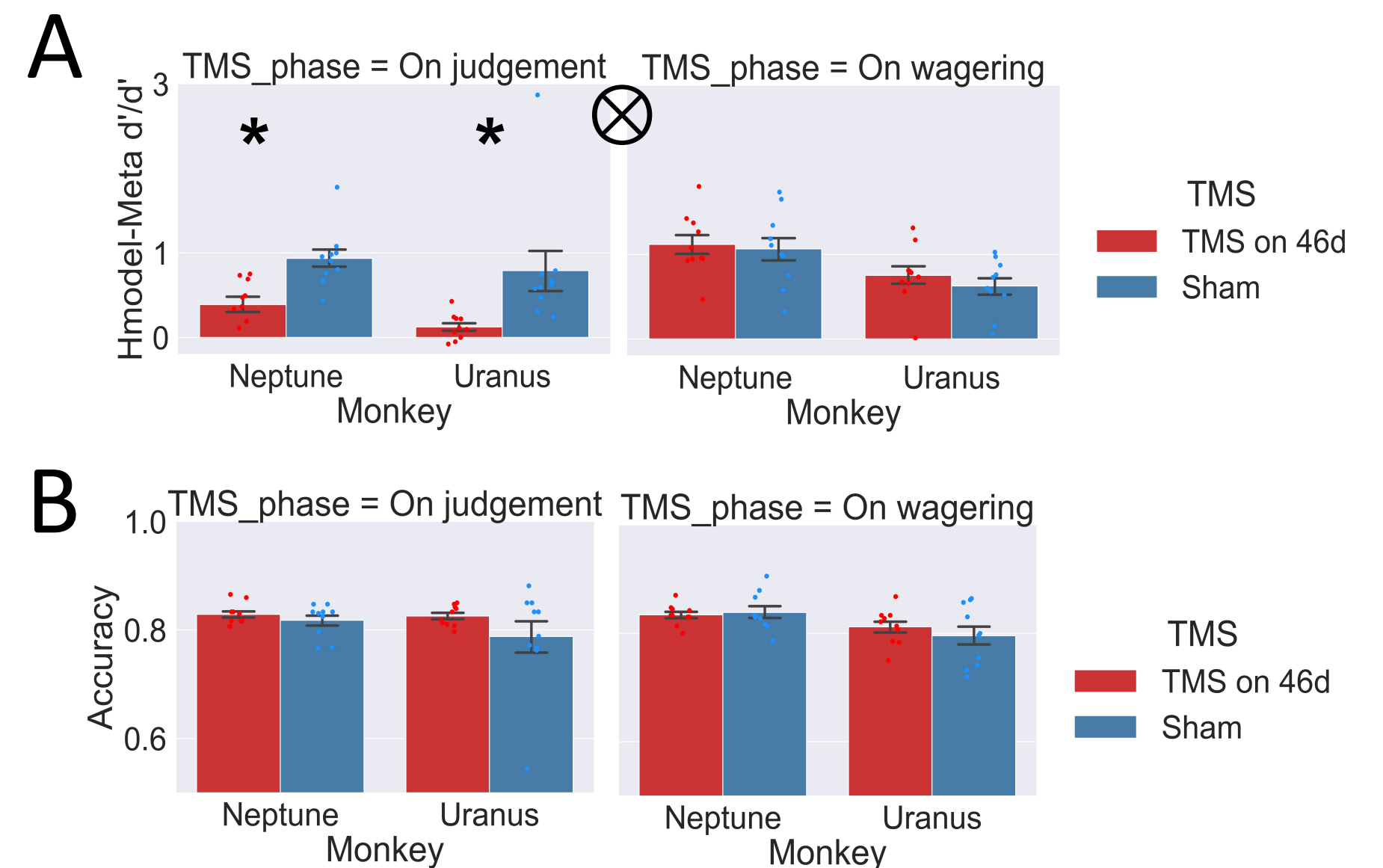
Finding three: Critical functional role of Area 46d in metacognition & Essential introspective information is computed before the actual wagering. We tested whether TMS of BA46d would affect metacognition on perceptual decision-making. We performed a 2 (TMS phase: on-judgement/on-wagering) × 2 (TMS: TMS-46d/TMS-sham) mixed-design repeated-measures ANOVA for metacognitive efficiency with TMS phase as a within-subjects factor and TMS as a between-subjects factor. We found a significant interaction between TMS phase and TMS modulation in both monkeys (all p values < 0.05). The interaction was driven by lower metacognitive efficiency following TMS of BA46d than following sham treatment in the on-judgement phase condition (paired t tests: *all p values < 0.05*), whereas no difference in metacognitive efficiency was found in the on-wagering phase (paired t tests: all p values > 0.1); see Panel A.

We further verified that type 1 task performance were not affected by TMS. As expected, task performance (daily accuracy) were not different between the two TMS conditions in either the on-judgement phase or the on-wagering phase (paired t test, ps values > 0.1).

Together, these results reveal that TMS to the 46d affects the metacognitive performance specifically for the on-judgement block, indicating the metacognitive-evidence is already accumulated in the decisional stage, instead of in the wagering stage.

Highlights & Conclusion

Highlights

- Macaque monkeys express confidence via wagering time in mnemonic and perceptual decisions.
- Macaque monkeys demonstrate sophisticated metacognitive ability.
  - Dissociation between metacognition and cognition.
  - Dissociation between metamemory and metaperception.
- Metacognitive ability can be disrupted by single pulse TMS on Area 46d in macaque monkeys.
- Essential introspective information is computed before the actual wagering.
- Gray matter volume of IPFC increase disproportionally with metacognitive training.

Conclusion

Macaque monkeys demonstrate domain-specific metacognition across memory and perception via temporal wagering. Such metacognitive ability is supported by Area 46d. Behavioral, functional, and morphometric evidence reveal introspection in macaque monkeys.

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1. Fleming et al.(2010). *Science*, 329(5998): 1541-1543. 2. Morales et al. 2018). *The Journal of Neuroscience*, 38(14): 3534-3546. 3. Lau et al.(2012). *Consciousness and Cognition*, 21 (2012): 422–430 4. Reveley et al.(2017). *Cerebral cortex* 27(9): 4463-4477.

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