Functional and cortical morphometric basis of metacognitive introspection in Old World monkeys (Macaca mulatta)

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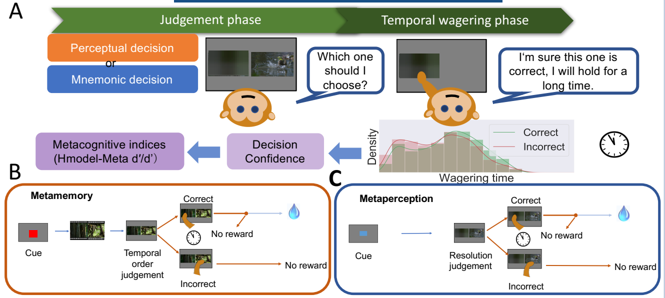
Introduction

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).

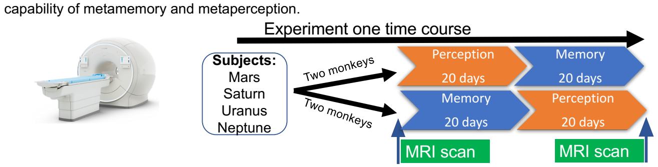
Method & Data Analysis



Confidence expression via 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 a another rule (e.g., choosing the picture with higher or lower resolution, counterbalanced in monkeys).

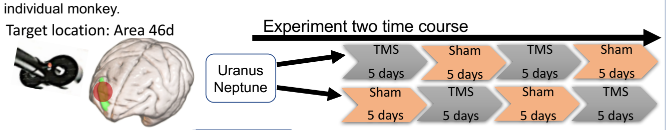
Temporal wagering: following mnemonic or perceptual judgement, macaque monkeys expressed their confidence by time-wagering: they could wait for a variable amount of time before they could receive a possible reward or initiate a new trial. This design allowed us to measure confidence on a trial-by-trial basis. We found monkeys can monitor their behaviors by distributing more time in correct trials (right bottom distribution plot in Panel A).

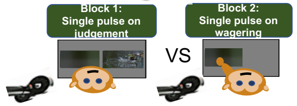
Meta-ability analysis: we then take wagering time and response to classify trials into four kinds: correct/high confidence (long WT), incorrect/high confidence (long WT), correct/low confidence (short WT), incorrect/low confidence (short WT), and to compute bias-free measures of metacognitive indices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



Experiment one 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.

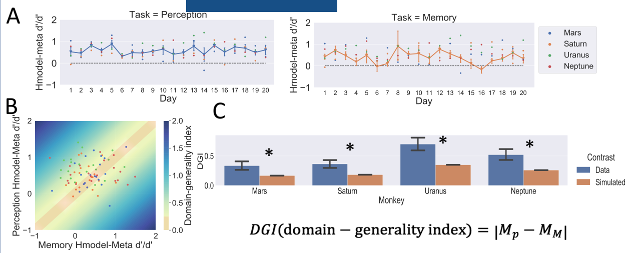


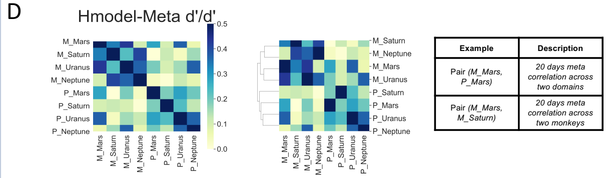


Experiment two time course. Uranus and Neptune received 20 days(10 days sham, 10 days TMS on 46d) of metaperception testing with single pulse TMS modulation.

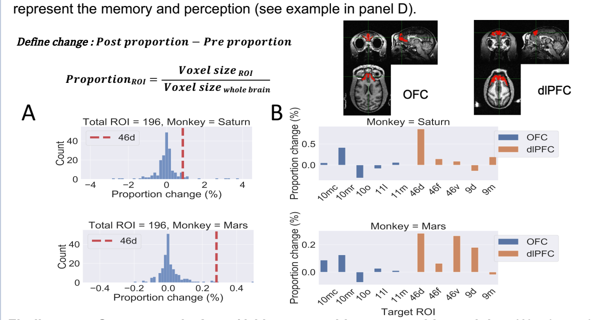
On judgement pulse vs on wagering pulse. In order to locate the timing of metacognitive computing, we also set up two blocks in each day (On_judgement: monkeys received a single pulse 100 ms after stimulus onset; On_wagering: single pulse 100 ms after they made their decision, indicating starting wagering).

Results



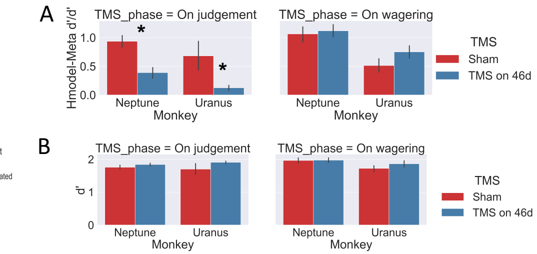


Finding one: Sophisticated metacognitive ability (Domain-specificity) in monkeys. First, we showed that monkeys have above zero metaperception and metamemory ability measured by Hmodel meta d'/d' (panel A), one sample T test against zero (all *Ps* < 0.05). Second, we found metacognition in monkeys is 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 *Ps* < 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).



Finding two: Gray matter in Area 46d increase with metacognitive training. We chose the subcortical structure in OFC (10mc, 10mr, 10o, 11l, 11m) and in dlPFC (46d, 46f, 46v, 9d, 9m) as target region (see the proportional change for each in panel B). To perform analysis for each monkey, we computed the voxel size for all subcortical structure in each monkey (196 in total), and calculated the voxel proportion for each ROI (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 ROI (see second equation above panel A).

Voxel-wise analysis identified significantly increased gray matter volume in the 46d in Saturn and Mars after training (Saturn: 509 0.85% of all voxels; Mars: 274, 0.28% of all voxels). Additionally, we try to determine whether the increment in 46d is surpass all other subcortical structure. So, we take all the subcortical structure as ROIs, and compute all the voxel proportion changes for all ROIs (see text above). We found the increment of 46d ranked third place in all ROIs for Mars (surpass 98% of ROIs), and ranked fourteenth place in all ROIs for Saturn (surpass 92.9% of ROIs), minimum statistic indicate the such increment is significant (*P* < 0.005).



Finding three: Critical functional role of Area 46d in metacognition & Essential introspective information is computed before the actual wagering. We first exam the metacognitive performance change following TMS modulation (see panel A). We found significant "TMS_phase × TMS" interaction of Hmodel meta d'/d' (P < 0.01). Such interaction was driven by lower Hmodel meta d'/d' value following single pulse TMS modulation on 46d relative to sham on judgement block (simple main effect, P < 0.05), whereas no deficit in Hmodel meta d'/d' was found in the on-wagering block (simple main effect, P > 0.1).

We then examined whether cognitive performance and mean confidence ratings might be affected by TMS. As expected, task performance (measured by d', see panel B) and mean wagering time were not different between the two TMS conditions in neither on-judgement block (all *Ps* > 0.1) nor on-wagering block (all *Ps* > 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 Area 46d 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.

References:
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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