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Medial prefrontal cortex supports perceptual memory

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eTOC Blurb

Schwiedrzik et al. provide evidence from intracranial recordings in epilepsy patients that medial prefrontal cortex, usually considered a non-sensory brain region, participates in the stabilization of perception across time.

Our visual environment constantly changes. Yet, we experience the world as a stable, unified whole. How is this stability achieved? It has been proposed that the brain preserves an implicit perceptual memory in sensory cortices [1] which stabilizes perception towards previously experienced states [2, 3]. The role of higher-order areas, especially prefrontal cortex (PFC), in perceptual memory is less explored. Since PFC exhibits long neural time constants, invariance properties, and large receptive fields which may stabilize perception against time-varying inputs, it seems particularly suited to implement perceptual memory [4]. Support for this idea comes from a neuroimaging study reporting that dorsomedial PFC (dmPFC) correlates with perceptual memory [5]. However, dmPFC also participates in decision making [6]. Hence, its contribution to perceptual memory may arise on a post-perceptual, decisional level [7]. To determine which role, if any, PFC plays in perceptual memory, we obtained direct intracranial recordings in six epilepsy

patients while they performed sequential orientation judgements on ambiguous stimuli known to elicit perceptual memory [8]. We find that dmPFC activity in the high gamma frequency band (HGB, 70-150 Hz) correlates with perceptual memory. This effect is anatomically specific to dmPFC (not directly adjacent lateral PFC) and functionally for memories of preceding percepts (not of preceding decisions). Further, dmPFC appears to play a causal role, as a patient with a lesion in this area showed impaired perceptual memory. Thus, dmPFC integrates current sensory information with prior percepts, stabilizing visual experience against the perpetual variability of our surroundings.

We evaluated perceptual memory (PM) by sequentially presenting ambiguous stimuli and determining whether prior percepts affected perception of orientation in successive stimuli (Fig. 1A). On each trial, subjects saw two ambiguous displays: a rectangular dot lattice, which can be perceived as aligned to one of two dominant orientations (0° or 90°); then, a hexagonal dot lattice, which can be perceived as aligned to one of three dominant orientations (0°, 60°, or 120°). After each respective stimulus, subjects reported which orientation they had perceived with a mouse click, selecting one of four orientations which were randomly assigned to four locations on a response screen to prevent recurring stimulus-response mappings. PM is evident when subjects systematically perceive the same orientation (0°) in both lattices [8]. We did not ask subjects to explicitly memorize orientation, but assessed implicit PM in the form of serial dependencies in perception between two successively presented stimuli. Indeed, subjects displayed PM, prompting them to perceive the same orientation in the first and second dot lattice ($\beta_{1\text{st percept}}$=2.49, p<0.001).

While subjects performed the task, we recorded neural activity from surface and depth electrodes implanted in PFC (Fig. 1B). We investigated activity at 102 visually responsive sites in the superior

frontal gyrus (SFG), the main anatomical region constituting dmPFC. To assess whether any neural effects were specific to dmPFC, we also examined activity from 61 visually responsive sites on the lateral surface of PFC in the rostral middle frontal gyrus (MFG). Like dmPFC, MFG is involved in memory and decision making [9, 10]. To determine whether either of these regions supports PM, we analyzed HGB responses to the second stimulus. We only compared trials in which subjects perceived the 0° orientation, but sorted them depending on their history: 'perceptual memory' trials, where subjects perceived 0° in the first and the second dot lattice; and 'no perceptual memory' trials, where subjects perceived any orientation but 0° in the first and 0° in the second dot lattice. Hence, we matched conditions with identical percepts but different perceptual histories. HGB activity was significantly stronger on trials with PM than on trials without PM in medial PFC (Fig. 1C, see Figure S1F for other frequency bands), but not in lateral PFC (Fig. 1D; area × memory interaction 280-360 ms and 760-780 ms). Thus, dmPFC is actively involved in integrating PM with current perceptual information.

To assess whether dmPFC is also involved in the encoding of PM, we analyzed responses to the first stimulus in the trial, again matched for identical percepts. We sorted trials depending on whether they would lead to PM: 'future perceptual memory' trials, where subjects perceived 0° in the first and the second dot lattice; and 'no future perceptual memory' trials, where subjects perceived 0° only in the first dot lattice. We found no significant effects during the first stimulus (FDR, q=0.05), and Bayesian statistics provided evidence against perceptual memory effects in dmPFC (median BF_{10} 'perceptual memory' vs. 'no perceptual memory' 0.1). Thus, dmPFC partakes in the retrieval, but not the encoding of PM, paralleling its role in short-term memory in rodents [6].

To differentiate whether memory effects were perceptual or arose post-perceptually for successive decisions independently of perception [7], we also had subjects make decisions about orientation on stimuli that did not contain orientation information. We then assessed whether these decisions affected perception of subsequently presented hexagonal dot lattices (as in the main experiment; Fig. S1A). Behaviorally, there was no effect of preceding decisions on orientation perception (p=0.232, McNemar test). Thus, subjects implicitly memorized percepts, not decisions. dmPFC did not show a significant difference in HGB activity between trials in which subjects chose twice the same orientation, and trials in which they did not (Fig. 1E; task × repetition interaction 100-780 ms; see Fig. S1E for lateral PFC). Together, this suggests that the memory effects observed here are perceptual and not a post-perceptual decision bias.

Are the neural effects in dmPFC a cause or a consequence of PM? We had the rare opportunity to assess behavior in a high functioning patient who had prior surgery that resected 18% of left SFG (Fig. 1F). Remarkably, and in contrast to all other epilepsy patients, this subject did not have PM for orientation (Fig, 1G, single subject $\beta_{\text{1st percept}}$=0.09, p=0.826; group $\beta_{\text{lesion}\times\text{1st percept}}$=-2.35, p<0.001). Thus, dmPFC is causally involved in perceptual stabilization.

Taken together, we report a functionally and anatomically specific involvement of dmPFC in PM. Thus, this form of memory is not limited to visual cortex but interfaces with higher-order areas whose functional properties optimally accommodate perceptual stabilization [4, 5]. Our results expand the known functional repertoire of PFC, showing that it partakes in perception and suggesting a general role of dmPFC in contextualizing behavior. Important questions to be addressed in future studies include where PM is initially encoded, how confidence interacts with

PM, whether dmPFC also participates in PM in the absence of an overt report, and which precise computations give rise to the integration of past and current percepts.

Supplemental Information

Supplemental information includes experimental procedures, one table and one figure and can be found with this article at *bxs.

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Author Contributions

Conceived and designed the experiments: C.M.S. and L.M.; collected the data: L.M., D.M.G., and P.M.; attending neurosurgeons: W.D. and A.D.M.; supervised recordings and IRB approval

process: T.T., O.D., and A.D.M.; analyzed the data: C.M.S., S.S.S., L.M., and H.W.; wrote the manuscript: C.M.S., L.M., and S.S.S.; revised the manuscript: all authors.

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Figure Legend

Figure 1: **(A)** Subjects sequentially judged the perceived orientation of dot lattices. Stimulus 1 is bistable (0°, 90°); stimulus 2 is tristable (0°, 60°, 120°). Subjects selected the perceived orientation from a response screen after each respective stimulus. Perceptual memory is evidenced by an increased likelihood to perceive the same orientation in both stimuli. A dynamic random dot mask prevented between-trial carry-over effects. **(B)** We recorded from 102 medial (blue) and 61 lateral (red) PFC sites. Green marks the superior frontal gyrus, purple the rostral middle frontal gyrus. **(C)** Neural activity in the HGB was significantly stronger (effect size D_r>0) for the 2nd stimulus in 'perceptual memory' trials than in 'no perceptual memory' trials in medial PFC (FDR, q=0.05) ~70 ms after the onset latency (170 ms) of the region. **(D)** There was no significant difference between 'perceptual memory' trials and 'no perceptual memory' trials in the HGB in lateral PFC (FDR, q=0.05) throughout the response to the 2nd stimulus. **(E)** To differentiate decisional from perceptual effects, subjects had to make decisions about orientation in the absence of orientation information in the first stimulus on a subset of trials. Behaviorally, this had no effect on orientation perception in subsequent tristable stimuli, and there were no differences between 'decision repetition' and 'no decision repetition' trials in the HGB in medial PFC (FDR, q=0.05). Shading bars in C, D, E denotes 95% confidence intervals (CIs) of effect size (D_r), red outlines indicate significant time points (FDR), dashed lines mark the independently determined onset latencies of the respective area. **(F)** A subject with a circumscribed lesion in dmPFC. Turquoise outlines indicate the outer lesion boundary on anatomical MRIs in radiological convention (left is right). **(G)** The lesion patient did not exhibit perceptual memory effects while the non-lesioned subjects

show a systematic tendency to perceive the same orientation (0°) in both dot lattices, i.e., a higher probability to perceive 0° in the second, tristable stimulus, after perceiving 0° in the first stimulus than after perceiving any other orientation (left panel: lesion patient vs. the group of non-lesioned subjects, error bars denote 95% CIs). The perceived orientation in the 1st stimulus was a significant predictor of orientation perception in the 2nd stimulus in all patients but the lesion patient (right panel: beta weight per subject, error bars denote SEM).

Supplemental Information

Document S1. Experimental Procedures, one table and one figure.