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## What "wins" in VMPFC: scenes, situations, or schema?

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Lieberman et al. (2019) analyzed data from a range of sources, including active voxels during functional magnetic resonance imaging, that pertained to forward inference (asking where is there increased neural activity when a task is performed), reverse inference (asking what task is being performed when there is activity in a brain region), and causal evidence from lesioned patients and transcranial magnetic stimulation. Their specific focus was on the medial prefrontal cortex (MPFC) in its dorsal (DMPFC; BA 9), anterior (AMPFC; BA 10), and ventral (VMPFC; BA 11) extents, and their functions in psychological domains traditionally ascribed to MPFC, namely, social cognition, the self, emotion, value and, more recently, mental time travel (the ability to move in subjective time to remember past experiences and conceive future events). The results confirmed the involvement of MPFC across domains but also convincingly disclosed functional segregation within MPFC, with DMPFC strongly associated with social cognition and VMPFC with its affective aspects, AMPFC with self-related processing, and VMPFC with processing of value and emotion. The results also revealed the involvement of AMPFC and VMPFC in mental time travel, and this latter link is the focus of this commentary.

Lesion studies strongly implicate VMPFC in mental time travel. Patients with bilateral VMPFC damage recall the past and imagine future events with sparse detail and can, on occasion, confabulate. These findings align with the consistent engagement of VMPFC during fMRI studies of episodic remembering and future thinking. VMPFC-lesioned patients also discount future rewards steeply, further highlighting their poor consideration of the future. However, Lieberman et al.'s (2019) head-to-head multi-term reverse inference comparisons showed that, of the psychological domains considered, it was not mental time travel that won the competition for dedicated voxels in VMPFC. This could suggest that much of what VMPFC contributes concerns the affective, evaluative, and self-related processes inherent to mental time travel. However, the authors also reported that VMPFC contained a considerable

proportion of "no-winner" voxels which supported a function that was significantly related to each domain, but not preferentially so. As yet, we do not know what that function is.

A few years ago, we found that VMPFC patients had difficulty imagining future events and also atemporal, fictitious events (Bertossi et al., 2016). At that point we hypothesized that VMPFC supported 'scene construction', a process underpinning the ability to mentally represent any complex event, for example by activating relevant schematic knowledge about typical scenes or events (see also Gilboa and Marlatte, 2017). Interestingly, Lieberman et al.'s (2019) single-term reverse inference maps for the term 'scene' and (even more so) 'event' revealed VMPFC regions that closely overlapped with the no-winner voxels (see their Figure 5). The authors argued that VMPFC may not just represent the visual aspects of scenes but, more generally, bits of (spatial, temporal, evaluative, social) knowledge that are associated with scenes or situational contexts.

We agree that VMPFC is unlikely to specifically support scene construction. Instead we suggest it implements functions upstream of, and instrumental to, scene construction (and mental time travel). This view evolved from our recent in-depth consideration of the effects, across cognition, of either amnesia-inducing focal bilateral hippocampal damage or bilateral VMPFC lesions (McCormick et al., 2018). Three of the dissociations we noted between hippocampal and VMPFC-damaged patients are germane here. First, studies of mind-wandering (i.e., the drift of attention away from external input towards inner experience) suggest that hippocampal patients mind-wander as frequently as healthy controls, but their perceptually-decoupled thoughts are devoid of episodic content and scene imagery. In contrast, VMPFC patients have a reduced tendency to mind-wander compared to both healthy and brain-damaged controls, perhaps implying that VMPFC facilitates the endogenous initiation of inner experience. Second, hippocampal patients' attempts at scene imagery are spatially fragmented and typically contain significantly fewer spatial elements than those of healthy controls, but a similar number of other details relating to scene content. VMPFC

patients, on the other hand, construct scenes that are globally impoverished (De Luca et al., 2018). This may be further evidence of the VMPFC's role in endogenous processing, because the cues in scene construction tasks are somewhat unconstrained. Third, hippocampal patients are unable to describe even single scenes from past or future events. By contrast, VMPFC patients, while impaired at constructing entire events, seem able to recall and describe individual scenes from events when the cues are specific (Kurczek et al., 2015), suggesting that scene construction per se is not the remit of the VMPFC but instead it may be a necessary component for the temporal unfolding of a dynamic mental event.

These observations coalesce in our simple model, summarized in Figure 1. In this architecture, VMPFC (in green) initiates the activation of schematic and other knowledge in neocortex that is relevant (shown edged in green) for a specific event, while inhibiting elements that are not relevant (shown edged in grey). This information is conveyed to the hippocampus (in red), which constructs a single scene snapshot from that event. VMPFC then engages in iterations via feedback loops with neocortex and hippocampus to mediate the schema-based retrieval, monitoring and sequencing necessary for building the successive scenes that comprise the unfolding mental event (McCormick et al., 2018). We propose that some or all of these processes may be what is activating Lieberman et al.'s (2019) VMPFC no-winner voxels.

Importantly, this idea specifies clear avenues for future investigation. Orthogonalizing and manipulating memory cues could help to disambiguate whether, and how, VMPFC supports scene, event, or situational processing in general, or only when they entail endogenous initiation, strong schema, or multiple transitions between scenes. Moreover, there is a dearth of knowledge concerning how scenes and events unfold millisecond to millisecond. A neuroimaging technique such as magnetoencephalography could throw new light on VMPFC-hippocampal interactions, including whether VMPFC drives oscillatory

activity in the hippocampus during scene and event (re)construction, as would be predicted by our model.

Insert Figure 1 about here

**Competing interests statement**

The authors have no competing interests to declare.

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**Figure Caption**

**Figure 1.** A simple model of scene and event construction involving the VMPFC (in green) and hippocampus (in red). See text and McCormick et al. (2018) for further details.

