Response to O’Callaghan et al. by Pierre Mégevand, David M. Groppe, and Ashesh D. Mehta

We thank O’Callaghan and colleagues for their thoughtful review of our work. The authors frame our findings in the context of the large-scale brain networks that connect the parahippocampal place area (PPA) with other brain regions subtending memory, emotions, cognitive control, and referential processing in addition to vision. They suggest that the PPA could represent a ‘nexus’ in the pathophysiology of visual hallucinations in various medical conditions that do not target the parahippocampal cortex per se.

Characterizations of information processing form a spectrum from local and modular to distributed and network-based, with both facets likely to exist at varying degrees across brain areas. The multimodal convergence (using functional MRI, intracranial EEG and direct electrical stimulation) of our findings supports a modular organization for visual scene processing in the PPA (see also Davidesco et al., 2013, for selective responses to exemplars of faces in the fusiform cortex). It is worth considering that electrical stimulation of the cortex most often does not result in any obvious conscious percept, and that perhaps areas that are most likely to have the strongest phenomenological correlation could represent sites with a greater degree of modular organization. On the other hand, assessment of the effects of stimulation in areas with more of a distributed network organization might have higher yield by examining for more modulatory influences to information processing rather than producing highly salient phenomenology.

How could one test the authors’ hypothesis that visual hallucinations would arise from the influence of remote network activity upon the PPA? Perhaps the strongest evidence would come from applying multifocal stimulation to remote cortical areas in order to impact the PPA and trigger hallucinations. Multifocal stimulation is not routinely performed in current clinical protocols, but it is likely only a question of time before such an experiment becomes feasible. Direct electrical stimulation with simultaneous functional MRI (Jones et al., 2014) would allow delineating the neural network associated with hallucinations triggered by PPA stimulation. Because not all neural connections are reciprocal (Entz et al., 2014; Keller et al., 2014), cortico-cortical evoked potentials would help delineate the incoming effective connectivity of the PPA. The observation that visual hallucinations alter activity in the PPA in a variety of medical conditions would provide additional evidence.

Visual hallucinations are fleeting, often haunting experiences (Sacks, 2012). Direct brain stimulation, combined with the array of neurophysiological and neuroimaging methods currently at our disposal, offers an unprecedented chance to investigate and perhaps solve their neural underpinnings.

References:


