Response to Commentary by Tune and Asaridou on Davey et al. (2015), *Automatic and Controlled Semantic Retrieval: TMS reveals distinct contributions of posterior middle temporal gyrus and angular gyrus*, Journal of Neuroscience, 35(46), 15230-15239, doi: 10.1523/JNEUROSCI.4705-14.2015

There is considerable controversy about the contribution of left temporo-parietal cortex, particularly posterior middle temporal gyrus (pMTG) and angular gyrus (AG), to semantic cognition. Some accounts suggest that temporo-parietal regions provide a "thematic hub", while anterior temporal cortex instead captures knowledge of taxonomic categories (Schwartz, Kimberg et al. 2011). An alternative view is that AG and pMTG contribute to different aspects of semantic retrieval across these domains of knowledge. Davey et al. (2015) aimed to distinguish these two views by comparing tasks that required identity matching (knowing that a picture is an 'Alsatian') and thematic association matching (matching this animal with 'bone'). Repetitive Transcranial Magnetic Stimulation (rTMS) to AG and pMTG interfered with both thematic and identity matching trials. This is inconsistent with the predictions of the thematic hub account, which would predict no disruption of identity matching.

A second question is whether AG and pMTG support more automatic and controlled retrieval respectively. To test this hypothesis, we contrasted the effects of TMS on thematic associations that were strong and easy-to-retrieve (e.g., dog with bone), with weaker relationships that had higher controlled retrieval demands (dog with beach). Neuroimaging work has already shown that pMTG and AG respond differently to hard and easy semantic tasks (Noonan, Jefferies et al. 2013), and have different patterns of functional connectivity at rest (see Figure 1 in Davey et al., 2015); however, these data are correlational. As noted by Tune and Asaridou, there are several reasons why the application of rTMS to AG and pMTG might fail to yield causal evidence of dissociable functions – these regions are spatially adjacent, show a complex pattern of inter-connections, and a poor choice of task may fail to capture key differences in their functions. Nevertheless, we found the predicted differences: stimulation of pMTG replicated previous findings showing greater disruption of weak than strong associations (Whitney, Jefferies et al. 2011) when this variable was included as a continuous predictor in the model (Analysis 2). AG produced the reverse pattern. This occurred even when controlling for performance on a non-semantic perceptual task, ruling out non-specific or visual effects of TMS.

As Tune and Asaridou argue, a well-specified account of the link between mental processes and cortical function is likely to be complex (see Figure below). Our results demonstrate that AG and pMTG do not fit the functional profile of thematic hubs, and that these regions make non-identical contributions to semantic cognition. This conclusion adds to earlier work showing equivalent disruption of weak but not strong associations following TMS to pMTG and left inferior frontal gyrus (LIFG; Whitney et al., 2011). Thus, there are *similar* effects of TMS in two *spatially separated* sites implicated in semantic control (pMTG and LIFG), plus *different* effects of TMS for *neighbouring sites* implicated in controlled vs. automatic aspects of retrieval (pMTG and AG). pMTG is located at the convergence of multiple large-scale networks, which might allow semantic retrieval in ATL to be constrained by regions important for executive control and attention. AG has strong connections to ATL and the medial core of the default mode network, which could facilitate rapid integration of strongly-activated conceptual information. These speculations provide plausible working hypotheses that are best tested, as noted by Tune and Asaridou, using converging neuroscientific methods.

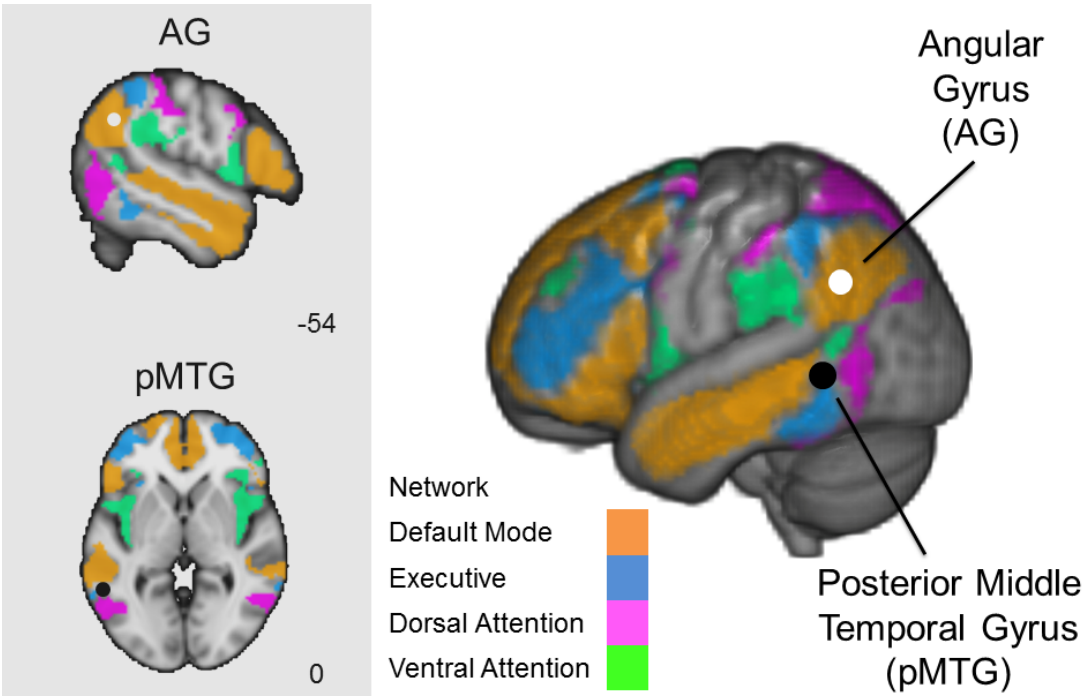

Figure: The stimulation sites used by Davey et al. (2015) are superimposed on maps of resting state networks from Yeo et al. (2011). pMTG, implicated in semantic control by a meta-analysis of fMRI studies (Noonan et al., 2013), lies at the intersection of multiple networks including the default mode network (shown in orange) and networks thought to contribute to the control of cognition (executive, dorsal attention and ventral attention systems). This spatial location might allow pMTG to control semantic retrieval. In contrast, the AG site, implicated in automatic semantic retrieval by a second meta-analysis (Humphreys & Lambon Ralph, 2014), lies squarely within the default mode network. These spatial patterns help to explain why pMTG shows greater functional connectivity to left inferior frontal gyrus (LIFG) and inferior frontal sulcus – regions implicated in semantic control (see Figure 1 in Davey et al., 2015). In contrast, AG shows greater connectivity to anterior temporal cortex (also shown in Figure 1; Davey et al., 2015).

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