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Exploring the role of the posterior middle temporal gyrus in semantic cognition: Integration of anterior temporal lobe with executive processes

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ABSTRACT

Making sense of the world around us depends upon selectively retrieving information relevant to our current goal or context. However, it is unclear whether selective semantic retrieval relies exclusively on general control mechanisms recruited in demanding non-semantic tasks, or instead on systems specialised for the control of meaning. One hypothesis is that the left posterior middle temporal gyrus (pMTG) is important in the controlled retrieval of semantic (not non-semantic) information; however this view remains controversial since a parallel literature links this site to event and relational semantics. In a functional neuroimaging study, we demonstrated that an area of pMTG implicated in semantic control by a recent meta-analysis was activated in a conjunction of (i) semantic association over size judgements and (ii) action over colour feature matching. Under these circumstances the same region showed functional coupling with the inferior frontal gyrus — another crucial site for semantic control. Structural and functional connectivity analyses demonstrated that this site is at the nexus of networks recruited in automatic semantic processing (the default mode network) and executively demanding tasks (the multiple-demand network). Moreover, in both task and task-free contexts, pMTG exhibited functional properties that were more similar to ventral parts of inferior frontal cortex, implicated in controlled semantic retrieval, than more dorsal inferior frontal sulcus, implicated in domain-general control. Finally, the pMTG region was functionally correlated at rest with other regions implicated in control-demanding semantic tasks, including inferior frontal gyrus and intraparietal sulcus. We suggest that pMTG may play a crucial role within a large-scale network that allows the integration of automatic retrieval in the default mode network with executively-demanding goal-oriented cognition, and that this could support our ability to understand actions and non-dominant semantic associations, allowing semantic retrieval to be 'shaped' to suit a task or context.

Introduction

Across our lifetime we acquire a large body of conceptual knowledge, only a subset of which is relevant for any given task or context; thus automatic spreading activation within semantic representations is often insufficient for efficient semantic cognition (Thompson-Schill et al., 1997; Badre et al., 2005; Jefferies, 2013). Automatic spreading activation can facilitate the retrieval of features and associations that are *dominant* for a particular concept (e.g., carrot-peel). When semantic retrieval needs to be focussed on aspects of knowledge that are *not* the strongest response for the inputs, additional control mechanisms can be engaged to guide semantic retrieval. For example, control is needed to recover weak associations (carrot-horse) and to match words on the basis of specific sensory-motor features, such as actions or colour (e.g., carrot with traffic cone), since the functional characteristics of these concepts are more central to their meaning (Thompson-Schill et al., 1997; Badre et al., 2005; Whitney et al., 2011; Noonan et al., 2013; Davey et al., 2015a).

Different brain regions have been implicated in the *representation* and *controlled retrieval* of semantic information. The ventral anterior temporal lobes (ATLs) have been argued to form a key repository of conceptual information, following studies of patients with semantic dementia (SD). These patients have relatively focal bilateral atrophy focussed on ATL, associated with a gradual deterioration of knowledge and multimodal semantic deficits, first affecting fine-grained distinctions between concepts, and then eroding more basic distinctions (Mummery et al., 2000; Hodges and Patterson, 2007; Patterson et al., 2007). Deficits in SD patients suggest they show a loss of central

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semantic information (Bozeat et al., 2000; Jefferies and Lambon Ralph, 2006) and studies employing inhibitory transcranial magnetic stimulation (TMS) in healthy participants have provided converging evidence for a necessary role of this region in comprehension (Pobric et al., 2007, 2010). Functional magnetic resonance imaging (fMRI) studies reveal activation of ATL during diverse semantic judgements (Binder et al., 2009; Visser et al., 2010; Rice et al., 2015). Finally, analyses of inter-regional signal correlations during task free (i.e. resting-state) functional scans have shown that ATL is part of a large scale assembly that includes medial prefrontal and posterior cingulate cortices, commonly referred to as the *default mode network* (DMN, Raichle et al., 2001; Buckner et al., 2008; Yeo et al., 2011; Jackson et al., 2016).

Converging neuroscientific methods have also identified brain regions beyond ATL which are important for multimodal semantics, specifically left inferior frontal gyrus (LIFG) and posterior middle temporal gyrus (pMTG). These regions are thought to contribute to the *control* of semantic retrieval. Patients with semantic aphasia (SA), who have lesions affecting these regions following stroke, fail the same range of verbal and non-verbal semantic tasks as SD patients; however, unlike SD cases, they often retrieve information that is irrelevant or inappropriate for the task, show strong effects of cues and miscues, and perform poorly in the face of strong distracters or ambiguous meanings (Thompson-Schill et al., 2002; Jefferies and Lambon Ralph, 2006; Jefferies et al., 2008, 2010; Corbett et al., 2009). Converging evidence from fMRI (Poldrack et al., 1999; Badre et al., 2005; Snijders et al., 2010; Noonan et al., 2013; Davey et al., 2015b) and TMS (Hoffman et al., 2010; Whitney et al., 2011; Davey et al., 2015a) supports the view that both of these regions contribute to semantic control. Indeed, in a recent neuroimaging meta-analysis, LIFG and pMTG were the sites activated most strongly and consistently across many different contrasts designed to tap semantic control (Noonan et al., 2013). In addition, when high-control semantic tasks were contrasted with demanding phonological judgements, pMTG and the anterior part of LIFG showed a specifically semantic response, suggesting that these two regions lie outside of the multiple-demand network (MDN), which is recruited during executively-demanding tasks across domains (Duncan, 2010).

These findings therefore provide some evidence that semantic cognition may be underpinned by at least three component processes, supported by distinct brain networks. (1) Domain-general executive control implemented by the MDN (Duncan, 2010) and the fronto-parietal control system (Power and Petersen, 2013) may support the capacity to engage and sustain a particular type of semantic retrieval in line with the task instructions, as well as the application of top-down constraints to support goal-driven aspects of cognition beyond semantics (Duncan and Owen, 2000; Duncan, 2010; Fedorenko et al., 2013; Noonan et al., 2013). For example, in a feature-matching task (in which globally unrelated words must be linked together on the basis that they both have a particular feature specified in the task instructions), there is a need to apply a pre-specified goal during semantic retrieval, and the implementation of this goal may involve the executive system. (2) Activation is thought to spread automatically between highly-related concepts within the representational system (underpinning semantic priming effects for strong associates). This allows dominant features and associations to be retrieved in the absence of executive control, and is supported by ATL and potentially other regions in the DMN (Wirth et al., 2011; Lau et al., 2013; Power and Petersen, 2013; Jackson et al., 2016). (3) A third network might support situations in which there is *no explicit goal* to indicate which aspect of knowledge should be brought to the fore, but the pattern of retrieval that is required for success is not the dominant one given the stimuli — i.e., semantic retrieval must be controlled to identify and sustain a linking context. The retrieval of relatively weak global associations is a good example of such a task: here, the instructions do not establish which types of associations or features should be the focus for retrieval — instead, it is necessary to establish a linking context from the concepts themselves and retrieve features relevant to this context.

Fig. 1 illustrates the spatial distribution for these three putative networks (MDN, DMN, and semantic control) from prior published investigations. This figure shows that regions implicated in semantic control by the meta-analysis of Noonan et al. (2013, in green) are only partially overlapping with the MDN (from Fedorenko et al., 2013, in red). Non-overlapping areas in LIFG and pMTG appear to be important for demanding semantic tasks (relative to easier semantic judgements) but not executive control across domains. Moreover, these semantic control regions are spatially intermediate between the MDN (implicated in executive control) and the DMN (implicated in automatic retrieval, from Yeo et al., 2011, in blue); this location could allow semantic control regions to integrate two distributed networks that are anti-correlated at rest and yet both crucial for semantic cognition, e.g., when semantic knowledge, not a task goal, defines the attentional focus.

The proposal that the control of semantic retrieval is partially distinct from executive control is broadly consistent with functional dissociations that have been identified within left inferior frontal cortex. Within the language domain, studies have reported a functional gradient in left inferior frontal gyrus (IFG), with ventral anterior aspects of IFG implicated in semantic control specifically, and dorsal posterior IFG contributing more broadly to language control, including phonological tasks (Poldrack et al., 1999; Wagner et al., 2001a, 2001b; Devlin et al., 2003; Gough et al., 2005; Snyder et al., 2007). Dorsal IFG, bordering inferior frontal sulcus (IFS), is recruited when participants select specific aspects of knowledge in line with an externally-specified goal (i.e., instructions to match words by colour or shape in the absence of a global semantic relationship; Badre et al., 2005). This selection process may be important for many language tasks, such as lexical and phonological retrieval. In contrast, ventral/anterior IFG shows an increased response when weak and strong semantic associations are contrasted (e.g., salt-grain > salt-pepper) — i.e., when participants shape retrieval to converge on a distant link between two concepts in the absence of an explicit goal. This ability to recover a non-dominant conceptual link does not generalise easily to other aspects of language processing. Recent work using single-subject analyses identified regions within the multiple-demand network, in dorsal and posterior IFG/IFS, that respond to difficult verbal working memory judgements involving non-words (Fedorenko et al., 2013): these regions are adjacent to, but spatially distinct from, areas of IFG that show a greater response to easier meaning-based trials involving words in sentences (Fedorenko et al., 2012; Blank et al., 2014). Moreover, analyses of resting-state connectivity have implicated anterior aspects of prefrontal cortex in a cingulo-opercular control system, which includes regions that display sustained activity during task-set maintenance, while dorsal prefrontal regions couple with a fronto-parietal system engaged by ongoing selection and implementation (Power and Petersen, 2013): this pattern may relate to the functional distinction between anterior and dorsal LIFG. Thus, a more semantic response in anterior/ventral parts of IFG may be broadly in line with the proposal that anterior areas in IFG establish and maintain priorities for what is to be retrieved, while the short-term process of selection itself is implemented in posterior regions of IFG (Badre and D'esposito, 2007). Badre and colleagues referred to this functional specialisation within IFG as "controlled retrieval" and "selection" respectively (Badre et al., 2005).

The functional contribution of IFG has been considered in detail while the significance of the second region identified by Noonan and colleagues, pMTG, remains controversial. Although this site is implicated in semantic control, a parallel literature links pMTG, together with angular gyrus (AG), to the comprehension of actions and events (Johnson-Frey et al., 2005; Liljeström et al., 2008), and to relational semantics (Humphreys and Lambon Ralph, 2014; Price et al., 2015), and these adjacent areas of temporoparietal cortex can show a similar response to contrasts tapping event knowledge (Wagner et al., 2005; Sachs et al., 2008; Kim, 2011). One theoretical account suggests that AG and/or pMTG provide a "thematic hub", capturing aspects of knowledge relating to the associations between concepts — such as