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Evidence for degraded low frequency verbal concepts in left resected temporal lobe epilepsy patients

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ABSTRACT

According to a large neuropsychological and neuroimaging literature, the bilateral anterior temporal lobe (ATL) is a core region for semantic processing. It seems therefore surprising that semantic memory appears to be preserved in temporal lobe epilepsy (TLE) patients with unilateral ATL resection. However, recent work suggests that the bilateral semantic system is relatively robust against unilateral damage and semantic impairments under these circumstances only become apparent with low frequency specific concepts. In addition, neuroimaging studies have shown that the function of the left and right ATLs differ and therefore left or right ATL resection should lead to a different pattern of impairment. The current study investigated hemispheric differences in the bilateral semantic system by comparing left and right resected TLE patients during verbal semantic processing of low frequency concepts. Picture naming and semantic comprehension tasks with varying word frequencies were included to investigate the pattern of impairment. Left but not right TLE patients showed impaired semantic processing, which was particularly apparent on low frequency items. This indicates that, for verbal information, the bilateral semantic system is more sensitive to damage in the left compared to the right ATL, which is in line with theories that attribute a more prominent role to the left ATL due to connections with pre-semantic verbal regions.

1. Introduction

1.1. Semantic memory

Semantic memory refers to the meaning of words, pictures, sounds and general information about the world. Damage to the bilateral anterior temporal lobes (bATL) leads to impaired semantic performance in Alzheimer's disease, semantic dementia (SD) and herpes simplex encephalitis (HSE), suggesting that the bATL is a core region for semantic representation (Lambon Ralph, 2014; Lambon Ralph et al., 2017; Rogers et al., 2004). This is further supported by a range of functional neuroimaging studies in healthy participants (Devlin et al., 2000; Hoffman et al., 2015; Humphreys et al., 2015; Vandenberghe et al., 1996; Visser et al., 2010).

Classical models suggest that conceptual knowledge arises from networks of modality-specific brain regions distributed throughout the cortex (for reviews see: Capitani et al., 2003; Humphreys and Forde, 2001; Martin, 2007). The newer hub-and-spoke's model suggest that these modality specific (i.e., “spoke”) regions interact with the transmodal ATL “hub”, whose function is to distil coherent concepts from these “spoke” regions (Lambon Ralph, 2014; Lambon Ralph et al., 2017; Rogers et al., 2004). This model suggests that the brain must contain a central semantic hub to support generalizations across concepts that have similar conceptual relations but very different property profiles. For example, dogs and parrots look and behave very differently, yet share many conceptual relations that humans can easily use to support categorical generalizations (e.g., are animals, breath air, are pets etc.). The bATL is a good candidate to serve as a central hub as it connects with many regions throughout the brain (Binney et al., 2012; Lambon Ralph et al., 2017; Rogers et al., 2004).

1.2. Semantic impairments in left and right temporal lobe epilepsy patients

The ideas of Lambon Ralph, Patterson and colleagues originate from

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SD patient studies. The semantic impairments in SD patients are caused by progressive bilateral ATL atrophy. Therefore, studies on temporal lobe epilepsy (TLE) patients with unilateral left or right ATL lobectomy can advance our knowledge on the role of the bATL and specifically on differences between left and right ATL. However, studies on TLE patients without ATL lobectomy, in which dysfunction of this area is heterogeneous, show an inconsistent pattern on left/right differences. Whereas some studies have showed that left but not right TLE patients are impaired on expressive naming tasks (Drane et al., 2013; Giovagnoli et al., 2005; Voltzenlogel et al., 2006, 2015), other studies revealed naming impairments in both left and right TLE patients (Giovagnoli et al., 2016a; Messas et al., 2008; Seidenberg et al., 2002). Furthermore, the literature base on the semantic impairments in resected TLE patients is scarce. A few studies have examined remote memory problems using famous faces or scenes, thereby probing semantic memory (Barr et al., 1990; Drane et al., 2013; Lah et al., 2004).

Barr et al. (1990) were the first to describe that left but not right resected TLE patients were significantly impaired at recalling famous people's names. This result was replicated by Lah et al. (2004), who found that naming deficits were evident in recall but not in recognition. Therefore, Lah et al. (2004) suggested that patients show a retrieval problem rather than damage to a semantic store. In addition, they showed that both left and right resected TLE patients were impaired when asked to answer questions about famous events. In the same study, these results were repeated on a verbal fluency task for famous persons and events: left TLE patients were impaired on the former, whereas both left and right TLE patients were impaired on the latter category. According to Lah et al. this fits with Damasio's (1989) model, which suggests that the ATL is not involved in general semantics but is involved in knowledge for unique entities.

A recent study by Drane et al. (2013) provided another view. Their study showed a double dissociation: right resected TLE patients had problems recognizing faces but once recognized they could always name the famous person. In contrast, left TLE patients could often recognise a face but were unable to name it. Based on this, Drane et al. (2013) suggested that the right ATL plays a fundamental role in accessing semantic information from a visual route, whereas the left ATL serves to link semantic information to the language system, which is required for naming.

The studies above were limited to remote memory on faces and/or events. In contrast, two recent studies have showed semantic memory impairments in resected TLE patients using a new semantic battery which focused on probing low frequency concepts (Lambon Ralph et al., 2012; Rice et al., 2018). These studies showed that patients performed well on standard semantic tasks probing concepts at the basic level (although semantic impairment was reflected by a n increase in response times on these tasks). However, patients were impaired for more demanding concepts referring to specific and abstract information. Furthermore, in the former study both left and right TLE patients showed semantic impairments on verbal tasks, although these were more severe for left TLE patients (Lambon Ralph et al., 2012). However, in the latter study, semantic impairments were found in the left TLE but not in the right TLE patient group (Rice et al., 2018).

The authors of these two studies pointed out that many current standard semantic memory tests are not sensitive to mild semantic impairments in TLE as they tend to use highly frequent concepts. This is important as the observed absence of semantic problems in these patients has cast doubt on the semantic role of the ATL. Taking into account the well-defined episodic memory impairments in TLE patients, it is logical that these impairments dominate the research field taking away the focus from potential semantic problems. As such, some influential review articles have suggested that the semantic role of the ATL should be considered with caution as unilateral ATL lobectomy does not commonly lead to semantic impairments (Hickok and Poeppel, 2004; Simmons and Martin, 2009).

1.3. Models explaining the frequency and lateralization effects in the semantic system

As explained above, the hub-and-spoke's model suggests that a transmodal hub in the bilateral ATL forms concepts through connections with modality-specific regions (Lambon Ralph et al., 2017; Rogers et al., 2004). The more frequently a concept is processed, the stronger its bilateral representation becomes, making it more readily available and more robust to damage. After unilateral damage, the remaining ATL can continue to support comprehension for strongly-instantiated high frequency concepts; thus small semantic impairments are easily overlooked on standard semantic tests (Bell and Giovagnoli, 2007; Rice et al., 2018, 2015a; Rogers et al., 2004; Schapiro et al., 2013). In other words, the remaining semantic system in the unilateral ATL is still able to construct highly frequent concepts but struggles when probing low frequent, specific concepts.

In the first computational model of the hub-and-spoke's model, the left and right ATL represented conceptual knowledge in a unified manner as part of a bilateral coupled system (Rogers et al., 2004). In agreement, repetitive transcranial magnetic stimulation (rTMS) to either the left or right ATL results in equivalent levels of semantic impairment for both verbal and nonverbal semantic tasks (Lambon Ralph et al., 2009; Pobric et al., 2010, 2007). However, such a model is unable to explain the different neuropsychological patterns seen in left and right TLE patients. Therefore, newer implementations of the model suggest that graded hemispheric specialisation emerges as a consequence of connectivity with modality-specific regions (Binney et al., 2012; Rice et al., 2018, 2015a, 2015b; Schapiro et al., 2013; Visser and Lambon Ralph, 2011). For example, left > right differences reflect the stronger connectivity of the ATL with the left-lateralized language network (for a more detailed explanation see the review of Rice et al., 2015b). In line with this, a large meta-analysis of functional neuroimaging data showed that the bilateral ATL are involved in all tasks and modalities, with a relatively increased reliance on the left ATL during verbal production and comprehension (Rice et al., 2015a).

However, when considering verbal tasks, we need to distinguish between naming and comprehension tasks. Neuropsychological data from SD patients shows a left-side dominance during expressive tasks due to connections with left-hemisphere phonological regions, whereas this left lateralisation effect was less strong during comprehension tasks (Lambon Ralph et al., 2001). This aligns with TLE studies that have shown that naming impairments are most prominent in left TLE compared to right TLE patients with a less clear lateralization pattern for comprehension tasks (Barr et al., 1990; Drane et al., 2013; Giovagnoli et al., 2005; Lah et al., 2004; Lambon Ralph et al., 2012; Voltzenlogel et al., 2006, 2015). Taking into account these neuropsychological data as well as the large meta-analysis on the neuroimaging data (Rice et al., 2015b), this suggests that both verbal naming and comprehension tasks are left lateralised with a more dominant lateralisation effect for naming.

1.4. The present study

The current study will investigate semantic problems in TLE patients with left or right ATL resection. The hypothesis is that left TLE patients perform particularly poorly on verbal semantic tasks, whereas the performance of right TLE patients is generally intact. This would be in agreement with a left lateralisation of verbal semantic information within the bilateral semantic system.

Semantic problems in TLE patients are often overlooked on standard semantic tests, but can be revealed by probing the meanings of low frequency words (Lambon Ralph et al., 2012). Therefore, the current study investigated this frequency effect in more detail by including multiple frequency levels. Moreover, hemispheric differences are likely to be overlooked when restricting to tasks on high frequency words, making it essential to include low frequent words to investigate the full