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Refractory effects in stroke aphasia: A consequence of poor semantic control

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Abstract

This study examined the full range of effects associated with "semantic access impairment" – namely, refractory variables (semantic relatedness, speed of presentation and item repetition), inconsistency, the absence of frequency effects and facilitation by cues – in a series of stroke patients with multimodal semantically impairment. By investigating all of these factors in a group of patients who were not specifically selected to show "access" effects, we were able to establish (1) whether this pattern is a common consequence of infarcts that produce semantic impairment and (2) if these symptoms co-occur. All of the patients showed effects of cueing and an absence of frequency effects in comprehension. Patients whose brain damage included the left inferior prefrontal cortex (LIPC) also showed marked effects of refractory variables; in contrast, two patients with temporal–parietal but not frontal lesions were less sensitive to these variables. Parallel results were obtained for cyclical naming and word–picture matching tasks suggesting that the LIPC plays a role in semantic selection as well as lexical retrieval. Rapid presentation and item repetition is likely to have increased the selection demands in both of these tasks in a similar fashion. Unlike patients with classical "semantic access impairment", our semantically impaired stroke patients showed significant test–retest consistency, indicating that their difficulties did not result from an unpredictable failure of semantic access—instead, their deficits were interpreted as arising from failures of semantic control.

Keywords: Semantic memory; Aphasia; Semantic dementia; Access impairment; Refractory

1. Introduction

Semantic memory encompasses the meaning of words, objects and faces, and includes general conceptual and factual knowledge. Previous neuropsychological single case studies suggest that there may be two distinct patterns of semantic impairment—described as disorders of "storage" and "access" (Forde & Humphreys, 1995; Warrington & McCarthy, 1983; Warrington & Shallice, 1979). Patients who purportedly have degradation of the semantic store show strong effects of word/concept frequency. They also show highly consistent performance when the same concepts are probed repeatedly. In contrast, a number of individuals with extremely poor comprehension in the context of global aphasia have been reported to have "semantic access impairment". Such patients are less consistent, insensitive to frequency and show "refractory" effects in comprehension tasks. The defining characteristic of a refractory semantic deficit is that processing becomes poorer for a short time after the retrieval of conceptual knowledge, particularly for items that are semantically related. Consequently, patients with "access" deficits become progressively less accurate throughout "cyclical" semantic tasks in which sets of items are presented repeatedly. They show effects of speed of presentation (response stimulus interval or RSI), item repetition, and semantic relatedness in such tasks (Crutch & Warrington, 2005; Warrington & McCarthy, 1983). Cueing also facilitates semantic retrieval in these patients (e.g. Warrington & Shallice, 1979).

Many of the characteristics of a semantic storage deficit are shown by patients with semantic dementia (SD). These patients have a progressive deterioration of semantic knowledge following bilateral atrophy of the inferior and lateral aspects of the anterior temporal lobes (Hodges, Salmon, & Butters, 1992; Mummery et al., 2000; Nestor, Fryer, &, Hodges, 2006; Snowden, Goulding, & Neary, 1989). SD patients have poorer knowledge of lower frequency items (Bozeat, Lambon

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Ralph, Patterson, Garrard, & Hodges, 2000; Hodges, Graham, & Patterson, 1995; Lambon Ralph, Graham, Ellis, & Hodges, 1998; Warrington, 1975) and are highly consistent—both across test sessions (Coughlan & Warrington, 1981) and when the same items are probed using different semantic tasks (Bozeat et al., 2000). In addition, aspects of knowledge that are shared by lots of items (e.g. zebras have four legs) are more robust in the face of this damage than knowledge of specific entities (e.g. zebras have stripes; Bozeat et al., 2003; Lambon Ralph, Graham, Patterson, & Hodges, 1999; Warrington, 1975).

Rogers et al. (2004) implemented a computational model of the anterior temporal lobe semantic system in which conceptual representations form through the distillation of information required for mappings between different verbal and non-verbal modalities. The anterior temporal lobes are ideal for forming such representations as they have extensive connections with cortical areas that represent modality-specific information (Gloor, 1997). The Rogers et al. model shows several characteristics of the "semantic storage deficit" seen in SD when it is damaged—i.e. strong frequency effects, an advantage for superordinate-level knowledge, and highly consistent performance across different semantic tasks. Frequently encountered items form stronger representations in the temporal lobe semantic system, making information about them more robust in the face of semantic degradation. In addition, as the semantic system collapses, fine distinctions (e.g. between terriers and poodles) are more vulnerable than broader divisions (e.g. between animals and plants), as the properties that are necessary for making general distinctions are shared across many items. Patients with herpes simplex encephalitis, who also have damage to the anterior temporal lobes, similarly show the hallmarks of semantic storage disorder (Warrington & Shallice, 1984; Wilson, 1997).

In contrast, a number of individual stroke/tumour cases have been described with impairments of semantic access (Cipolotti & Warrington, 1995; Crutch & Warrington, 2003, 2004; Ferrand & Humphreys, 1996; Forde & Humphreys, 1995, 1997; McNeil, Cipolotti, & Warrington, 1994; Warrington & Cipolotti, 1996; Warrington & Crutch, 2004; Warrington & McCarthy, 1983, 1987). These patients commonly have profound aphasia and large lesions encompassing left frontal, parietal and sometimes posterior temporal areas—however, the anterior temporal lobes are apparently spared. Warrington and colleagues proposed that these patients have damage to the mechanisms that access semantic knowledge, making semantic retrieval unreliable from trial to trial.

The contrast between these two patterns of impairment has the potential to tell us a great deal about the neural basis of semantic memory. However, the distinction between "storage" and "access" disorders has been criticised on both empirical and theoretical grounds (Rapp & Caramazza, 1993). Some patients show a mixture of "storage" and "access" effects, suggesting that these syndromes may not be so readily distinguishable (see Gotts & Plaut, 2002 for a recent review). In addition, Rapp and Caramazza noted that in a literature dominated by single case studies, not all of the characteristics of storage/access impairment had been tested in both patient groups: patients with disorders of "storage" and "access" have rarely been directly compared using the same tasks. Warrington and Cipolotti (1996) addressed this concern for a subset of storage/access characteristics. They found that strong frequency effects, an insensitivity to speed of presentation and consistent performance across repeated administrations of the same semantic trials co-occurred in four "storage" patients with SD. The opposite pattern was found in two patients with "access" deficits resulting from stroke or tumour.

Rapp and Caramazza (1993) also suggested that some of the distinguishing features of access and storage deficits are poorly motivated. For example, it is unclear why "access" patients are insensitive to frequency since more frequent concepts might be easier to access, as well as being more robust in the face of semantic degradation. Gotts and Plaut (2002) presented a neurobiologically constrained computational model of storage/access disorders that overcomes this difficulty. They modelled "storage" deficits by damaging the neurons that represent semantic knowledge (like Rogers et al., 2004 described above). In contrast, "access" disorders were explained in terms of damage to neuromodulatory signals that interact with synaptic depression. Synaptic depression is a type of neural refractoriness because it reduces the responsiveness of neurons for a short period after they have fired. Certain neuromodulators, for example acetylcholine, promote ongoing neural activity and reduce synaptic depression: deficiencies of these neurotransmitters would therefore cause synaptic depression to spread across semantically related items, producing increased sensitivity to presentation rate and stimulus repetition—i.e. a refractory behavioural impairment. This neuromodulatory deficit could also eliminate normal frequency effects because there is more synaptic depression when the initial activation in the system is higher.

Other explanations of refractory effects, however, have focussed on the location of the cortical damage (anterior temporal versus frontal or temporal–parietal) as opposed to the nature of damage. Schnur, Schwartz, Brechr, Rossi, and Hodgson (2006) examined semantic blocking effects in picture naming for eighteen aphasic patients. The patients were asked to name sets of line drawings presented individually one after another. Items were semantically related or unrelated, presented at a fast or slow rate and repeated several times within each block. This "cyclical" naming paradigm produced a greater build up of refractoriness in a subgroup with Broca's aphasia (which typically follows frontal lobe damage) compared with aphasia syndromes associated with more posterior brain damage. This difference was proposed to reflect the role of the left inferior prefrontal cortex (LIPC which overlaps with Broca's area) in lexical selection (see also Schnur, Lee, Coslett, Schwartz, & Thompson-Schill, 2005 for a lesion analysis that support this conclusion). Functional neuroimaging studies of normal participants have observed that the LIPC shows greater activation when semantic tasks that require control/selection are contrasted with those that need less control (Demb et al., 1995; Gold & Buckner, 2002; Schnur et al., 2005; Wagner, Pare-Blagoev, Clark, & Poldrack, 2001). Deficits of semantic control might produce the hallmarks of "semantic access impairment" because when semantically related items are presented repeatedly at a fast rate, competition between the items will be strong and the requirement for semantic control will increase. Similarly, phonemic cues in picture naming