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.

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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...
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 deficit (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 aphasics. 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
will boost activation of the target word, making it more likely to win the semantic competition despite weakness of semantic control. Poor semantic control might produce inconsistency between tasks requiring different degrees of control. However, this theory might not predict test–retest inconsistency because the trials within a test will require varying degrees of semantic control and this should promote consistency when tests are repeated.

Although Thompson-Schill and her colleagues have argued that the LIPC is important in semantic selection, Schnur et al.’s explanation of refractory effects in picture naming for aphasic patients centred on competition at the lexical–semantic (or “lemma”) level of speech production. Refractory effects in picture naming latencies for healthy participants have also been accounted for in these terms (Belke, Meyer, & Damian, 2005; Damian, Vigliocco, & Levelt, 2001; Kroll & Stewart, 1994; Maess, Friederici, Damian, Meyer, & Levelt, 2002). By this view, refractoriness might not be expected to extend to semantic tasks that do not require overt lexical retrieval, such as word–picture matching. Indeed, patients with poor lexical retrieval (but no general semantic impairment) can show exaggerated refractory effects that affect picture naming accuracy (Lambon Ralph, Sage, & Roberts, 2000; McCarthy & Kartsounis, 2000; Wilshire & McCarthy, 2002). However, Schnur et al. did not examine cyclical word–picture matching in their aphasic group in order to assess this hypothesis directly. In addition, although within classical aphasiology the LIPC is thought to underpin word retrieval (whereas deficiencies in semantic processing are associated with lesions to the temporoparietal junction/Wernicke’s area), there is increasing evidence to suggest that the LIPC is involved in semantic control more generally. First, functional neuroimaging studies of healthy participants show that this region is sensitive to the control requirements of semantic tasks (see references above) and is activated by both verbal and non-verbal semantic tasks (Bright, Moss, & Tyler, 2004; Mummery et al., 1999; Vandenberghhe, Price, Wise, Josephs, & Frackowiak, 1996). Secondly, consideration of the neuropsychological literature indicates that semantic (not just lexical) impairment can accompany both temporal–parietal and frontal lobe lesions. For example, transcortical sensory aphasia (TSA) – which is defined as comprehension impairment in the context of fluent speech and good repetition – can result from both left temporoparietal and frontal infarcts: TSA patients with lesions in these two regions show highly similar aphasia profiles (Berthier, 2001). Consequently, lesions of the LIPC might be expected to produce refractory effects in comprehension tasks such as word–picture matching as well as picture naming.

In a recent study (Jefferies & Lambon Ralph, 2006), we compared the nature of comprehension deficits in patients with semantic dementia and stroke aphasia. A major motivation for the study was the observation that patients with these two conditions fail the same tasks and yet have very different areas of brain damage. While SD patients have bilateral anterior temporal lobe atrophy, our semantically impaired stroke patients had a combination of left frontal and temporoparietal lesions in line with Berthier (2001). The stroke aphasic participants obtained broadly equivalent scores to the SD cases on both verbal and non-verbal semantic tasks: they failed tests of picture association and sound-picture matching. However, the groups showed qualitatively different types of semantic deficit. These differences partly overlapped with the distinction between semantic “storage” and “access” impairment. The SD patients showed strong correlations between different semantic tasks and substantial consistency when a set of items was assessed several times. In addition, they were highly sensitive to frequency in a range of tasks and generally did not respond to cues in picture naming. The stroke patients also showed consistency across different input modalities for the same semantic task (e.g. picture versus word tests of semantic association) but not between tasks that required different types of semantic judgement (e.g. simple matching tasks versus judgements of semantic association). They were also insensitive to frequency and their picture naming was highly cueable. Aphasic patients with lesions exclusively in left temporoparietal cortex had similar semantic deficits to those who also had left prefrontal lesions, suggesting that in addition to the LIPC, temporal–parietal cortex may play a role in semantic control. This suggestion is consistent with recent neuroimaging and neuropsychological evidence suggesting that these two regions, which are highly interactive, both make an important contribution to executive functioning (Collette et al., 2005; Garavan, Ross, Li, & Stein, 2000; Peers et al., 2005). Consequently, damage to either region might produce a similar disruption to semantic control, impairing both verbal and non-verbal comprehension in a similar way.

The current study examined the strength of refractory effects in eight of the semantically impaired stroke patients examined by Jefferies and Lambon Ralph (2006). The study had four key aims:

1. To establish the frequency of refractory/access effects amongst stroke aphasic patients with multimodal semantic impairments. Although the majority of cases of semantic access deficits reported to date have been patients with severe, global aphasia, these previous studies have reported cases specifically selected to show refractory phenomena and do not reveal whether refractory/access deficits are common amongst semantically impaired stroke aphasic patients. The study by Schnur et al. (2006) suggests that refractory effects in picture naming are fairly widespread amongst Broca’s aphasics and more sporadic in non-Broca’s patients, but their study did not focus on comprehension deficits.

2. To compare refractory effects in naming and word–picture matching. If damage to the LIPC produces refractory effects in picture naming due to competition at the “lemma” level of speech production (as proposed by Schnur et al., 2006), patients with damage to this region would not be expected to show similar deficits in a comprehension task like word–picture matching. If, in contrast, refractory effects in naming accuracy are indicative of poor semantic control, both tasks should be affected because they require similar types of semantic control (i.e. selecting a word to produce in naming versus selecting a picture in word–picture matching).
3. To explore the relationship between deficits of semantic control, refractory effects and lesion location. If refractory effects are associated with the LIPC, as proposed by Schnur et al. (2006), we should observe them in every patient with damage in this region. However, the two cases in the current study with damage restricted to left temporal–parietal regions might also show refractory effects given that these two regions appear to work together to underpin cognitive control (e.g. Peers et al., 2005). This hypothesis is supported by our previous work in which we observed similar deficits of semantic control following left prefrontal and temporal–parietal lesions (Jefferies & Lambon Ralph, 2006).

4. We examined the full range of effects associated with “semantic access impairment”—e.g. facilitation by cues, inconsistency and the absence of frequency effects, as well as the build up “refractoriness” and how this is affected by semantic relatedness, speed of presentation and item repetition. As noted by Rapp and Caramazza (1993), the access/storage distinction predicts that these effects will co-occur but it is hard to establish if this is true because most previous studies have investigated single cases with a subset of these variables: in particular, cueing has rarely been investigated at the same time as the other variables (see Gotts & Plaut, 2002 for a review). We examined all of these purported elements of “access” disorder in eight patients, enabling us to consider the extent to which they occurred together across a case-series. To our knowledge, this is the first study to investigate the full range of refractory/access effects in multiple cases.

2. Methods
2.1. Participants

This work was approved by the local health authority ethics committee and informed consent was obtained. Eight aphasic stroke patients were recruited from stroke clubs and speech and language therapy services in Manchester, UK. Every case had chronic impairment from a CVA at least a year previously. The patients were selected to show multimodal comprehension deficits such that they failed both the picture and word versions of the Camel and Cactus Test of semantic association (CCT; Bozeat et al., 2000). This test involved deciding which of four pictures/words was most associated with a probe item (e.g. does camel go with cactus, tree, sunflower or rose). The patients were recruited in order to investigate the nature of multimodal semantic impairment following stroke (Jeffries & Lambon Ralph, 2006). They were not selected to show refractory effects in comprehension and had a variety of aphasia syndromes. Four patients had transcortical sensory aphasia. The remainder had less fluent speech and/or poorer repetition. Table 1 shows biographical/neuroimaging details and aphasia classifications based on the Boston Diagnostic Aphasia Examination (Goodglass, 1983) and some additional repetition tests from the PALPA battery (Kay, Lesser, & Coltheart, 1992). Imaging confirmed damage to the LIPC in 5/6 cases who had a left frontal lesion (only a report was available for the final patient due to contraindication for MRI). An additional two patients had temporoparietal infarcts that did not encompass left prefrontal regions.

A patient with semantic dementia, GE, was also examined to provide a comparison with the stroke patients. GE was a 50-year-old man who had deficits typical of SD. He first experienced difficulties 2 years before in his job as a production manager. He had a highly specific impairment of semantic memory that affected both verbal and non-verbal tasks. He showed word-finding difficulties despite his fluent speech and he had very poor confrontational naming. He was surface dyslexic in reading aloud. In contrast, phonology, syntax, visual-spatial abilities, day-to-day memory and executive skills were well preserved. MRI revealed bilateral anterior temporal lobe atrophy.

2.2. Background neuropsychological and semantic tests

The patients were examined on a range of general neuropsychological assessments, including the Visual Object and Space Perception battery (Warrington & James, 1991), forwards and backwards digit span (Wechsler, 1987), and a number of executive tests—the Coloured Progressive Matrices test of non-verbal reasoning (Raven, 1962), the Wisconsin Card Sort Test (WCST; Milner, 1964; Stuss et al., 2000), the Brixton Spatial Rule Attainment task (Burgess & Shallice, 1996) and the Elevator Counting subtests with and without distraction from the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994).

Semantic processing was assessed with the following tests: the Pyramids and Palm Trees Test (PPT), in which subjects decide which of two items is more associated with a target—e.g. pyramid with pine tree or palm tree (Howard & Patterson, 1992); the similar Camel and Cactus Test described above (CCT; Bozeat et al., 2000); the concrete and abstract word synonym task; word–picture matching (with 10 choices) and naming using a set of 64 black and white line drawings from the Snodgrass and Vanderwart set (Snodgrass & Vanderwart, 1980); category fluency for six categories (animals, birds, fruit, household items, tools and vehicles) and verbal fluency for three letters (F, A, S). In both fluency tests, participants produced as many exemplars as possible within 1 min.

2.3. Experimental tasks

2.3.1. Cyclical word–picture matching

This experiment investigated three factors using a fully crossed design: presentation speed in which the response-stimulus interval was manipulated (RSI = 0 s versus 5 s), semantic relatedness, and repetition of trials. Items were drawn from six categories: foreign animals, fruit, birds, tools, vehicles, musical instruments. Within each category there were six items. On each trial, the patient selected between six pictures. For semantically related sets, the six pictures within a trial were from the same category and the trials within a block probed these items in a pseudorandom order. For semantically unrelated sets, both the trials within a block and the items within a trial were from different categories. All of the items within the semantically related/unrelated sets were presented once and then again three more times in a pseudorandom order (which prevented the items from being tested twice in a row). Items were presented in both the semantically related/unrelated sets and at both fast and slow speeds. The order of items across these conditions was counterbalanced. There were 576 trials in total (36 items × 4 repetitions × 2 speeds × 2 related/unrelated conditions). Testing occurred over 3–6 sessions, depending on the tolerance of the patient. There were four practice items before the start of each block of the experiment.

The experiment was presented on a laptop using E-prime software. A fixation point appeared on the screen to signal the start of each trial. The name of the target item was presented through speakers and, at the same time, the six choices were presented on the screen. Participants indicated their choice by pointing to one of the pictures. The experimenter then pressed a button which advanced the experiment on to the next trial. In the 0 s RSI condition, the next trial appeared immediately. When the RSI was 5 s, a blank screen was presented for 5 s between trials. Participants were given 10 s to make a response. If they did not respond within this time, the next trial was presented and an error was recorded. One block of slow, unrelated items was not tested for NY because his performance in this condition was at ceiling.

For the semantically related and unrelated blocks using a fast presentation speed, the items were retested 5 min after the end of the main experiment in order to establish the duration of response suppression (for a similar method, see Martin, Pink, Laine, & Ayala, 2004; Renvall, Laine, & Martin, 2005).

2.3.2. Cyclical picture naming

Four CVA patients, KH, NY, SC, PG, were tested on this experiment. The remaining four CVA cases and one SD case performed near floor on tests of picture naming and so were excluded. The experiment employed the same structure and items as above, with each target presented singly for naming. Again, seman-
Table 1
Background details for comprehension impaired stroke aphasic patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Full-time education (leaving age)</th>
<th>Neuroimaging summary</th>
<th>Left frontal lesion</th>
<th>Years since CVA</th>
<th>Aphasia classification</th>
<th>BDAE comprehension percentile</th>
<th>BDAE fluency percentile</th>
<th>BDAE repetition percentile</th>
<th>PALPA nine word repetition (% correct)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NY</td>
<td>63</td>
<td>M</td>
<td>15</td>
<td>Left frontal–temporal–parietal (and right frontal–parietal)</td>
<td>✓</td>
<td>4.5</td>
<td>Conduction</td>
<td>47</td>
<td>37</td>
<td>40</td>
<td>81</td>
</tr>
<tr>
<td>SC</td>
<td>76</td>
<td>M</td>
<td>16</td>
<td>Left occipital–temporal (and right frontal–parietal)</td>
<td>×</td>
<td>5.5</td>
<td>Anomic/TSA</td>
<td>37</td>
<td>90</td>
<td>60</td>
<td>98</td>
</tr>
<tr>
<td>PG</td>
<td>59</td>
<td>M</td>
<td>18</td>
<td>Left frontal and capsular (CT)</td>
<td>✓</td>
<td>5</td>
<td>TSA</td>
<td>20</td>
<td>40</td>
<td>80</td>
<td>91</td>
</tr>
<tr>
<td>KH</td>
<td>73</td>
<td>M</td>
<td>14</td>
<td>Left occipital–temporal and frontal</td>
<td>✓</td>
<td>1.5</td>
<td>Mixed transcortical</td>
<td>30</td>
<td>30</td>
<td>40</td>
<td>80</td>
</tr>
<tr>
<td>BB</td>
<td>55</td>
<td>F</td>
<td>16</td>
<td>Left frontal and capsular (CT)</td>
<td>✓</td>
<td>2.5</td>
<td>Mixed transcortical</td>
<td>10</td>
<td>17</td>
<td>55</td>
<td>96</td>
</tr>
<tr>
<td>ME</td>
<td>36</td>
<td>F</td>
<td>16</td>
<td>Left occipital–temporal</td>
<td>×</td>
<td>6.5</td>
<td>TSA</td>
<td>33</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>LS</td>
<td>71</td>
<td>M</td>
<td>15</td>
<td>Left temporal–parietal–frontal</td>
<td>✓</td>
<td>3</td>
<td>TSA</td>
<td>13</td>
<td>90</td>
<td>90</td>
<td>96</td>
</tr>
<tr>
<td>KA</td>
<td>74</td>
<td>M</td>
<td>14</td>
<td>Left frontal–parietal (CT)</td>
<td>✓</td>
<td>1</td>
<td>Global</td>
<td>0</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Patients are arranged in order of word–picture matching scores (see Table 2). BDAE, Boston Diagnostic Aphasia Examination (Goodglass, 1983). Auditory comprehension percentile is derived from word discrimination, commands and complex ideational material subtests. Fluency percentile is derived from phrase length, melodic line and grammatical form ratings. Repetition percentile is average of word and sentence repetition subtests. Percentile scores from 0 to 30 were considered “severely impaired”, 31 to 59 as “intermediate” and 60 to 100 as “good”. TSA (transcortical sensory aphasia) was defined as good or intermediate fluency/repetition and poorer comprehension. An experienced speech and language therapist verified these classifications from the BDAE. PALPA, Psycholinguistic Assessments of Language Processing in Aphasia (Kay et al., 1992).
Table 2
Background neuropsychological assessment

<table>
<thead>
<tr>
<th>Task</th>
<th>Maximum cut-off</th>
<th>Normal cut-off</th>
<th>CVA</th>
<th>Semantic dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NY</td>
<td>SC</td>
</tr>
<tr>
<td>Visual-spatial processing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VOSP dot counting</td>
<td>10</td>
<td>8</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>VOSP position discrimination</td>
<td>20</td>
<td>18</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>VOSP number location</td>
<td>10</td>
<td>7</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>VOSP cube analysis</td>
<td>10</td>
<td>6</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Executive function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raven’s coloured matrices (percentiles)</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>5</td>
</tr>
<tr>
<td>WCST (number of categories)</td>
<td>6</td>
<td>1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Brixton spatial anticipation (correct)</td>
<td>54</td>
<td>28</td>
<td>34</td>
<td>25</td>
</tr>
<tr>
<td>TEA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Counting without distraction</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Counting with distraction</td>
<td>10</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Digit span</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forwards</td>
<td>–</td>
<td>5</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Backwards</td>
<td>–</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3
Semantic tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Maximum mean (S.D.)</th>
<th>Control mean (S.D.)</th>
<th>CVA</th>
<th>Semantic dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NY</td>
<td>SC</td>
</tr>
<tr>
<td>Word–picture matching&lt;sup&gt;a&lt;/sup&gt;</td>
<td>64</td>
<td>63.7 (0.5)</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td>Picture PPT</td>
<td>52</td>
<td>51.2 (1.4)</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>Word PPT</td>
<td>52</td>
<td>51.1 (1.1)</td>
<td>42</td>
<td>51</td>
</tr>
<tr>
<td>Picture CCT</td>
<td>64</td>
<td>58.9 (3.1)</td>
<td>36</td>
<td>46</td>
</tr>
<tr>
<td>Word CCT</td>
<td>64</td>
<td>60.7 (2.06)</td>
<td>39</td>
<td>56</td>
</tr>
<tr>
<td>Concrete synonyms</td>
<td>25</td>
<td>23.7 (1.3)</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Abstract synonyms</td>
<td>25</td>
<td>23.0 (2.1)</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Picture naming</td>
<td>64</td>
<td>62.3 (1.6)</td>
<td>55</td>
<td>28</td>
</tr>
<tr>
<td>Letter fluency (FAS)</td>
<td>–</td>
<td>44.2 (11.2)</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>Category fluency (six categories)</td>
<td>–</td>
<td>95.7 (16.5)</td>
<td>25</td>
<td>17</td>
</tr>
</tbody>
</table>

Table shows raw scores. CVA patients are arranged in order of word–picture matching scores. TA, testing abandoned; NT, not tested; PPT, Pyramids and Palm Trees Test; CCT, Camel and Cactus Test.

<sup>a</sup> Word–picture matching using standard presentation (i.e. minimal delay between trials).
battery of semantic tests. These data indicate that the semantically impaired CVA patients and the SD patient (GE) failed the full range of verbal and non-verbal semantic tests. The stroke aphasic group also performed poorly on a range of tests of executive function, whereas GE was more intact. A fuller discussion of these data is provided in Jefferies and Lambon Ralph (2006).

3.2. Cyclical word–picture matching

3.2.1. Response accuracy for stroke aphasic group

Fig. 1 shows means and standard errors for the stroke aphasic cases on the word–picture matching task (N = 8). Analysis of variance revealed that performance was poorer for the semantically related versus unrelated blocks (F(1, 7) = 17.7, p = .004). There were no main effects of speed of presentation and stimulus repetition although the interaction between repetition and semantic relatedness approached significance (F(3, 21) = 2.9, p = .06). The decrease in accuracy between the first and fourth presentations approached significance for the semantically related items (t(7) = 2.0, uncorrected p = .08) but not the unrelated sets. Repetition also interacted with speed (F(3, 21) = 5.1, p = .008). Accuracy between the first and second presentations increased at the slow speed (t(7) = -2.8, uncorrected p = .03) but decreased at the fast speed (t(7) = 2.2, uncorrected p = .06). Therefore, as a group, the stroke aphasic patients showed mild refractory effects in word–picture matching.

The CVA patients showed equivalent performance on the first presentation and 5 min after the experiment was completed (related set: 77% versus 76%, t(7) < 1; unrelated set: 92% versus 96%, t(7) = -1.8). This indicated that they had recovered completely from the build-up of refractoriness after 5 min. There was also no evidence of longer-term facilitation following stimulus repetition.

3.2.2. Response accuracy for individual patients

Fig. 2 shows the performance of each individual stroke aphasic patient. These data were first analysed with logistic regression because this method allowed us to consider the influence of the main effects of relatedness, speed and repetition as well as any interactions between them (see Table 4). The main effects were examined first and then multiplicative interactive terms were added to each model. Additional analyses that explored the effects of each variable separately using chi-square produced very similar outcomes; these are reported below only when they generated divergent results.

All of the patients showed strong effects of relatedness. Six of them also showed effects of either speed or repetition or both (the latter effect emerged as a relatedness by repetition interaction because there was a build up of refractoriness for related sets but improvement in performance for unrelated sets due to repetition priming). The two stroke cases who did not show any effect of either speed or repetition, ME and SC, were the only cases who had temporoparietal lesions that spared the left prefrontal cortex. Separate analysis using chi-square revealed the same pattern of findings (except that for KH the marginally significant effect of speed reported in Table 4 reached conventional significance levels).

Table 4

Word–picture matching accuracy for individual patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>CV A</th>
<th>Semantic dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NY</td>
<td>SC</td>
</tr>
<tr>
<td>Related (%)</td>
<td>91</td>
<td>92</td>
</tr>
<tr>
<td>Unrelated (%)</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Relatedness (Wald)</td>
<td>12.2*</td>
<td>11.5*</td>
</tr>
<tr>
<td>Fast (%)</td>
<td>93</td>
<td>96</td>
</tr>
<tr>
<td>Slow (%)</td>
<td>97</td>
<td>95</td>
</tr>
<tr>
<td>Speed (Wald)</td>
<td>3.7*</td>
<td>n.s.</td>
</tr>
<tr>
<td>Related items Trial 1 (%)</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>Related items Trial 2 (%)</td>
<td>81</td>
<td>97</td>
</tr>
<tr>
<td>Related items Trial 3 (%)</td>
<td>79</td>
<td>92</td>
</tr>
<tr>
<td>Related items Trial 4 (%)</td>
<td>86</td>
<td>89</td>
</tr>
<tr>
<td>Relatedness by repetition (Wald)</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Figures indicate percentage of items correct. Wald values derived from logistic regressions computed for individual patients. Wald values for relatedness and speed were derived from an analysis that also included repetition. Interaction terms were entered in addition to main effects. All effects that reached p < .1 are shown. *p < .05. **p < .01. Effects that are not shown in the table (including main effect of speed and speed by relatedness interaction) did not reach significance. Patients are arranged in order of word–picture matching scores using standard presentation (see Table 3).
The SD patient, GE, also showed substantially poorer performance for semantically related sets (see Table 4). However, he was insensitive to speed of presentation and item repetition (accuracy = 67%, 69%, 72% and 67% on the first to fourth presentations, respectively). There were no interactions between these three variables.

### 3.2.3. Reaction times

Six patients (NY, SC, PG, KH, BB and ME) performed relatively well in the word–picture matching task: they achieved scores above 50% in every condition. For these patients, there were sufficient correct responses to examine the impact of relatedness, speed and repetition on response latency. The results...
are shown in Table 5. The patients as a group showed a main effect of relatedness, \(F(1, 5) = 203.6, p < .0001\), and an interaction between relatedness and repetition, \(F(3, 15) = 4.9, p = .01\). Response times typically decreased for the unrelated items through repetition priming but increased for the related items due to a build up of refractoriness (as shown by RT differences between Trials 1 and 4 for related versus unrelated trials in Table 5; \(t(6) = 3.4, p = .02\)).

Data for individual cases were analysed using between-subjects ANOVA treating items as cases. Reaction times were slower for related versus unrelated trials for every case, \(F(1, >164) > 79.3, p < .0001\). None of the patients showed main effects of speed of presentation. Two patients became significantly slower to respond with item repetition (ME: \(F(3, 479) = 7.3, p < .0001\); PG: \(F(3, 474) = 7.2, p = .0001\) and one became faster (KH: \(F(3, 476) = 2.5, p = .06\). The repetition by relatedness interaction also reached significance for ME (\(F(3, 479) = 2.6, p = .05\)) and PG (\(F(3, 474) = 4.2, p = .006\)). Therefore, although ME did not show refractory effects in word–picture matching accuracy, she did show this pattern in the latency data.

### 3.2.4. Consistency across repetitions

Despite showing refractory effects in word–picture matching, all of the stroke patients showed some consistency across item repetitions. Contingency coefficients were calculated between adjacent presentations of items in the same speed/relatedness conditions, resulting in three scores for each patient: first–second, second–third and third–fourth presentations. All three contingency coefficients were significant for four cases: KH (\(C = .31–.47, p < .001\)), KA (\(C = .29–.45, p < .001\)), LS (\(C = .27–.42, p < .002\)) and BB (\(C = .19–.32, p < .01\)). Two out of three were significant for ME (\(C = .15–.30\)) and PG (\(C < .1–.34\)). One out of three was significant for NY (\(C < .1–.27\)) and SC (\(C < .1–.25\)). The SD patient, GE, showed a very strong degree of consistency on every comparison (\(C = .44–.51, p < .0001\)).

To allow a direct comparison with some previous studies (e.g. Cipolotti & Warrington, 1995; Warrington & Cipolotti, 1996; Warrington & McCarthy, 1983), we also used the binomial expansion to calculate the number of items that would be correct 0–4 times by chance given the probability of a correct response in general. The observed and expected distributions were then compared using chi-square. Significant consistency should produce deviation from the distribution predicted from the binomial expansion. As this technique does not examine consistency item-by-item, the inclusion of different conditions (e.g. related/unrelated; fast/slow) is likely to inflate consistency. For this reason, the related fast/slow conditions were examined in separate analyses (the unrelated trials were not examined due to ceiling effects). Using this method, only two stroke aphasic patients deviated significantly from the consistency expected by chance (KH in both analyses and NY in the slow presentation condition only; \(\chi^2(4) > 10.2, p < .02\)). Contingency coefficients were therefore a better way of examining response consistency in our study. The SD patient, GE, still showed highly significant consistency when items were presented repeatedly at both a fast and slow rate (\(\chi^2(4) > 11.1, p < .02\)).

### 3.3. Cyclical naming

#### 3.3.1. Group analysis

Accuracy was much lower for naming than word–picture matching (below 50% for every patient tested in at least one condition): therefore, the analysis below focuses on naming accuracy rather than latency. The results for the whole group are shown in Fig. 3 (self-corrections were not included as correct). Logistic regression that included data from all four cases revealed main effects of semantic relatedness (\(Wald = 10.7, p < .001\)), speed of presentation (\(Wald = 40.8, p < .001\)) and patient identity (\(Wald = 9.2, p = .002\)) but not repetition (\(Wald < 1\)). The interaction between relatedness and repetition approached significance (\(Wald = 3.1, p = .08\)).

Performance on the unrelated items following a 5 min delay was significantly better than it had been on the first presentation (56% versus 68%, McNemar Exact two-tailed \(p = .02\)). Therefore, the patients showed longer-term facilitation of the unrelated set following stimulus repetition. However, the related
Fig. 3. Refractory effects in picture naming for stroke aphasic patients. Error bars show standard errors.

set did not show this advantage following the delay (57% versus 58%).

3.3.2. Individual cases

Table 6 shows the data for individual patients. Three out of four cases showed substantial effects of speed of presentation on picture naming (using logistic regression including speed, relatedness and repetition as predictors; KH: Wald = 12.3, \( p = .0004 \); NY: Wald = 11.2, \( p = .001 \); PG: Wald = 19.0, \( p < .0001 \)). The fourth case, SC, showed a much smaller effect of speed that approached significance in logistic regression (Wald = 3.2, \( p = .07 \)) and reached conventional significance levels in a McNemar test (one-tailed \( p = .02 \)). Semantic relatedness and repetition had more variable effects on performance. PG showed significantly poorer performance for items that were semantically blocked (Wald = 19.0, \( p < .0001 \)). KH showed a small effect of relatedness that approached significance in chi-square (Fisher’s exact test, one-tailed \( p = .075 \)) but not logistic regression (Wald = 1.8, \( p = .18 \)). NY and SC showed no effect of relatedness (Wald = 1.3 and <1, respectively). Stimulus repetition could either improve or impair performance, depending on the patient. NY showed poorer performance following repetition (Wald = 5.1, \( p = .02 \)). Although PG did not show this effect in the experiment as a whole (Wald < 1), a McNemar test revealed that his performance fell between the first and second presentations in the related and fast condition (two-tailed \( p = .004 \)). In contrast, KH showed some improvement with repetition (Wald = 3.3, \( p = .07 \)) and SC showed no effect of stimulus repetition (Wald < 1).

Logistic regression was used to examine interactions between relatedness, repetition and speed (by entering each interaction term in addition to the three main effects). The only significant interaction was for NY between repetition and speed (Wald = 5.4, \( p = .02 \)). This reflected the fact that performance decreased with repetition in the fast condition (from 80% to 54% from Trial 1 to Trial 4) but remained stable in the slow condition (Trial 1 = 75%, Trial 4 = 78%).

3.3.3. Consistency across repetitions

Contingency coefficients between adjacent presentations of items in the same speed/relatedness conditions (first–second, second–third and third–fourth presentations) were highly significant for every patient. For KH, PG and SC, \( C = .43–.56, \ p < .0001 \). Consistency for NY was a little weaker (\( C = .24–.34, \ p < .003 \)). The four conditions (related/unrelated by slow/fast) were also examined using the binomial expansion method outlined above. For three patients (SC, PG and KH), the distribution of responses significantly differed from that expected by chance in all four conditions (\( \chi^2 = 25.7–9.5, \ p < .05 \)). For NY, this result was only obtained in the unrelated slow condition (\( \chi^2 = 8.8, \ p = .003 \)).

3.3.4. Consistency between naming and word–picture matching

KH showed significant consistency between naming and word–picture matching for the same items, including only trials from semantically related blocks (as word–picture matching performance was near ceiling for unrelated trials; \( C = .21, \ p = .0004 \)). In contrast, NY, PG and SC did not show consistency across the two tasks (\( C < 1 \)).

3.3.5. Naming errors

Incorrect responses were typically omissions and semantic errors. The patients frequently produced the same semantic error several times when items were repeated; these perseverative responses accounted for 63% of all semantic errors. Faster presentation speeds led to a larger number of omissions (fast = 60% of errors; slow = 52% of errors) and a smaller number of semantic errors (22% versus 30% of errors); Fisher’s exact test \( = 6.8, \ p = .03 \). Semantic relatedness and repetition did not have any significant effect on naming errors.

3.4. Additional phenomena associated with “semantic access impairment”

3.4.1. Effect of word frequency in synonym judgement

Despite the strength of the frequency manipulation in the synonym judgement task, not one of the semantically impaired stroke patients was significantly affected by this variable (see Fig. 4). KH showed the largest numeric advantage for high over low frequency words but this did not reach significance (Fisher’s exact test: one-tailed \( p = .1 \)). As a group, the CVA patients did not show a frequency effect (\( \pi(7) = 1.3, \) n.s.). In contrast, the SD

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Picture naming accuracy for individual patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NY</td>
</tr>
<tr>
<td>Fast</td>
<td>66</td>
</tr>
<tr>
<td>Slow</td>
<td>78</td>
</tr>
<tr>
<td>Related</td>
<td>70</td>
</tr>
<tr>
<td>Unrelated</td>
<td>74</td>
</tr>
<tr>
<td>Trial 1</td>
<td>78</td>
</tr>
<tr>
<td>Trial 2</td>
<td>74</td>
</tr>
<tr>
<td>Trial 3</td>
<td>72</td>
</tr>
<tr>
<td>Trial 4</td>
<td>66</td>
</tr>
</tbody>
</table>

Figures indicate percentage of items correct. Patients are arranged in order of word–picture matching scores using standard presentation (see Table 3).
Table 7

Summary of results

<table>
<thead>
<tr>
<th>Stroke aphasia</th>
<th>Semantic dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>NY</td>
<td>SC</td>
</tr>
<tr>
<td>Left frontal lesion</td>
<td>✓</td>
</tr>
<tr>
<td>Refractoriness</td>
<td>✓</td>
</tr>
<tr>
<td>Consistency</td>
<td>✓</td>
</tr>
<tr>
<td>Frequency</td>
<td>×</td>
</tr>
<tr>
<td>Cueing</td>
<td>✓</td>
</tr>
</tbody>
</table>

Patients are arranged in order of word–picture matching scores using standard presentation (see Table 3).

3.5. Summary

The results are summarised in Table 7. As a group, the semantically impaired stroke aphasic patients showed many of the symptoms of semantic access impairment—i.e. refractory effects in naming and word–picture matching, an absence of significant frequency effects and strong effects of phonemic cueing in picture naming. However, all of the patients showed some degree of test–retest consistency, contrary to the pattern expected for access impairment. There was also some variation in the access effects across the patients. Two patients without left frontal lobe lesions, ME and SC, failed to show refractory effects in word–picture matching, at least in terms of accuracy. In contrast, all the other cases who did have damage to the left frontal lobe, showed refractory effects in this task. This difference between ME/SC and the other patients appears to have been one of degree as SC did show some weak refractory effects in picture naming accuracy and ME showed refractory effects in word–picture matching latency.

In contrast to the stroke aphasic patients, a patient with SD showed none of the effects associated with semantic access impairment: he was not influenced by any of the refractory variables, did not readily cue in picture naming and was highly sensitive to word frequency in a synonym judgment task. He also showed very strong consistency when items were repeated. Although the SD patient resembled the semantically impaired stroke aphasic group in that he showed effects of semantic relatedness in word–picture matching, previous research has suggested that relatedness effects might occur for different reasons in “storage” and “access” patients (Crutch & Warrington, 2005). Poorer performance for semantically related arrays might reflect the relative robustness of superordinate-level knowledge in SD and the spreading of refractoriness across semantically related concepts in patients with stroke aphasia.

4. Discussion

This study examined the full range of effects associated with “semantic access impairment” — namely, refractory variables (speed of presentation, item repetition and semantic blocking), inconsistency, absence of frequency effects and facilitation by cues — in a series of eight semantically impaired stroke patients and a patient with semantic dementia (SD).
To our knowledge, this is the first time that all of these factors have been investigated simultaneously in a group of stroke aphasic cases: previous studies have focussed on single patients and have typically investigated only a subset of these factors.

Our findings indicate that refractory/access effects are a frequent property of semantic impairment in stroke aphasia. Patients were included in this study if they failed both verbal and non-verbal semantic tasks – they were not selected on the basis of any refractory/access phenomena – and yet every patient showed at least some effect of speed of presentation and/or item repetition in semantic processing as well as several other symptoms of a semantic ‘access’ disorder. Schnur et al. (2006) also observed that refractory effects were widespread amongst stroke aphasic patients in picture naming (although they did not select their cases on the basis of semantic impairment and they did not examine performance at a comprehension task).

In contrast to the stroke aphasic patients, a patient with SD did not show any of the hallmarks of a semantic access disorder. He showed the opposite pattern: marked test–retest consistency, very strong effects of word frequency on comprehension, no benefit from phonological cues in picture naming and no effect of variables such as speed of presentation and item repetition that affect the build up of refractoriness in the semantic system. Although it would be useful to confirm these findings in a larger sample of SD patients, our results are consistent with a number of other studies that have suggested that SD produces a degradation of semantic knowledge (Bozeat et al., 2000; Rogers et al., 2004; Warrington, 1975; Warrington & Cipolotti, 1996).

An item that is poorly understood will produce poor performance, however, it is tested, regardless of the availability of cues or the presentation context (e.g. time since the previous trial).

Within the stroke aphasic group, the proposed symptoms of “access” impairment co-occurred to some extent but not entirely. Strong effects of phonemic cueing and an absence of frequency effects were seen universally but refractory variables were weak (and sometimes absent) for two cases (SC and ME). There was also variation amongst the six patients who did show refractory effects: some were affected by speed of presentation but not item repetition (e.g. LS), whereas others showed the opposite pattern (e.g. KA). All of the patients in our study showed some degree of test–retest consistency, whereas “access” patients are said to show unreliable retrieval of semantic knowledge from trial to trial.

Refractory effects were relatively weak for two patients (SC and ME) with temporoparietal junction (TPJ) infarcts and more marked for six aphasic patients with left frontal lesions. Nevertheless, ME and SC did show some impact of refractory variables (in response latencies/picture naming), and they showed effects of phonemic cueing in picture naming and an absence of frequency effects in comprehension as strongly as the group as a whole. Similarly, in our previous study, there were no substantial differences between the aphasic patients with and without prefrontal lesions (Jefferies & Lambon Ralph, 2006).

4.1. Theoretical interpretation

Differences between comprehension-impaired stroke aphasic and SD patients in the impact of refractory/access variables can be interpreted as reflecting damage to two interacting components of semantic cognition. First, SD patients have damage to a modal semantic representations formed in the anterior temporal lobes through the distillation of information specific to particular input or output modalities. The model of Rogers et al. (2004) described above provides an instantiation of this system (see Damasio, 1989; Damasio, Tranel, Grabowski, Adolphs, & Damasio, 2004; Martin, Haxby, Lalonde, Wiggs, & Ungerleider, 1995; Wernicke, 1874, for related theories).

Secondly, our ability to use semantic knowledge flexibly according to the requirements of the task/situation requires these semantic representations to interact with executive processes that help to direct and control semantic activation in a task-appropriate fashion. The Rogers et al. model cannot be a complete account of semantic cognition because it activates all information for a particular concept in a rigid way. We know many different things about objects and only particular aspects of our knowledge are relevant for a particular task or context. For example, we know that pianos are both heavy and played by pressing keys with the fingers: if the task is to move a piano across a room, information about fine motor movements must be disregarded (Saffran, 2000). Stroke aphasic patients with multimodal semantic deficits may have damage to these semantic control processes (Jefferies & Lambon Ralph, 2006).

Deficits of semantic control should produce strong refractory effects because when semantically related items are presented repeatedly at a fast rate, activation will spread between items and will not fully decay between trials. As a result, the entire set of items will become highly active giving rise to strong competition with the target. This competition will become more intense as the experiment progresses and consequently patients with deficits of semantic control will increasingly struggle to make accurate and rapid semantic judgements. Deficits of semantic control might also account for other “access” phenomena. For example, phonemic cues in picture naming will boost activation of the target word and exclude phonologically dissimilar semantic competitors, ameliorating the effects of poor internal control.

This distinction between degraded semantic knowledge in SD and deregulated semantic cognition in stroke aphasia might also explain the differential effects of word frequency. Frequent items might have stronger representations in the semantic system making them more robust to damage in SD (e.g. Rogers et al., 2004). These concepts will also be encountered regularly as the semantic system degrades and this continued exposure may afford them some protection (Lambon Ralph et al., 1998).

In contrast, concept frequency will not predict the degree of semantic degradation for stroke aphasic patients who have poor semantic control but intact semantic representations. As concepts can be used in many different ways, judgements about more frequent concepts will not necessarily require less semantic control — indeed, because frequently encountered objects are associated with a greater range of items/contexts which may be
irrelevant for a particular semantic judgement, it is possible that they will require greater control.

As noted above, our stroke aphasic patients deviated from the traditional notion of an access deficit because the patients did not show the expected pattern of unreliable retrieval of semantic knowledge from trial to trial. Instead, every aphasic patient showed some degree of test–retest consistency. This pattern is again consistent with the notion that the patients’ refractory effects resulted from poor semantic control. According to this view, consistency should be relatively high when semantic tests are repeated because the trials within a test will have differing control requirements which will predict the likelihood of success. For example, more control might be required in the word–picture matching task for arrays of closely associated items. In contrast, consistency should be low for semantic tasks that probe knowledge of the same items in different ways because the control requirements of these tasks will differ. This is exactly the pattern that we observed in a previous study employing the same semantically impaired stroke patients (Jeffries & Lambon Ralph, 2006). Significant consistency was observed across different versions of the same semantic test – e.g. between the picture and word versions of the Camel and Cactus Test (CCT) – but there was no consistency between tests that examined knowledge of the same items in different ways (e.g. between word–picture matching and the CCT). For the semantically impaired stroke patients, CCT success was predicted by ratings of the control requirements for each trial (e.g. the ease with which the relevant semantic relationships could be identified and distracters rejected). In contrast, performance for the SD patients was predicted by the degree of semantic degradation for each item, as revealed by other semantic tests.

Why were our semantically impaired stroke patients more consistent than the “access” cases in the literature, given that they showed many of the symptoms of semantic access impairment? First, methodological factors could have contributed to previous failures to observe significant consistency. Studies have typically analysed consistency data using the binomial expansion but have shown some degree of test–retest consistency. This pattern is again consistent with the notion that the patients’ refractoriness resulted from poor semantic control. The refractoriness may have been weaker for their sensitivity to refractory variables may have been linked to lexical retrieval, as proposed by Schnur et al. (2006). Schnur et al. suggested that refractoriness in picture naming is again consistent with the notion that the patients’ refractory variables may have been linked to lexical retrieval, as proposed by Schnur et al. (2006). Schnur et al. suggested that refractoriness in picture naming and word–picture matching have similar control requirements: in both tasks, the most appropriate item (word or picture) must be selected from a set of semantically related competitors. Cyclical presentation might be expected to increase competition in each of these tasks in the same way.

The LIPC and TPJ may be components of a single distributed functional system underpinning semantic control and executive processing more generally, explaining why lesions of these two regions produce similar behavioural deficits in semantic tasks (Jeffries & Lambon Ralph, 2006). Functional imaging studies of normal participants indicate that activation within LIPC is sensitive to the control/selection demands of semantic tasks: for example, this region is more active when there are a larger number of possible responses in a semantic task and when inter-item association strength is reduced (Demb et al., 1995; Gold & Buckner, 2002; Schnur et al., 2005; Wagner et al., 2001). In addition, the prefrontal cortex has strong connectivity with the TPJ (Gloor, 1997; Parker et al., 2005): lesions in the two regions produce comparable deficits of visual attention and they show coupled activation during functional imaging studies of executive processing (Collette et al., 2005; Garavan et al., 2000; Peers et al., 2005). In line with these arguments, our stroke aphasic patients with lesions encompassing either left prefrontal cortex or the TPJ showed executive deficits comitant with their difficulties in semantic tasks: in contrast, semantic deficits are seen in SD in the absence of executive impairment (Jeffries & Lambon Ralph, 2006).

Although the semantic deficits resulting from LIPC and TPJ lesions overlap substantially, the present study points to some subtle differences, with lesions encompassing the LIPC producing a greater sensitivity to refractory variables such as speed of presentation. Schnur et al. (2006) similarly proposed that LIPC lesions result in greater refractory effects in picture naming. It will be necessary to confirm this finding in a larger study given that there are single “access” cases in the literature who showed substantial effects of refractory variables following temporo-parietal damage (Forde & Humphreys, 1995; Warrington & McCarthy, 1987) and because, in our case series, the differences between the patients with and without prefrontal lesions was one of degree.

In conclusion, we have demonstrated that many of the symptoms of “semantic access impairment” – including refractoriness, effects of cueing and the absence of frequency effects – are common in semantically impaired stroke aphasic patients. However, while “access” cases are supposedly inconsistent from trial to trial, the patients in this study did show significant test–retest consistency. This suggests that their deficits did not result from probabilistic failures of access to semantics. Instead, their sensitivity to refractory variables may have been linked
to their difficulties controlling activation within the semantic system.

Acknowledgements

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