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Support for anterior temporal involvement in semantic error production in aphasia: New evidence from VLSM

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ABSTRACT

Semantic errors in aphasia (e.g., naming a horse as "dog") frequently arise from faulty mapping of concepts onto lexical items. A recent study by our group used voxel-based lesion-symptom mapping (VLSM) methods with 64 patients with chronic aphasia to identify voxels that carry an association with semantic errors. The strongest associations were found in the left anterior temporal lobe (L-ATL), in the mid- to anterior MTG region. The absence of findings in Wernicke's area was surprising, as were indications that ATL voxels made an essential contribution to the *post-semantic* stage of lexical access. In this follow-up study, we sought to validate these results by re-defining semantic errors in a manner that was less theory dependent and more consistent with prior lesion studies. As this change also increased the robustness of the dependent variable, it made it possible to perform additional statistical analyses that further refined the interpretation. The results strengthen the evidence for a causal relationship between ATL damage and lexically-based semantic errors in naming and lend confidence to the conclusion that chronic lesions in Wernicke's area are not causally implicated in semantic error production.

1. Introduction

Incidental speech errors in otherwise healthy speakers have been used to comic effect in literature, film, and politics, as when the playwright William Shakespeare gave his bumbling constable Dogberry the line "O villain! thou wilt be condemned into everlasting *redemption* for this" (i.e., *damnation*; 1600/1905, IV.ii.51). Retrieving the wrong word becomes a more serious affair when the rate of error is high enough to disrupt fluent conversation. This can happen in the speech of healthy individuals, but it happens quite often in neurological conditions that disrupt the function of left hemisphere (LH) language networks, such as aphasia.

A common assumption is that lexical access errors in LH patients, while more frequent and more extreme than the errors of healthy speakers, do not differ from them in kind (Dell, Schwartz, Martin, Saffran, & Gagnon, 1997; Freud, 1891; Schwartz, Saffran, Bloch, & Dell, 1994). Among other things, both healthy speakers and patients are vulnerable to the two major classes of error: those that relate to the target in meaning (semantic errors) and those that relate to the target in sound (phonological errors). The high frequency with which these error types occur in patients has made them an important object of study for researchers interested in the neural underpinnings of semantic and phonological processes in language.

Studies of lexical access errors in patients necessarily begin with identification and classification of errors. With respect to the semantic-phonological distinction, some errors are unambiguous; for example, few would dispute that horse → dog is a semantic error, whereas horse → hearse is a phonological error. Problems arise in deciding how broadly or narrowly to define these categories, that is, when to lump and when to split. For example, should semantic errors be confined to taxonomically related nouns, e.g., horse → dog, animal, or pony? Or should the category also include errors that are thematically associated with the target (e.g., horse → cart)? Should noun (horse → cart) and non-noun (horse → trot) errors be lumped or split? And what about multi-word descriptions (horse → "it runs races"; "it goes 'neigh'")? Some errors with a clear semantic relation to the target also share some of its phonemes (e.g., horse → race); how should these "mixed" errors be classified? In the ideal case, scoring decisions like these are rationalized in relation to an explicit theory; more often, however, the rationale is idiosyncratic or unreported. Yet such decisions can have a major influence on the outcome of studies.

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1.1. Schwartz et al. (2009)

We recently carried out voxel-based lesion-symptom mapping (VLSM) to identify brain regions associated with semantic picture naming errors in 64 patients with chronic left hemisphere stroke and aphasia (Schwartz et al., 2009). Motivated by the interactive two-step model of lexical access (Dell, 1986; Dell et al., 1997) and by the hypothesis that semantic error production is primarily the consequence of faulty mapping from semantics to abstract word entities (i.e., "lemmas"), this anatomical study sought to localize the lesions responsible for semantic errors that arise via this cognitive mechanism. Three VLSM analyses were carried out. In the first, unfiltered analysis, the dependent variable was semantic error proportion relative to total trials. In the second and third analyses, we regressed out the variance in the semantic error proportion that was shared with verbal and nonverbal comprehension measures, respectively. These secondary, filtered, analyses helped rule out the contribution to semantic errors of alternative mechanisms, such as failure to conceptualize the pictured target correctly, a shared requirement with nonverbal comprehension, or failure to edit out potential errors as a consequence of verbal comprehension deficits. There was only one brain region where the lesion status of voxels correlated with semantic errors in both the filtered and unfiltered analyses. That region was the left anterior temporal lobe (L-ATL), where we identified a large cluster of supra-threshold voxels occupying Brodmann areas (BA) 38 and 21, with peak *t*-values in mid-to–anterior middle temporal gyrus (MTG). Surprisingly, no effects were found in Wernicke's area (posterior BA 22) or the angular gyrus (BA 39), even in the unfiltered analysis. These posterior areas feature prominently in classical and contemporary anatomical models of semantics and naming (e.g., Binder, Desai, Graves, & Conant, 2009; Cloutman et al., 2009; DeLeon et al., 2007; Hart & Gordon, 1990; Hillis, Kane, et al., 2001; Hillis, Wityk, et al., 2001; Hillis et al., 2006; Mesulam, 1998; Noonan, Jefferies, Corbett, & Lambon Ralph, 2010), although the anatomical claims have not gone unchallenged (e.g., Binder et al., 2009; Dronkers, Wilkins, Valin, Redfern, & Jaeger, 2004; Indefrey & Levelt, 2004; Mesulam, Wieneke, et al., 2009).

There is a growing literature looking at how left temporal regions anterior and inferior to Wernicke's area contribute to semantic processing. These newer studies demonstrate a contribution of anterior and lateral inferotemporal regions to narrative comprehension (Scott, Blank, Rosen, & Wise, 2000; Sharp, Scott, & Wise, 2004; Warren, Crinion, Lambon Ralph, & Wise, 2009); word and picture comprehension (Antonucci, Beeson, Labiner, & Rapcsak, 2008; Pobric, Jefferies, & Lambon Ralph, 2010; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996); amodal or supra-modal semantic processing (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Lambon Ralph, Sage, Jones, & Mayberry, 2010; Patterson, Nestor, & Rogers, 2007; Rogers et al., 2004); naming, especially of categories and stimuli whose feature structure invites many perceptually-related competitors (e.g., living things; famous people; landmarks: Antonucci et al., 2008; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Damasio, Tranel, Grabowski, Adolphs, & Damasio, 2004; Gorno Tempini & Price, 2001; Grabowski et al., 2001; Mesulam, Rogalski, et al., 2009; Tranel, 2006; Tyler et al., 2004); and the mapping between semantics and lexical phonology (Cloutman et al., 2009; Foundas, Daniels, & Vasterling, 1998; Hickok & Poeppel, 2004; Lüders et al., 1991; Mummery et al., 1999; Raymer, Maher, Foundas, Heilman, & Rothi, 1997; Trébuchon-Da Fonseca et al., 2009).

The Schwartz et al. (2009) findings agree with this focus on semantic processing outside posterior temporal and temporoparietal regions, but, here too, there are some surprises. First, according to Schwartz et al.'s (2009) filtered analyses, voxels in L-ATL play a role in naming that is independent of whatever role they might also play in verbal or nonverbal comprehension. At least at first blush, this does not fit well with the theory that neurons in this region code for amodal semantic information (e.g., Patterson et al., 2007; but see Section 4) or that they form convergence zones that mediate *two-way* mappings between words and concepts (Damasio et al., 1996, 2004). Moreover, as errors in our study were gathered from the Philadelphia Naming Test (PNT), which assesses basic-level naming of non-unique categories of objects, the well-documented specialization of the left temporal pole for the naming of known people, landmarks, and other unique entities (e.g., Damasio et al., 2004; Gorno Tempini & Price, 2001; Grabowski et al., 2001; Tranel, 2006; Tyler et al., 2004) cannot explain the effects we obtained in this region.

Outside the ATL, Schwartz et al. (2009) identified clusters of voxels that were associated with semantic errors in the unfiltered analysis but not after controlling for nonverbal comprehension. One of these clusters was located in lateral, superior BA 37. Other research has linked BA 37 to "pure" anomia (Antonucci, Beeson, & Rapcsak, 2004; Benson & Ardila, 1996; Cloutman et al., 2009; Foundas et al., 1998; Raymer et al., 1997), which, by definition, does not derive from a semantic deficit. Questioning this, the Schwartz et al. (2009) data suggest that in the lateral superior division of BA 37, at least, lesions create semantic errors by virtue of their impact on conceptualization or other semantic processes shared with comprehension. We will return to the topic of pure anomia below.

It should be evident from even this cursory discussion that the Schwartz et al. (2009) study reached conclusions that are controversial on several grounds. Given this, we performed a new VLSM analysis, using a more inclusive definition of semantic errors. We explain the benefits of such a re-analysis below in detail, beginning with the consideration of how semantic errors were defined in the previous study, compared with others.

1.2. Semantic error coding reconsidered

The original study was motivated by the interactive two-step model of lexical access (Dell, 1986; Dell et al., 1997) and by the hypothesis that semantic error production is primarily the consequence of faulty mapping from semantics to abstract word entities (i.e., "lemmas"). The VLSM analyses were aimed at localizing lesions responsible for semantic errors that arise via this cognitive mechanism, with the filtered analyses used to control for alternative mechanisms. Semantic errors were obtained from the PNT (http://www.ncrrn.org/assessment/pnt), using the error taxonomy and scoring rules that are standard for this test and that were used in many prior empirical tests of the interactive two-step model (e.g., Dell et al., 1997; Kittredge, Dell, Verkuilen, & Schwartz, 2008; Ruml, Caramazza, Capasso, & Miceli, 2005; Schwartz, Dell, Martin, Gahl, & Sobel, 2006). The benefit of our having defined semantic errors in accordance with this scheme is that we could relate the findings directly to the model and this line of empirical research. There were also some significant downsides: The definition excluded other error types that bear directly on the broader question of how semantically-guided lexical access goes awry in aphasia. Other lesion-mapping studies have not been so restrictive in classifying semantic errors, and this could help explain discrepancies between those findings and ours (e.g., Antonucci et al., 2008; Cloutman et al., 2009). Moreover, using the more restrictive definition gave us fewer errors to analyze, which almost certainly affected the reliability of the dependent variable and, hence, power to detect smaller effects in the VLSM.

To be specific, the naming scores that Schwartz et al. (2009) mapped anatomically were comprised of pure semantic errors – substituted nouns that related to the target either taxonomically or associatively and that were not also phonologically related. Mixed (semantic plus phonological) errors were excluded to keep