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An area essential for linking word meanings to word forms: Evidence from primary progressive aphasia

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ABSTRACT

We investigated the relationship between deficits in naming and areas of focal atrophy in primary progressive aphasia (a neurodegenerative disease that specifically affects language processing). We tested patients, across multiple input modalities, on traditional naming tasks (picture naming) and more complex tasks (sentence completion with a name, naming in response to a question) and obtained high resolution MRI. Across most tasks, error rates were correlated with atrophy in the left middle and posterior inferior temporal gyrus. Overall, this result converges with prior literature suggesting that this region plays a major role in modality independent lexical processing.

1. Introduction

Everyone has had the frustrating experience of being unable to retrieve a word from memory. In most cases, one is able to retrieve neither the pronunciation nor the spelling of the word. Although occasional instances of difficulty are not generally a cause for concern, brain lesions or neurological disease can cause a pathological level of naming deficits. Interestingly, difficulty with naming can be the residual deficit after incomplete recovery from nearly any vascular aphasia syndrome (e.g. Broca's Aphasia or Wernicke's Aphasia). It can also be one of the earliest manifestations of neurodegenerative syndromes, including all variants of Primary Progressive Aphasia (PPA). In the present study, we investigated the relationship between naming deficits and location of atrophy in individuals with PPA, a neurodegenerative condition in which language is disproportionately impaired for at least two years, without impairment in other cognitive domains other than praxis (Mesulam, 1982).

Naming is complex in that it involves, at the very least, mapping from various modalities of input (visual, auditory, tactile, etc.) to a semantic representation and then linking that to a word form for output in a particular mode (spoken, written). A deficit in any one of these processes can cause naming errors. In the current study, we evaluate areas of the brain associated with naming across various input modalities, and evaluate the possibility that there is an area critical for accessing spoken word forms (lexical representations) from a modality-independent semantic representation. Damage to this access or "linking" process would result in anomia, or the inability to name an object, although sensory and semantic processing remains intact (Deleon et al., 2007). For example, an individual with anomia would be unable to access the name "shoe" although they could select a shoe (versus glove) if given the name.

In a series of previous studies of acute stroke, we and others have identified areas of hypoperfusion and/or infarct associated with modality-independent naming impairment before the opportunity for reorganization of structure/function relationships. These studies have converged in support of the conclusion that an area in left posterior inferior temporal cortex (within Brodmann Area, BA, 37) when acutely compromised results in anomia (Deleon et al., 2007; Hillis et al., 2002a; Raymer et al., 1997). Furthermore, poor perfusion of this area (leading to tissue dysfunction) is associated with anomia, while reperfusion results in recovery from anomia (Hillis et al., 2002a, 2006b).

Although we have found this area to be critical for accessing modality-independent word forms from meaning, functional imaging studies in healthy participants have indicated that this relatively posterior part of the inferior temporal cortex (including inferior lateral BA 37) may be engaged in a variety of modality-independent lexical tasks in addition to naming (Cohen, Jobert, Le Bihan, & Dehaene, 2004). Cohen and colleagues dubbed this

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area, lateral to the midfusiform area critical to reading, the "lateral modality independent area" (LIMA). Whether or not this area is "specialized" for naming, the area is not likely to be the only area critical for modality-independent naming, but one important node in a neural network supporting naming.

Most of the evidence that posterior inferior temporal cortex is critical for modality-independent naming comes from stroke. Stroke studies might be biased as a method for identifying lesions associated with particular deficits, because some areas of the brain are particularly vulnerable to ischemia. Areas that are especially vulnerable to ischemia are more likely to be revealed as associated with deficits than areas less vulnerable to ischemia. PPA affects some regions of the brain that are less frequently damaged by stroke such as the anterior temporal pole, in addition to regions that stroke commonly affects (e.g. insula and superior temporal gyrus). Therefore, studying PPA provides another opportunity to test hypotheses about structure/function relationships, about naming in particular. It is especially useful to study all variants of PPA, because they all have naming deficits, but are associated with distinct areas of atrophy. Three variants of PPA (semantic, nonfluent agrammatic, logopenic) have been recognized that are characterized by their behavioral performance on language tasks and their pattern of brain atrophy (Gorno-Tempini et al., 2004, 2011; Mesulam, Weineke, Thompson, Rogalski, & Weintraub, 2009b; Mesulam et al., 2009a; Wilson et al., 2009). All three are frequently associated with naming impairment early in the course and throughout the course, and naming impairment is a defining criterion of both svPPA and lvPPA.

Of the three variants, svPPA is associated with the most severe naming deficits. SvPPA is characterized by severe naming and single-word comprehension deficits across input and output modalities (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Coccia, Bartolini, Luzzi, Provinciali, & Ralph, 2004; Hurley, Paller, Rogalski, & Mesulam, 2012; Luzzi et al., 2007). Naming errors are often empty nouns ("thing", "stuff"), circumlocutions, or semantic paraphasias, with both coordinate (cat → 'dog') and super-ordinate (cat → 'animal') errors observed (Jefferies & Lambon Ralph, 2006). Some patients with svPPA have progressive impairment in naming objects, with spared naming of actions, and their naming impairment is worse in the written than the spoken modality (Hillis, Oh, & Ken, 2004; Hillis et al., 2006a), although often severely impaired in the spoken modality as well. In contrast to the other variants, speech in svPPA is fluent, with intact syntax but limited content. This variant is associated with atrophy in the anterior and inferior temporal lobes bilaterally, but generally with greater atrophy on the left (Gorno-Tempini et al., 2011; Wilson et al., 2009). Due in large part to the multi-modal nature of the naming and comprehension deficits, there are claims that the anterior temporal lobes involved in amodal semantic processing (Corbett, Jefferies, Ehsan, & Lambon Ralph, 2009; Jefferies & Lambon Ralph, 2006).

Nonfluent agrammatic variant PPA (nfvPPA) is characterized by agrammatism and/or apraxia of speech (AOS) (Ash et al., 2009; Gorno-Tempini et al., 2004; Mesulam, Weineke, Thompson, Rogalski, & Weintraub, 2009; Rogalski et al., 2011). Agrammatism is characterized by the production of simple phrases and omissions of grammatical morphemes. Furthermore, syntactic processing becomes more apparent as the difficulty of the structure increases (passives, object relative clauses, etc.). AOS refers to slow, effortful speech articulation with numerous and varied off-target productions of words, especially polysyllabic words, with an awareness of misarticulations, but impaired motor planning. This variant is associated with atrophy in the left posterior frontoinsular region (posterior inferior frontal gyrus, insula, premotor, and supplementary motor areas) (Gorno-Tempini et al., 2004, 2011; Wilson et al., 2009).

In a small number of cases, modality-specific impairment in naming, specific to the spoken modality, has been reported in nfvPPA (Hillis, Tuffiash, & Caramazza, 2002b; Hillis et al., 2004, 2006a). The naming deficit in these cases has also been specific to impaired naming of actions rather than objects (Hillis et al., 2002b; see also Bak, O'Donovan, Xuereb, Boniface, & Hodges, 2001). For example, individuals with nfvPPA have been reported who could name objects both orally and in writing, but could name actions only in writing. Their deficit could not be attributed to a motor speech problem because they are able to say the names of objects without difficulty. Rather, they have difficulty accessing the spoken word form of actions. Because this pattern of performance has only been reported in nfvPPA, we expect that the area of atrophy associated with this component of naming is the posterior frontal cortex, and there is some evidence for this conclusion (Bak, O'Donovan, Xuereb, Boniface, & Hodges, 2001; Hillis et al., 2006a).

Logopenic variant PPA (lvPPA) is characterized by slow, hesitant speech that is often related to word finding pauses and moderately impaired confrontation naming (Gorno-Tempini et al., 2004, 2008). Observed errors include circumlocutions (e.g. "the thing you wear on your feet" for shoe) and phonological errors ("sue" for shoe). In addition, errors processing complex sentence structures seem to be more related to word length than syntactic complexity. These deficits are believed to generally stem from impaired phonological short-term memory, as the main distinguishing feature is disproportionally impaired phrase and sentence repetition. In contrast to svPPA, single word comprehension is relatively preserved. This variant is associated with atrophy in the left temporoparietal junction area (posterior temporal, supramarginal, and angular gyri) (Gorno-Tempini et al., 2011; Wilson et al., 2009).

Although there are differences in language deficits, difficulty naming can be one of the first symptoms and can remain a prominent symptom throughout the course in all PPA variants (Budd et al., 2010; Etcheverry et al., 2012; Grossman et al., 2004; Hurley et al., 2009, 2012; Kremin et al., 2001; McMillan et al., 2004; Mesulam et al., 2013; Rogalski, Rademaker, Mesulam, & Weintraub, 2008). However, there are fewer studies that have investigated naming across these PPA variants. It is important to investigate all variants, because naming severity is likely to be associated with atrophy in left temporal pole in svPPA (because that is where they have most atrophy), left superior temporal gyrus and inferior parietal lobule in lvPPA (because that is where they have the most atrophy), and left inferior frontal gyrus in nfvPPA (because that is where they have the most atrophy). Those that have studied all variants have reported both spoken naming and comprehension to be related to atrophy in the temporal lobes (anterior temporal and inferior temporal lobe) (Amici et al., 2007; Rogalski et al., 2011). However, these studies have not generally investigated naming across different modes of input (auditory and visual) and across actions and objects. Therefore in the current study, we investigated the relationship between modality-independent naming deficits for actions and objects and atrophy across all variants of PPA. Specifically, we tested naming when the input was visual or visual plus tactile or pure auditory. Finally, we tested participants on two complex naming tasks (Naming to Sentence Completion (Grass is... → green); responsive naming (Where do nurses work? → hospital). Although these tasks are more complex than simple naming (and can be failed for other reasons, such as failure to understand the question), they both require producing the correct name for the given input. We hypothesized that there might be one area of the brain (posterior inferior temporal cortex) critical for access to lexical representations from semantic representations (naming), and therefore atrophy in that area would be associated with impairment on all tasks that required naming (although other areas of atrophy might also disrupt