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A nonverbal route to conceptual knowledge involving the right anterior temporal lobe

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ABSTRACT

The semantic variant of primary progressive aphasia (PPA-S) is diagnosed based on impaired single-word comprehension, but nonverbal impairments in face and object recognition can also be present, particularly in later disease stages. PPA-S is associated with focal atrophy in the left anterior temporal lobe (ATL), often accompanied by a lesser degree of atrophy in the right ATL. According to a dual-route account, the left ATL is critical for verbal access to conceptual knowledge while nonverbal access to conceptual knowledge depends upon the integrity of right ATL. Consistent with this view, single-word comprehension deficits in PPA-S have consistently been linked to the degree of atrophy in left ATL. In the current study we examined object processing and cortical thickness in 19 patients diagnosed with PPA-S, to evaluate the hypothesis that nonverbal object impairments would instead be determined by the amount of atrophy in the right ATL. All patients demonstrated inability to access conceptual knowledge on standardized tests with word stimuli: they were unable to match spoken words with their corresponding pictures on the Peabody Picture Vocabulary Test. Only a minority of patients, however, performed abnormally on an experimental thematic verification task, which requires judgments as to whether pairs of object pictures are thematically-associated, and does not rely on auditory or visual word input. The entire PPA-S group showed cortical thinning in left ATL, but atrophy in right ATL was more prominent in the subgroup with low verification scores. Thematic verification scores were correlated with cortical thickness in the right rather than left ATL, an asymmetric mapping which persisted when controlling for the degree of atrophy in the contralateral hemisphere. These results are consistent with a dual-route account of conceptual knowledge: breakdown of the verbal left hemispheric route produces an aphasic syndrome, which is only accompanied by visual object processing impairments when the nonverbal right hemispheric route is also compromised.

1. Introduction

The anterior temporal lobe (ATL) was ignored in classic accounts of language and cognition (Mesulam et al., 2015), in part because it is rarely the center of stroke lesions. This has changed dramatically through the study of patients with focal neurodegeneration in ATL, most frequently caused by TDP-43 proteinopathy and Pick's disease (Mesulam et al., 2014a, 2014b; Rohrer et al., 2011). The most consistent symptoms shown by such patients are inability to name objects (anomia) and loss of single-word comprehension, but nonverbal impairments in object and face recognition are also common (Mesulam et al., 2014a, 2014b). Collectively, these symptoms suggest a fundamental problem in employing conceptual/semantic knowledge, so this syndrome is either referred to as the semantic variant of primary progressive aphasia (PPA-S) or as semantic dementia (SD) (Gorno-Tempini et al., 2004, 2011; Mesulam et al., 2003, 2014a, 2014b; Snowden et al., 1989). PPA-S and SD may be distinguished based on the prominence of nonverbal impairments (being more central to the latter) (Adlam et al., 2006; Mesulam et al., 2003), but they are also often treated interchangeably (see (Gorno-Tempini et al., 2011)). Regardless of these changes in nosology, such patients provide a valuable opportunity to study how conceptual knowledge is arranged in the human brain.

Warrington (1975) provided the first modern description of SD. She

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identified three patients with neurodegenerative etiology, all of whom showed no visuoperceptual impairments in viewing geometric shapes, common objects, or faces. Warrington assessed their ability to access conceptual knowledge by asking them to define (describe aloud) pictures of common objects (e.g. animals), to define the spoken names of those same objects, and to match spoken names with pictures on the Peabody Picture Vocabulary Test (PPVT) (Dunn, 2007). All three patients showed impairments on the PPVT and word definitions, and two of three patients produced abnormal picture definitions, thus presenting with a mixture of verbal and nonverbal conceptual deficits.

The standard neurological diagnoses for these patients would have been concurrent Wernicke-like aphasia (Wernicke, 1874) and associative agnosia (Lissauer, 1890), attributable to dysfunction in the left perisylvian language network and the ventral visual stream, respectively (Geschwind, 1965). Warrington offered an alternative mechanism based on a construct that was emerging at that time in the field of cognitive psychology: semantic memory (Tulving, 1972). Difficulties with both word and picture stimuli were parsimoniously explained as commonly stemming from damage to a unitary long-term memory system, which was dedicated to the storage of conceptual knowledge. The proposed storage mechanism rendered the route of access immaterial (verbal, nonverbal), as each pathway eventually leads to the same damaged knowledge system (i.e. a unitary system). Warrington's semantic memory framework was widely adopted afterwards (Snowden et al., 1989). Morphometric magnetic resonance imaging (MRI) eventually implicated the anterior portion of the temporal lobes as the common denominator in virtually every case of SD (Mummery et al., 2000, 1999; Rosen et al., 2002), with some degree of atrophy usually being present in the ATLs in both hemispheres. Based on this evidence, Warrington's unitary storehouse was proposed to be localized to ATL (Adlam et al., 2006; Rogers et al., 2004), which has been characterized as the brain's primary “semantic hub” (Lambon Ralph, 2014; Patterson et al., 2007).

Despite favoring a unitary account of conceptual impairments, in her initial report Warrington (1975) noted that the “correspondence of the deficits for words and for visual objects is far from complete”. For example, while patient E.M. successfully defined 93% of the picture stimuli in that study, she was only able to define 65% of the corresponding word stimuli. Similar verbal/nonverbal splits in performance are now known to be common in SD (Bozeat et al., 2000; Lambon Ralph et al., 1999), and are perhaps most clearly demonstrated in the related and overlapping syndrome of PPA-S.

PPA-S has historically been described and diagnosed as an aphasic syndrome rather than as a disorder of semantic memory (Gorno-Tempini et al., 2011; Mesulam et al., 2009a; Mesulam, 1982). In its initial stages atrophy is often confined to ATL in the left hemisphere, as evidenced by a consecutive case-series analysis where 8 out of 11 early-stage PPA-S patients showed left unilateral rather than bilateral atrophy according to cortical thickness analysis (Mesulam et al., 2013). Patients in that study and others (Mesulam et al., 2009a) produced fewer specific details when defining nouns than when defining pictures of those same items. PPA-S patients are also slower and less accurate when matching noun stimuli, and generate lower amplitude N400 potentials in response to nouns, compared to judgments of picture stimuli, and these verbal abnormalities correlate with cortical thickness in left ATL (Hurley et al., 2012). Likewise, patient scores on the PPVT, which is commonly used to assess single-word comprehension, are correlated with cortical thickness in left ATL (Rogalski et al., 2011a). In summary, verbal impairments often outweigh nonverbal impairments in PPA-S and SD, and critical substrates of verbal comprehension have been localized to the left rather than right ATL.

Discrepancies in performance based on route of access conflict with a basic unitary storehouse model, which have prompted a variety of elaborations to that model and the development of alternative accounts. According to a *dual-route account* of ATL functionality, ATL is part of a verbal route to conceptual knowledge in the left hemisphere, and part of a nonverbal route to conceptual knowledge in the right hemisphere (Gefen et al., 2013; Hurley et al., 2012; Mesulam et al., 2013; Nilakantan et al., 2017). The dual-route account thus describes a functional asymmetry in ATL: the left ATL is critical for conceptual access via word form input (written or spoken), while the right ATL mediates access via nonverbal object input (e.g. visual images).

Selective disruption of the verbal route has been well-characterized in PPA-S, and many theories and descriptions of ATL now include provisions for left-hemispheric language specialization (Gainotti, 2014; Lambon Ralph, 2014; Lambon Ralph et al., 2001; Mesulam et al., 2013). Fewer attempts have been made to localize the nonverbal route, but the results from several studies suggest that right ATL atrophy is particularly disruptive to recognition of facial images. Whereas left ATL lesions are associated with failure to describe celebrities when provided with their names, right-hemispheric lesions are associated with failure to describe those same individuals based on pictures of their faces (Evans et al., 1995; Gainotti, 2007; Gainotti et al., 2003, 2010; Gefen et al., 2013; Snowden et al., 2004, 2012; Tranel, 2006). These studies support the hypothesized role of right ATL in nonverbal access, but some have argued that recognition of specific persons depends on different neural machinery compared to recognition of “common object” stimuli such as animals or tools (McMullen et al., 2000; Pitcher et al., 2009; Thompson et al., 2004; Wallis, 2013).

The Pyramids and Palm Trees Test (PPT) is commonly employed to assess conceptual knowledge of common objects, where a cue picture must be matched to a thematically associated target picture rather than a foil (Howard and Patterson, 1992).[1] The verbal version of the PPT includes a comparable test with written words rather than pictured objects. At least one of the aforementioned studies of person knowledge found correlations between famous face recognition and the picture version of the PPT, and between famous name recognition and the word version of the PPT, but no formal analyses were conducted in that study to directly demonstrate a relationship between PPT scores and leftward vs rightward ATL atrophy (Snowden et al., 2004). Another study including larger samples of both leftward and rightward patients found no differences between the word and picture versions of the PPT in either subgroup (Thompson et al., 2003). Butler et al. (2009) examined correlations between PPT scores and atrophy (via voxel-based morphometry) in a large sample of degenerative patients including SD and other syndromes. Word and picture scores were both correlated with atrophy in both the left and right ATLs. When picture scores were included as a covariate, however, there was a specific association between word scores and left (but not right) ATL atrophy. Likewise, when word scores were included as a covariate, picture scores were selectively correlated with atrophy in right ATL. Further clinico-anatomic investigations are thus needed to help clarify what role the ATLs in each hemisphere play in nonverbal object processing.

There are two inherent methodological challenges when attempting to assess nonverbal object processing, and previous studies may be critiqued on both points. Firstly, it is extremely difficult to eliminate verbal components from ostensible “nonverbal” tests. For example, patients are often asked to define pictures aloud, and although this ensures that the stimuli themselves are nonverbal, the subsequent production of definitions depends upon speech output, and may thus encourage verbal mediation. When patients with aphasia or motor speech impairments provide imprecise definitions this may partially reflect difficulties with word finding and/or other aspects of language production rather than corruption of conceptual knowledge.

The second inherent challenge is to disentangle conceptual from perceptual stages of object processing. Receptive fields of neurons in the occipitotemporal ventral visual stream become increasingly

[1] As defined by Estes and colleagues, a thematic relationship is “a temporal, spatial, causal, or functional relation between things that perform complementary roles in the same scenario or event” (Estes et al., 2011).