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Language networks associated with computerized semantic indices

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ABSTRACT

Tests of generative semantic verbal fluency are widely used to study organization and representation of concepts in the human brain. Previous studies demonstrated that clustering and switching behavior during verbal fluency tasks is supported by multiple brain mechanisms associated with semantic memory and executive control. Previous work relied on manual assessments of semantic relatedness between words and grouping of words into semantic clusters. We investigated a computational linguistic approach to measuring the strength of semantic relatedness between words based on latent semantic analysis of word co-occurrences in a subset of a large online encyclopedia. We computed semantic clustering indices and compared them to brain network connectivity measures obtained with task-free fMRI in a sample consisting of healthy participants and those differentially affected by cognitive impairment. We found that semantic clustering indices were associated with brain network connectivity in distinct areas including fronto-temporal, fronto-parietal and fusiform gyrus regions. This study shows that computerized semantic indices complement traditional assessments of verbal fluency to provide a more complete account of the relationship between brain and verbal behavior involved organization and retrieval of lexical information from memory.

Introduction

The question of how conceptual knowledge is represented, organized and accessed from memory continues to be the subject of much research in multiple disciplines including neuroscience (Caramazza and Mahon, 2006; Chan et al., 1993; Mahon and Caramazza, 2009; Patterson et al., 2007; Pylkkanen et al., 2006), neuropsychology (Salmon et al., 1999; Troster et al., 1998; Weber et al., 2009), psycholinguistics (Levelt, 1989; Tverski and Hemenway, 1984), and computer science (Miller and Fellbaum, 1991; Rada et al., 1989; Resnik, 1999). Following Tulving (1972) this field of inquiry has drawn a distinction between a cognitive system that represents temporally dated events (episodic memory) and a system that constitutes a mental thesaurus of symbols that indexes information about cognitive referents and relations holding between them (semantic memory). The two types of memory have since been demonstrated to have different, albeit interdependent and interconnected, underlying neural mechanisms (Cabeza and Nyberg, 2000; Prince et al., 2007; Tulving et al., 1994).

The test of generative semantic verbal fluency (SVF) is an instrument widely used to elicit responses from subjects when studying semantic memory, executive function, and language. On this test, one is asked to say as many words as possible in one minute that denote objects belonging to a certain semantic category (e.g., animals, fruits, vegetables, tools). The performance on the SVF test is typically measured by counting the number of correct responses (SVF score). Lower SVF scores have been widely reported in patients with various stages of Alzheimer's disease (AD) dementia and mild cognitive impairment (MCI) (Chan et al., 2001; Ober et al., 1986; Rosen, 1980; Troyer et al., 1998). Furthermore, performance on SVF tests often shows early and more pronounced decline relative to other language, attention, and executive abilities (see Lezak (2004) and Henry et al. (2004) for review). The traditional SVF scores reflecting the number of words generated on this task assess performance consisting of several abilities including but not limited to semantic memory. Structural and functional neural imaging studies found that lower SVF scores are associated with lesions and atrophy in the anterior and inferior left temporal lobe regions as well as impairment in fronto-temporal connectivity (Libon et al., 2009). Evidence collected in fMRI studies supports the involvement of multiple frontal, temporal and posterior areas during word generation tasks such as SVF that include (but are not limited to) the left inferior frontal gyrus, the left inferior temporal gyrus, the hippocampus, the left superior occipital gyrus, and the left inferior medial parietal lobe (Birn et al., 2010; Wheatley et al., 2005). Furthermore, the basal ganglia exerts inhibitory control over motor, cognitive/executive, and affective systems which would make it an important part in a variety of tasks including aspects of the SVF performance. The involvement of multiple brain areas in generating words on SVF tests suggests that verbal behavior resulting from this task is supported by multiple neural mechanisms. However, the correspondence

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between various aspects of the generative verbal fluency behavior and distinct neural mechanisms is currently much less clear because of the difficulty involved in isolating quantifiable characteristics of the responses produced during SVF testing.

The overarching objective of the current study was to investigate the utility of a computational linguistic approach to capturing distinct components of verbal behavior manifest on SVF tests and to relate them to the underlying brain networks identified with task-free fMRI. Using task-free fMRI in connection with behavioral performance on a specific task is well-motivated by the fact that the patterns of temporally correlated low-frequency fluctuations observed in a resting state constitute the brain's intrinsic architecture that predicts the brain's functional responses to stimulation (Keller et al., 2011).

Clustering of responses on SVF tests

Optimal performance on SVF tests depends to a large extent on how well semantic information is organized into conceptually related clusters and whether the person is able to use an efficient strategy that accesses these clusters during the test (Estes, 1974; Hodges and Patterson, 1995; Laine, 1988). The size of semantic clusters and the efficiency of switching between clusters have been found to have different neuroanatomical correlates. Semantic cluster size was found to be associated with the left temporal lobe function, whereas the processing associated with switching was associated with the function of the frontal lobe (Rich et al., 1999; Troyer et al., 1997; Troyer, 2000).

While manual assessment of clustering and switching behavior has proven to be useful, it has traditionally relied on subjective evaluations of semantic similarity between at least two (Rich et al., 1999; Troyer et al., 1997, 1998) or three (Laine, 1988) adjacent words to define semantic clusters. For example, the qualitative assessment proposed by Troyer et al. (1997) relies on manual categorization of words produced on the SVF test (e.g., Zoological Categories, Human Use, and Living Environment) with further more fine-grained subcategorizations (e.g. living environment category composed of African, Australian, Arctic/Far North, Farm, North American and Water Animals). In addition to their subjectivity, these manual qualitative approaches are time consuming and are difficult to implement and standardize, which may be responsible for some of the conflicting results obtained with these methods in studies of Alzheimer's disease noted in previous work (Raoux et al., 2008).

Independently of these efforts, a number of fully automated approaches to representing the degree to which any two words in a given language are semantically related have been developed in the field of computational linguistics based on lexical databases such as WordNet, as well as corpora of text (Pedersen et al., 2007; Rada et al., 1989; Resnik, 1999). Many of these approaches utilize variations on a technique called Latent Semantic Analysis (LSA: (Landauer and Dumais, 1997)), a variant of factor analysis designed for representing lexical semantics. In addition to the LSA approach to semantic representation, several other alternatives have been proposed to model how semantic information is represented in the brain including neural networks (McClelland and Rogers, 2003), Random Indexing (Kanerva, 2009), Latent Dirichlet Allocation (LDA) modeling (Blei et al., 2003), and distributional memory models (Baroni and Lenci, 2010; Baroni et al., 2010).

The application of LSA to semantic representation is described in detail in the Methods section. In brief, LSA relies on the co-occurrence of words in a large corpus of text consisting of various types of discourse including newspaper articles, books, speeches and other sources of typical word usage to represent the semantic content of a word or a term as a set of co-occurrence counts with other words used in the same context. These semantic representations can then be directly and automatically compared to each other to assign a numeric value indicative of the strength of semantic relatedness between them. Apart from improved scalability and objectivity as a result of automation, these computational approaches allow quantification of semantic relations on a continuous rather than a categorical scale which allows us to (a) directly control and systematically vary how measures such as the cluster size, for example, are calculated, and (b) develop new semantic indices not possible with categorical judgments. We have previously reported on applications of these computerized semantic indices, either calculated from WordNet, a large lexical database (Pakhomov et al., 2012), or from a corpus of text (Pakhomov and Hemmy, 2014). In other prior work, computational models of word meanings derived from a very large corpus of text have been demonstrated to predict neural activation patterns observed with fMRI (Mitchell et al., 2008). These findings were based on representations for concrete nouns and thus provide a strong motivation for using distributional semantic approaches to represent the meaning of words produced in response to a verbal fluency task.

The mechanisms underlying *semantic* memory are negatively affected by aging (Meinzer et al., 2009) and are the target of several types of neurodegenerative diseases including the semantic variant of frontotemporal dementia (Grossman, 2002; Hodges et al., 2004; Knopman et al., 2008) and the Alzheimer's disease (AD) dementia (Hodges and Patterson, 1995). In our previous work, we found that computerized semantic indices were sensitive to clinical differences between mild cognitive impairment (MCI) and AD dementia (Pakhomov et al., 2012), and could be used to estimate future risk of developing dementia in healthy individuals (Pakhomov and Hemmy, 2014). The current study relies on a sample consisting of cognitively normal individuals as well as MCI and AD dementia patients in order to investigate the relationship between SVF performance and functional connectivity in the language network 'at rest' assessed with task-free fMRI. Thus, the disease status is used in this study as a naturally occurring research instrument that modulates both the behavioral performance on SVF tests and the connectivity of brain networks that underlie verbal behavior. Therefore, we expect that the degree of differential impairment in the connectivity of functional brain networks that is characteristic of AD dementia (Stam et al., 2007, 2009; Supekar et al., 2008) will introduce detectable systematic variability into both behavioral and neural measurements. The specific aims of this study were (a) to confirm previously found neural correlates of the performance on the SVF test, and (b) to determine if the new automated semantic clustering indices derived with the LSA-based computational linguistic approach are associated with connectivity in areas distinct from those related to the traditional SVF scores. Initially, our prediction was that the computerized semantic indices were associated with roughly the same brain networks as those associated with traditional SVF scores; however, while we did find some overlap between measures, we also found that they were associated with clearly distinct networks.

Methods

Participants

A random target sample of 60 participants (mean age = 72.46; SD = 10.8) was obtained from the Mayo Clinic Alzheimer's Disease Research Center (MCADRC). Of these participants, at the time of neuropsychological testing, 21 had a clinical diagnosis of probable AD dementia (DSM-IV/NINCDS-ADRDA criteria; (American Psychiatric Association, 1994; McKhann et al., 1984)), 20 had a clinical diagnosis of MCI (Petersen, 2004) with or without an amnestic component, and 19 were cognitively normal elders (CN). The final study sample consisted of 49 participants (11 CN, 17 MCI and 21 AD dementia) that were selected from the target sample of 60 participants based on availability of good quality task-free functional MRI scans (TF-fMRI). The demographic characteristics of this sample are reported in Table 1.

All participants, or appropriate surrogates, provided written informed consent for participation. The Mayo Clinic Institutional Review Board approved the study and the consenting processes