CORTEX XXX (2013) 1–10

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Research report

# A computational linguistic measure of clustering behavior on semantic verbal fluency task predicts risk of future dementia in the Nun Study

*Serguei V.S. Pakhomov* [a,*] *and Laura S. Hemmy* [b,c]

[a] *University of Minnesota Center for Clinical and Cognitive Neuropharmacology, United States*
[b] *Department of Psychiatry, University of Minnesota, MN, United States*
[c] *Geriatric Research Education and Clinical Center (GRECC), Minneapolis VA System, United States*

ARTICLE INFO

*Article history:*
Received 24 October 2012
Reviewed 14 January 2013
Revised 20 February 2013
Accepted 15 May 2013
Published online xxx

*Keywords:*
Semantic verbal fluency
Dementia
Latent semantic analysis
Clustering
Alzheimer's disease

ABSTRACT

Generative semantic verbal fluency (SVF) tests show early and disproportionate decline relative to other abilities in individuals developing Alzheimer's disease. Optimal performance on SVF tests depends on the efficiency of using clustered organization of semantically related items and the ability to switch between clusters. Traditional approaches to clustering and switching have relied on manual determination of clusters. We evaluated a novel automated computational linguistic approach for quantifying clustering behavior. Our approach is based on Latent Semantic Analysis (LSA) for computing strength of semantic relatedness between pairs of words produced in response to SVF test. The mean size of semantic clusters (MCS) and semantic chains (MChS) are calculated based on pairwise relatedness values between words. We evaluated the predictive validity of these measures on a set of 239 participants in the Nun Study, a longitudinal study of aging. All were cognitively intact at baseline assessment, measured with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery, and were followed in 18-month waves for up to 20 years. The onset of either dementia or memory impairment were used as outcomes in Cox proportional hazards models adjusted for age and education and censored at follow-up waves 5 (6.3 years) and 13 (16.96 years). Higher MCS was associated with 38% reduction in dementia risk at wave 5 and 26% reduction at wave 13, but not with the onset of memory impairment. Higher [+1 standard deviation (SD)] MChS was associated with 39% dementia risk reduction at wave 5 but not wave 13, and association with memory impairment was not significant. Higher traditional SVF scores were associated with 22–29% memory impairment and 35–40% dementia risk reduction. SVF scores were not correlated with either MCS or MChS. Our study suggests that an automated approach to measuring clustering behavior can be used to estimate dementia risk in cognitively normal individuals.



* *Corresponding author*. 7-125F Weaver Densford Hall, 308 Harvard Street SE, Minneapolis, MN 55455, United States.
E-mail address: pakh0002@umn.edu (S.V.S. Pakhomov).

0010-9452/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.cortex.2013.05.009

## 1. Introduction

Tests of phonemic and semantic verbal fluency (SVF) are widely used in the assessment of individuals with memory complaints and in the clinical diagnosis of Alzheimer's disease (AD). Patients are asked to generate as many words as they can either starting with a certain letter of the alphabet (phonemic fluency) or belonging to a certain semantic category (semantic fluency). The performance on the SVF test is typically measured by counting the number of correct words spoken by the patient in 1 min. Although individual performance on both the phonemic and semantic fluency tests is impaired in individuals with AD, semantic performance is significantly more affected than phonemic early in the disease course. Deficits evident on SVF have been shown to be sensitive and specific in differentiating between healthy controls and patients with AD (Canning et al., 2004) and have been found to be predictive of the development of AD in people with memory complaints prior to a clinical diagnosis (Fagundo et al., 2008), as well as progression of healthy individuals to mild cognitive impairment (MCI) and dementia (Loewenstein et al., 2012). In addition to clinical use, these relatively simple to administer tests of verbal fluency have been used extensively as part of standard neuropsychological test batteries to study cognitive effects of dementia (Gorno-Tempini et al., 2004; Hodges et al., 2004; Knopman et al., 2008; Libon et al., 2007). In particular, SVF deficits have been widely reported in patients with various stages of AD and MCI (Chan et al., 2001; Ober et al., 1986; Rosen, 1980; Troyer et al., 1998a, 1998b) and often show early and disproportionate decline relative to other language, attention, and executive abilities [see Lezak (2004) and Henry et al. (2004), for review].

Originally proposed by Troyer et al. (1997), additional qualitative metrics that examine the degree to which SVF responses are organized into groups of semantically related words (semantic clusters) and the frequency of transitions between these groups (switches) have also been extensively studied. Successful overall performance on the SVF test depends to a large extent on how well semantic information is organized into conceptually related clusters and whether one 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 from one cluster (after it has been exhausted) to another have been found to have different neuroanatomical correlates (Rich et al., 1999; Troyer, 2000; Troyer et al., 1997). Semantic cluster size was found to be associated with the left temporal lobe, whereas the processing associated with switching was associated more with the function of the frontal lobe. These studies suggested that cluster size and the amount of switching between clusters may index the strength of associations in the patient's lexical-semantic networks.

Studies of clustering and switching in AD also found smaller and fewer clusters produced on this task by people clinically diagnosed with AD (Ober et al., 1986; Rosen, 1980; Troster et al., 1998; Troyer et al., 1998a, 1998b) and significantly fewer switches (Raoux et al., 2008) than by healthy controls. The latter finding is not surprising as the number of switches in a time-limited task such as the SVF test is likely to be highly correlated with the total number of words produced on the test. This is particularly true of approaches such as the original Troyer et al. (1997) methodology in which single words unrelated to adjacent words are counted as clusters of zero size. This approach results in discounting these "singleton" clusters in the computation of the mean cluster size (MCS) but not the number of switches for any given SVF sample. When participants tend to produce small clusters, and a switch is defined as a transition between any two clusters (even those consisting of a single word), the number of switches is likely to be highly correlated with the total number of words produced, and thus not very informative. An alternative measure that normalizes the raw number of switches by the total number of words produced was proposed but was not found to add meaningful information (Troster et al., 1998).

Subsequent studies that examined clustering and switching performance in less impaired individuals with memory complaints (e.g., MCI) consistently found significant differences between healthy controls and MCI participants on the traditional SVF score and switching, but not so with cluster size. For example, Raoux et al. (2008) examined a set of 153 participants including 51 incident cases of AD at 2 and 5 years prior to diagnosis. Significant cross-sectional differences between controls and the incident AD cases were found at all three time points in the traditional SVF score and the number of switches, but no difference was found in MCS. In contrast, a recent study by Price et al. (2012) examined a group of 33 amnestic MCI participants matched on age, education and IQ with 33 healthy controls, and found significant differences in both the traditional SVF score and MCS measures. Both of these studies calculated the cluster sizes according to Troyer et al. (1997) guidelines with one major difference, however. Rosen's study excluded repetitions from the calculation of cluster sizes, whereas Price's study followed Troyer's methodology more strictly and included all repetitions and errors in computation of clusters. It is unclear at this point if the inclusion/exclusion of repetitions in cluster size determination is responsible for the inconsistency in the results and conclusions; however, this is a good example where the qualitative nature of the methodology is a problem that we are attempting to address with automation in the present study.

All prior studies of clustering and switching in relation to dementia have relied on subjective assessments of semantic similarity between at least two (Rich et al., 1999; Troyer et al., 1997, 1998a, 1998b) or three (Laine, 1988) adjacent words to define clusters. For example, the qualitative assessment proposed by Troyer et al. (1997) relies on manual determination if adjacent words belong to a top-level subcategory (e.g., zoological categories, human use, and living environment) with furthermore 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 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. Automated, computerized approaches to the assessment of clustering and switching behavior may help address some of the issues with qualitative approaches.

Please cite this article in press as: Pakhomov SVS, Hemmy LS, A computational linguistic measure of clustering behavior on semantic verbal fluency task predicts risk of future dementia in the Nun Study, Cortex (2013), http://dx.doi.org/10.1016/j.cortex.2013.05.009