Published in final edited form as:

Int J Geriatr Psychiatry. 2019 June ; 34(6): 863–867. doi:10.1002/gps.5081.

Verbal Fluency and Risk of Dementia

Angelina R. Sutin[1], **Yannick Stephan**[2], and **Antonio Terracciano**[1]

[1]Florida State University College of Medicine

[2]Euromov, University of Montpellier

Abstract

OBJECTIVE: Verbal fluency is a common neuropsychological test that is impaired in dementia. We test whether verbal fluency is a prospective risk factor for incident dementia, cognitive impairment not dementia (CIND), and conversion from CIND to dementia.

METHODS: Participants (*N*=18,189) from the Health and Retirement Study were administered a standard test of verbal fluency and were assessed for cognitive status every two years between baseline and six years follow-up.

RESULTS: Every standard deviation increase in verbal fluency was associated with an approximately 60% reduced risk of incident dementia, an approximately 25% reduced risk of incident CIND, and an approximately 25% reduced risk of conversion from CIND to dementia. These associations were independent of age, gender, education, race, ethnicity, and *APOE* risk status. The associations were slightly weaker (but still significant) for African-Americans and individuals with lower education. There was no interaction between verbal fluency and *APOE* risk status.

CONCLUSION: Verbal fluency is an easily-administered task that is predictive of incident cognitive impairment.

Keywords

verbal fluency; dementia; Alzheimer's disease; neurocognitive tests

Introduction

Verbal fluency is among the most common neuropsychological tests administered in both research and clinical settings.[1] Although a relatively simple task – typically naming as many examples of a category (e.g., animals) or a letter (e.g., "s") as possible in 60 seconds – it requires activation of multiple cognitive processes.[2] That is, it engages both verbal knowledge to produce the examples and executive function to monitor and remember what words have already been produced and inhibit repetitions.[3] It thus provides a great deal of general information about how well an individual is functioning cognitively.

Address correspondence to: Angelina R. Sutin, Ph.D., Florida State University College of Medicine, 1115 W. Call Street, Tallahassee, FL 32306, (850) 645-0438, Fax: (850) 645-1773, angelina.sutin@med.fsu.edu.

Conflict of Interest: None.

Verbal fluency has been associated with cognitive impairment. Individuals suffering from Alzheimer's disease and other dementias, for example, have impaired fluency.[4] Among individuals with mild cognitive impairment (MCI), it has been found to predict conversion to dementia,[5] particularly among individuals with Parkinson's disease.[6] This literature on verbal fluency and cognitive impairment has focused on either comparisons between patients with impairment and cognitively-healthy controls[7] or how fluency predicts conversion from mild to severe impairment.[8] There is also evidence that verbal fluency declines more over time for participants who developed dementia over the study period compared to participants who did not develop dementia.[9,10] Less is known, however, about whether fluency predicts long-term risk of developing dementia or more mild impairments in the general population.

To that end, we use data from the Health and Retirement Study to test verbal fluency as a prospective predictor of incident dementia over an up to six-year follow up in a large sample of community-dwelling adults. In addition to testing verbal fluency as a predictor of incident dementia, we also test whether it predicts incident cognitive impairment not dementia (CIND), conversion from CIND to dementia, and whether the association with dementia risk is moderated by age, gender, education, race, Hispanic ethnicity, or *APOE* risk status.

Methods

Participants and Procedure

Participants were drawn from the Health and Retirement Study (HRS), a longitudinal study of the health and well-being of Americans over the age of 50 and their spouses (regardless of age). More information about the study and how to access the data can be found at http://hrsonline.isr.umich.edu/. Participants are interviewed every two years in an extensive assessment that includes the modified Telephone Interview for Cognitive Status (TICSm), a measure of cognitive status (see below). Verbal fluency was first administered in 2010 as part of this regular cognitive assessment. Participants were selected for inclusion in the current analysis if they scored in the non-dementia range on the TICSm at baseline, completed the verbal fluency task at the 2010 baseline, and had at least one additional TICSm measurement through 2016 (the most recent assessment available). A total of 18,189 participants met these inclusion criteria to be included in the analysis.

A total of 20,488 participants had complete data available on all study variables at baseline. Of these participants, 798 (4%) were excluded because they scored in the dementia range at baseline, and 606 (3%) were excluded because they died without a follow-up. The remaining 895 (4%) participants with no follow-up data were older, had less education, and retrieved fewer words on the verbal fluency task ($p<.01$) at baseline than the 18,189 participants in the analytic sample; there were no differences in gender, race, or Hispanic ethnicity.

Measures

Verbal fluency.—Participants were given the following instructions: "Now I want to see how many different animals you can name. You will have 60 seconds. When I say, 'Begin', say the animal names as fast as you can." Fluency was the total number of animals named in 60 seconds.

Cognitive status.—Every two years in the HRS participants completed the modified Telephone Interview for Cognitive Status (TICSm). Participants were asked to (a) recall 10 words immediately and after a delay, (b) subtract 7 from 100 five times, and (c) count backward from 20. The TICSm score is the sum of performance on these three tasks with up to 20 points for immediate and delayed recall, up to five points for serial 7 subtraction, and up to two points for backward counting. From a possible total of 27 points, participants were classified into one of three groups at each assessment: Scores between 12 and 27 were classified as normal cognition, scores between 7 and 11 were classified as cognitive impairment not dementia (CIND), and scores 6 or less were classified in the dementia group. These cutoffs have been validated previously against a comprehensive neuropsychological assessment and clinical diagnosis of dementia.[11,12] National trends in dementia prevalence have been tracked from assessment of the TICSm in the HRS.[13] In addition, similar associations have been found for risk of dementia using the TICSm[14] as for a clinical diagnosis of Alzheimer's disease.[15]

Analytic Strategy

Cox proportional hazard models were used to test verbal fluency as a predictor of incident dementia and incident CIND over the 6-year follow-up. Specifically, time was measured in years from the assessment of verbal fluency and coded as time-to-incidence of dementia. Cases were censored at the last available cognitive assessment at which the participant did not score in the dementia range. We followed the same procedure for incident CIND. We also tested whether verbal fluency was associated with risk of conversion from CIND to dementia over the follow-up by selecting participants who scored in the CIND range at the baseline assessment. For dementia risk, sensitivity analyses excluded participants with CIND at baseline and participants with less than six years of follow-up data. All analyses controlled for age, gender, race, Hispanic ethnicity, and education. In a subsample of participants with genetic information (n=9,223), *APOE* risk status (any ε4 carrier versus non-carriers) was included as an additional covariate. Finally, we included interactions between verbal fluency and each sociodemographic factor and genetic risk to test whether the association between fluency and risk of dementia was moderated by age, gender, race, Hispanic ethnicity, education, or *APOE* risk status.

Results

Descriptive statistics for study variables are shown in Table 1. Over the up to 6-year follow-up and 94,742 person-years, a total of 1,326 participants developed dementia. Results of the Cox regression analysis are shown in Table 2. For every standard deviation increase in verbal fluency, there was a more than 60% decreased risk of dementia (Table 2). By comparison, every standard deviation increase in years of education was associated with a nearly 60% decreased with of dementia. When scaled in the raw number of words, rather than by standard deviation, each additional word produced during the verbal fluency task was associated with an approximately 7% reduced risk of incident dementia over the follow-up (HR=.93, 95% CI=.92, .94, p<.001). Sensitivity analyses indicated that the association between fluency and dementia risk was similar when excluding participants who scored within the range of CIND at baseline (Model 2) and when the sample was further restricted

to participants who had a full six years of follow-up data (Model 3). The results were also similar when genetic risk was included in the model (HR=.58, 95% CI=.53, .63; *n*=9,223; 751 incident dementia). Verbal fluency was likewise associated with a lower risk of CIND and, among participants with CIND at baseline, it was associated with a lower risk of conversion to dementia over the follow-up (Table 3).

The association between verbal fluency and risk of incident dementia was moderated by race and education. The association was apparent among African American participants (HR=.71, 95% CI=.63, .80, $p<.001$) but weaker than among white participants (HR=.56, 95% CI=.52, .61, p<.001). This difference was significant ($HR_{interaction}$ =1.33, 95% CI=1.16, 1.54, p<.001). Likewise, although apparent across the range of years of education, the association was weaker among participants with lower levels than higher levels of education ($HR_{interaction}$=.93, 95% CI=.88, .97, p=.003). The association between verbal fluency and risk of incident dementia was not moderated by age, gender, Hispanic ethnicity, or *APOE* risk status.

Discussion

The present research shows that a relatively simple task to assess verbal fluency is associated with risk of incident dementia. The fluency task correlates only modestly with the tasks that make up the TICSm,[16] which suggests that the relation is not due to overlap in cognitive processes between fluency and those used to identify dementia. In addition, although fluency is associated with education – individuals with more education tend to perform better on verbal fluency tasks[17] – it was an independent and slightly stronger predictor of dementia than educational attainment. Verbal fluency is thus one easily administrable task that provides information on dementia risk that is above and beyond the effect of education.

The association between fluency and dementia risk was apparent across age, gender, education, race, and ethnicity. The strength of these associations, however, was somewhat lower among individuals with lower education and among African Americans. At lower levels of education, verbal fluency may be detecting lack of education rather than cognitive processes that are vulnerable in dementia.[18] The association was also slightly weaker among African American participants. There are significant health disparities in dementia prevalence across ethnic groups. African American adults, for example, have greater than twice the risk of dementia compared to white adults.[19] Verbal fluency may have less predictive power among African Americans because the risk associated with ethnicity accounts for a large portion of the variance in risk. It is of note, however, that even in this high-risk group, higher verbal fluency was associated with an approximately 30% decreased risk of dementia.

Previous work on verbal fluency and dementia risk has focused on fluency as a predictor of conversion from MCI and other mild impairments to dementia.[8] Our results are consistent with this literature: among individuals with CIND, lower fluency was associated with greater risk of conversion to dementia. In addition, lower fluency is also associated with increased risk of developing CIND. Although most individuals with CIND will not go on to develop dementia,[20] CIND is an important outcome in its own right. Individuals with even mild

impairments have greater limitations in daily functioning[21] and functional disability[22] and greater declines in financial capacity over time.[23]

As with other risk factors, the association between verbal fluency and dementia risk may be the result of reverse causality:[24] The pathological processes associated with dementia may impair the ability to retrieve words quickly. Thus, rather than increasing risk, poor verbal fluency may be an early marker of the disease. The results, however, remained significant when we excluded cases that were classified with dementia within 4 years of follow up. Reverse causality would also predict stronger effects for conversion from CIND to dementia, but the effect size for conversion (in Table 3) was actually smaller than the effect found in the full sample (Table 2). These findings suggest that the association between fluency and dementia risk may not only be the result of reverse causality.

Although verbal fluency may be useful as an early marker of risk for AD, it is a non-specific marker for two reasons. First, although an easy task to administer, it is quite complex in terms of the number of basic cognitive functions needed to perform it. As such, it is not possible to differentiate specific cognitive functions, such as low verbal knowledge or impaired working memory, as risk factors for dementia. Second, it is implicated in a number of neurodegenerative diseases, including several types of dementia (e.g., Alzheimer's disease, frontotemporal dementia) and Parkinson's disease.[25] It thus lacks specificity as a risk factor for disease. In the current study, we were unable to differentiate the causes of cognitive impairment.

The present study had several strengths, including a large sample and a relatively long follow-up period. There are also some limitations that could be addressed in future research. As just mentioned, we could not differentiate between types of dementia. The performance-based measure indicated the presence of cognitive impairment but not the cause of the impairment. Future research could address whether verbal fluency is more or less predictive of specific neurodegenerative diseases, such as Alzheimer's disease or frontotemporal dementia. Another limitation was the relatively short follow-up of six years, which is not long enough to determine whether verbal fluency measured earlier in adulthood, such as in middle age, is predictive of dementia risk in older adulthood. We also could not rule out the possibility of reverse causality. In future work it would be useful to have measures of brain pathology, such as through brain scans, to be able to address the role of neurodegeneration in the relation between fluency and dementia risk. Such studies could be particularly informative with repeated longitudinal assessment of fluency over decades to examine the trajectories of verbal fluency with the progression from preclinical to clinical phase of the disease.

Conclusion

The present research indicates that low verbal fluency increases risk of dementia, incident CIND, and conversion from CIND to dementia. These associations were independent of socio-demographic factors and *APOE* risk status and apparent even after excluding participants with CIND at baseline and those with <6 years follow-up.

Acknowledgments

Financial Support: Research reported in this publication was supported by the National Institute On Aging of the National Institutes of Health under Award Number R01AG053297 and R21AG057917. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Lezak MD. Neuropsychological assessment. 4th ed New York: Oxford University Press; 2004.
2. Troyer AK, Moscovitch M, Winocur G. Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults. Neuropsychology. 1997;11:138–146. [PubMed: 9055277]
3. Shao Z, Janse E, Visser K, Meyer AS. What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. Front Psychol. 2014;5:772. [PubMed: 25101034]
4. Henry JD, Crawford JR, Phillips LH. Verbal fluency performance in dementia of the Alzheimer's type: a meta-analysis. Neuropsychologia. 2004;42:1212–1222. [PubMed: 15178173]
5. Gallucci M, Di Battista ME, Battistella G, Falcone C, Bisiacchi PS, Di Giorgi E. Neuropsychological tools to predict conversion from amnestic mild cognitive impairment to dementia. The TREDEM Registry. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2018;25:550–560. [PubMed: 28715933]
6. Pagonabarraga J, Kulisevsky J. Cognitive impairment and dementia in Parkinson's disease. Neurobiol Dis. 2012;46:590–596. [PubMed: 22484304]
7. Bertola L, Mota NB, Copelli M, et al. Graph analysis of verbal fluency test discriminate between patients with Alzheimer's disease, mild cognitive impairment and normal elderly controls. Front Aging Neurosci. 2014;6:185. [PubMed: 25120480]
8. Gainotti G, Quaranta D, Vita MG, Marra C. Neuropsychological predictors of conversion from mild cognitive impairment to Alzheimer's disease. J Alzheimers Dis. 2014;38:481–495. [PubMed: 24002185]
9. Raoux N, Amieva H, Le Goff M, et al. Clustering and switching processes in semantic verbal fluency in the course of Alzheimer's disease subjects: results from the PAQUID longitudinal study. Cortex. 2008;44:1188–1196. [PubMed: 18761132]
10. Amieva H, Jacqmin-Gadda H, Orgogozo JM, et al. The 9 year cognitive decline before dementia of the Alzheimer type: a prospective population-based study. Brain. 2005;128:1093–1101. [PubMed: 15774508]
11. Crimmins EM, Kim JK, Langa KM, Weir DR. Assessment of cognition using surveys and neuropsychological assessment: the Health and Retirement Study and the Aging, Demographics, and Memory Study. J Gerontol B Psychol Sci Soc Sci. 2011;66 Suppl 1:i162–171. [PubMed: 21743047]
12. Langa KM, Plassman BL, Wallace RB, et al. The Aging, Demographics, and Memory Study: study design and methods. Neuroepidemiology. 2005;25:181–191. [PubMed: 16103729]
13. Langa KM, Larson EB, Crimmins EM, et al. A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012. JAMA Intern Med. 2017;177:51–58. [PubMed: 27893041]
14. Terracciano A, Stephan Y, Luchetti M, Albanese E, Sutin AR. Personality traits and risk of cognitive impairment and dementia. J Psychiatr Res. 2017;89:22–27. [PubMed: 28153642]
15. Terracciano A, Sutin AR, An Y, et al. Personality and risk of Alzheimer's disease: New data and meta-analysis. Alzheimers Dement. 2014;10:179–186. [PubMed: 23706517]
16. Fisher GG, McArdle JJ, McCammon RJ, Sonnega A, Weir DR. New measures of fluid intelligence in the HRS. Ann Arbor, MI: University of Michigan;2013.
17. Kempler D, Teng EL, Dick M, Taussig IM, Davis DS. The effects of age, education, and ethnicity on verbal fluency. J Int Neuropsychol Soc. 1998;4:531–538. [PubMed: 10050357]
18. Sharp ES, Gatz M. Relationship between education and dementia: an updated systematic review. Alzheimer Dis Assoc Disord. 2011;25:289–304. [PubMed: 21750453]

19. Association As. 2017 Alzheimer's disease facts and figures. Alzheimer's & Dementia. 2017;13:325–373.

20. Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia--meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand. 2009;119:252–265. [PubMed: 19236314]

21. Jekel K, Damian M, Wattmo C, et al. Mild cognitive impairment and deficits in instrumental activities of daily living: a systematic review. Alzheimers Res Ther. 2015;7:17. [PubMed: 25815063]

22. Lindbergh CA, Dishman RK, Miller LS. Functional Disability in Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. Neuropsychol Rev. 2016;26:129–159. [PubMed: 27393566]

23. Martin RC, Gerstenecker A, Triebel KL, et al. Declining Financial Capacity in Mild Cognitive Impairment: A Six-Year Longitudinal Study. Arch Clin Neuropsychol. 2018.

24. Solomon A, Mangialasche F, Richard E, et al. Advances in the prevention of Alzheimer's disease and dementia. J Intern Med. 2014;275:229–250. [PubMed: 24605807]

25. Suhr JA, Jones RD. Letter and semantic fluency in Alzheimer's, Huntington's, and Parkinson's dementias. Arch Clin Neuropsychol. 1998;13:447–454. [PubMed: 14590609]

Key points:

- Individuals with cognitive impairment perform worse on verbal fluency tasks; we test whether verbal fluency prospectively predicts incident dementia
- Higher verbal fluency is protective against incident dementia, incident cognitive impairment not dementia (CIND) and conversion from CIND to dementia
- These associations were independent of socio-demographic factors and *APOE* risk status
- Lower risk of dementia was still apparent after excluding participants with CIND at baseline and those with <6 years follow-up

Table 1

Baseline Characteristics and APOE ε4 Risk Status of the full sample and by Cognitive status at follow-up

Variable	Non-impaired	Dementia	Total
	N=16,863	N=1,326	N=18,189
Age (years)	63.75 (10.92)	70.93 (12.17)	64.27 (11.17)
Education (years)	13.02 (2.95)	10.66 (3.67)	12.85 (3.07)
Gender (female)	59%	60%	59%
Race (African American)	18%	30%	19%
Race (other or unknown)	8%	10%	9%
Race (white)	74%	60%	72%
Ethnicity (Hispanic)	13%	20%	13%
APOE ε4 risk status[a]	13%	35%	12%
Verbal Fluency (words)	17.52 (7.09)	12.34 (5.45)	17.14 (7.11)

Note. Values are means (standard deviations) or percentiles.

[a] *N*=9,223 for *APOE* risk status.

Table 2

Cox Regression Predicting Risk of Incident Dementia from Baseline Verbal Fluency

Predictor	Model 1	Model 2	Model 3
Age (SD)	1.97 (1.85, 2.09)**	1.98 (1.78, 2.20)**	2.83 (2.03, 2.80)**
Education (SD)	.64 (.61, .67)**	.66 (.60, .73)**	.71 (.62, .83)**
Gender (female)	.97 (.87, 1.08)	1.12 (.93, 1.36)	1.14 (.86, 1.51)
Race (African American)	2.48 (2.18, 2.82)**	2.14 (1.70, 2.68)**	1.99 (1.40, 2.88)**
Race (other or unknown)	1.41 (1.15, 1.73)**	1.43 (.99, 2.08)	1.45 (.83, 2.54)
Ethnicity (Hispanic)	1.19 (.99, 1.43)	1.09 (.78, 1.51)	1.22 (.76, 1.98)
Verbal Fluency (SD)	.60 (.56, .64)**	.66 (.59, .73)**	.74 (.63, .87)**

Note. Model 1 *N*=18,189; Model 2 *N*=15,083; Model 3 *N*=11,605. Model 1 is the analysis on the full sample. Model 2 excludes participants with cognitive impairment not dementia (CIND) at baseline. Model 3 excluded participants with CIND at baseline and participants with less than six years of follow-up data. SD=standard deviation.

Table 3

Cox Regression Predicting Risk of Incident CIND and Conversion from CIND to Dementia from Baseline Verbal Fluency

Predictor	Incident CIND	Conversion to Dementia
Age (SD)	1.50 (1.45, 1.56)**	1.65 (1.52, 1.79)**
Education (SD)	.72 (.70, .75)**	.79 (.73, .85)**
Gender (female)	.89 (.84, .95)**	1.01 (.88, 1.15)
Race (African American)	2.10 (1.94, 2.28)**	1.56 (1.33, 1.84)**
Race (other or unknown)	1.40 (1.24, 1.58)**	1.07 (.84, 1.37)
Ethnicity (Hispanic)	1.23 (1.10, 1.38)**	1.13 (.90, 1.41)
Verbal Fluency (SD)	.76 (.73, .79)**	.77 (.72, .83)**

Note. N=15,083, n=3862 incident CIND; N=3,106; n=861 converted to dementia. SD=standard deviation.