Published in final edited form as:
Int Psychogeriatr. 2010 August ; 22(5): 785–794. doi:10.1017/S1041610209991657.

A novel approach to assessing memory at the population level: Vulnerability to semantic interference

Beth E. Snitz[1,*], **David A. Loewenstein**[2,3], **Chung-Chou H. Chang**[4,5], **Ching-Wen Lee**[5], **Joni Vander Bilt**[6], **Judith Saxton**[1], and **Mary Ganguli**[6,7,1]

[1] Department of Neurology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[2] Departments of Psychiatry and Behavioral Sciences and Neurology, University of Miami Miller School of Medicine, Miami, FL, USA

[3] Wien Center for Alzheimer's Disease and Memory Disorders, Mount Sinai Medical Center, Miami Beach, FL, USA

[4] Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[5] Department of Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

[6] Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[7] Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

Abstract

Background—There is increasing interest in identifying novel cognitive paradigms to help detect preclinical dementia. Promising results have been found in clinical settings using the Semantic Interference Test (SIT), a modification of an existing episodic memory test (Fuld Object Memory Evaluation) that exploits vulnerability to semantic interference in Alzheimer's disease. It is not yet known how broadly this work will generalize to the community at large.

Methods—Participants aged ≥65 years from the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) were administered the SIT at study entry. Independent of neuropsychological assessment, participants were rated on the Clinical Dementia Rating (CDR) scale, based on reported loss of cognitively-driven everyday functioning. In individuals free of dementia (CDR <1), the concurrent validity of the SIT was assessed by determining its association with CDR using multiple logistic regression models, with CDR 0 (no dementia) vs. 0.5 (possible dementia) as the outcome and the SIT test variables as predictors.

[*]Correspondence: Beth E. Snitz, PhD, Department of Neurology, University of Pittsburgh, 3471 Fifth Avenue, Suite 802, Pittsburgh, PA 15213, Phone: (international+) 412-692-4820, Fax: (international+) 412-692-4031, snitzbe@upmc.edu.

Conflict of Interest Declaration:
This study was supported by the following grants from the National Institutes of Health: R01 AG023651 and K24 AG022035. The sponsor had no direct role in the conduct and reporting of this study. There are no conflicts of interest to disclose for any of the authors.

Description of authors' roles:
B. Snitz: conceptualization and design, interpretation of results, writing. D. Loewenstein: conceptualization and design, interpretation of results, editing and writing. C-C. Chang: data analysis and interpretation, writing and editing. C-W. Lee: data analysis and interpretation, writing and editing. J. Vander Bilt: supervision of data collection and management, conceptualization and design, editing. J. Saxton: interpretation of results, editing. M. Ganguli: overall project design, obtaining grant support, conceptualization and design, interpretation of results, writing and editing.

Results—Poorer performance on all SIT variables but one was associated with higher CDR reflecting possible dementia (Odds Ratios 2.24 to 4.79). Younger age and female gender also conferred a performance advantage. Years of education and reading ability (a proxy for quality of education) evidenced a very weak association with SIT performance.

Conclusions—The SIT shows promise as a valid, novel measure to identify early preclinical dementia in a community setting. It has potential utility for assessment of persons who may be illiterate or of low education. Finally, we provide normative SIT data stratified by age which may be utilized by clinicians or researchers in future investigations.

Keywords

neuropsychological tests; norms; cognitive aging; Semantic Interference Test; Alzheimer's disease

One of the most challenging tasks in the cognitive assessment of older adults is the differentiation of normal from pathological cognitive aging. Mild cognitive impairment (MCI) with deficits reported in one or more cognitive domains, including episodic memory, executive functions, verbal abilities, visuospatial skills, attention, and perceptual speed is often found to reflect preclinical Alzheimer's disease (AD) and other dementias (Backman *et al.*, 2005; Masur *et al.*, 1994). However, there is growing interest in identifying novel cognitive paradigms that might help detect preclinical dementia even earlier, particularly as new, potentially disease-modifying treatments, appear on the horizon for AD.

In addition to episodic memory, it has been postulated that AD is also associated with altered structure of semantic memory, an individual's concept-based knowledge of the world (Hodges *et al.*, 1992). Buschke et al. (Buschke *et al.*, 1997) has argued that early AD is characterized by specific deficits that prevent effective use of semantic cues. On tests requiring recall of remembered words, mildly impaired AD patients are specifically prone to semantic intrusions that suggest incomplete processing of the target (Loewenstein *et al.*, 1991). Semantic intrusions include substituting the target item for a semantically similar exemplar (e.g., "*lighter*" for "*matches*") or for the superordinate semantic category to which the target belonged (e.g., "*jewelry*" for "*ring*"). These intrusions reflect an underlying deficit in inhibiting the activation of competing semantic exemplars within a general semantic category (e.g., "*objects that start a fire*" in the case of the first example). Therefore the use of an interference paradigm, in which semantically similar objects compete for expression in memory, may further highlight the specific information processing deficits associated with AD. This line of work has shown remarkable potential for distinguishing between individuals with normal cognition and mild dementia in case-control studies of specialty clinical samples of AD patients and research volunteers (Loewenstein *et al.*, 2007; Loewenstein *et al.*, 2004). However, it has yet to be determined how broadly this experience will generalize to dementia in the community at large.

The Semantic Interference Test (SIT) is a selective reminding task that employs two semantically related groups of household objects. It is based on a modification of the Fuld Object Memory Evaluation (OME) (Fuld, 1981) and involves actual common objects as stimuli which are tactually, visually and aurally encoded. Unlike the original OME which had five learning trials, the SIT paradigm presents the initial group of OME objects for three learning trials, followed by presentation of a new group of objects semantically related to the first group (e.g., *cup* is semantically related to *bowl; key* to *lock; playing card* to *domino*), and followed by an immediate recall and then a delayed recall of the initial list of objects. In addition to semantic intrusions from one list to another, this paradigm allows for evaluation of interference effects: proactive interference, in which new learning is inhibited by the competing effects of old learning, and retroactive interference, in which recall of previously learned material is impeded by competing intervening information. Loewenstein and colleagues found that a SIT composite measure of vulnerability to semantic interference was highly sensitive (84.6%) and

specific (96.2%) in differentiating mild AD patients from healthy older adults. Vulnerability to proactive interference, specifically, was most discriminative between patients with mild cognitive impairment (MCI) and healthy control participants (Loewenstein *et al.*, 2004). Further work showed that vulnerability to proactive interference on the SIT was highly predictive of progression to dementia within three years among older adults with MCI, more so than traditional neuropsychological measures of delayed recall (Loewenstein *et al.*, 2007).

Here we report the performance of this novel memory paradigm, which examines vulnerability to semantic interference, in a population-based epidemiologic study of older adults. Specifically, we examined associations between scores the SIT (Loewenstein *et al.*, 2003) and demographic characteristics, hypothesizing that better test performance would be associated with younger age and higher education. Further, we hypothesized that SIT performance would be associated with level of decline in cognitively driven everyday functioning, as independently measured by the Clinical Dementia Rating (CDR) scale (Hughes *et al.*, 1982). Additionally, we provide normative data for the SIT stratified by age level in 5-year bands that can be used by clinician or researchers in future investigations.

Methods

Study area, sampling, and recruitment

The small-town area selected for the study surrounds the confluence of the Monongahela and Youghiogheny rivers, in southwestern Pennsylvania in the USA. The study cohort was named the Monongahela-Youghiogheny Healthy Aging Team (MYHAT). As previously described (Ganguli *et al.*, 2009) the cohort was recruited by age-stratified random sampling from the voter registration lists for the selected towns. Given the history and stability (low rates of in- and out-migration) of the region's elderly residents, it is considered representative of the population. All procedures were approved by the University of Pittsburgh Institutional Review Board. Recruitment criteria were (a) age 65 years or older, (b) living within the selected area, (c) not already in a long-term care institution. Individuals were considered ineligible if they (d) were too ill to participate, (e) had severe vision impairment, (f) had severe hearing impairment, or (g) were incapacitated in decision-making ability. Over the approximately two-year recruitment period, a total of 2036 individuals were recruited.

Assessment (overview)

A single-stage assessment was employed to avoid both delays and potentially non-random attrition between screening and definitive assessment stages (Prince, 2000). The Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975) was administered and scored on the spot, applying a standard correction for age and education (Mungas *et al.*, 1996). Fifty-four individuals scoring < 21/ 30 (age-education corrected) were classified as having moderate to severe cognitive impairment and therefore not part of the target population for the MYHAT study. These individuals were not assessed further. The remaining 1982 participants, who scored ≥ 21 on the age-education corrected MMSE, proceeded to the full assessment, which included several components. Among the neuropsychological tests in the full assessment battery was the Wide Range Achievement Test (3rd edition) Reading subtest (WRAT-3 Reading), used to estimate literacy or academic reading level and as a proxy for quality of education (used in analyses below) (Manly *et al.*, 2002). The remainder of this report is focused on one specific test from the neuropsychological assessment, the SIT, and the Clinical Dementia Rating.

Fuld OME / Semantic Interference Test (SIT)

All participants were first administered the SIT as the first task in the neuropsychological battery. The objects are placed inside opaque black cloth bags before presentation to the

participant, who is first required to identify, by touch alone, the contents of the first bag (Bag A). These are 10 common household objects (*button, scissors, ball, ring, matches, cup, playing card, nail, key, and bottle*). After attempting to identify the objects by touch, the participant is allowed to view them as well; if still unable to name the object by touch or vision, the interviewer then provides the name. This learning trial is followed by a 60 second verbal fluency distracter task and then the participant is asked to recall the 10 objects. Selective reminders are only provided for the unrecalled objects. The testing then alternates between recall trials with selective reminders and 30 second verbal fluency tasks for two additional trials. The sum of the three learning trials for Bag A reflects episodic encoding and retrieval.

Next, the semantic interference paradigm requires the participant to identify, by touch, 10 new common household items (*belt, knife, whistle, bracelet, lighter, bowl, domino, screw-driver, lock, and can*) inside Bag B. As with Bag A objects, after identifying the new Bag B objects by touch, the objects are both visually and tactually presented. If the object cannot be identified by touch or vision, its name is provided by the examiner. Participants then complete a 60 second verbal fluency distracter task, and are then asked to recall Bag B objects (Bag B-Immediate Recall). This recall trial is susceptible to proactive interference (i.e., old learning of the previous Bag A items interferes with new learning of Bag B items). The participant is then asked to recall the Bag A objects (Short-Delay Recall), a recall trial that is vulnerable to retroactive interference (i.e., new learning of Bag B items interferes with retrieval of previously learned information). The Combined Interference Score consists of the sum of Bag B Immediate Recall score (Proactive Interference) and Bag A Short-Delay Recall score (Retroactive Interference). After a 20-min delay, during which non-memory tests in the battery are administered, participants are asked to recall Bag A items (Long-Delay Recall). Intrusions (retrieval of any item other than the to-be-remembered targets) during all learning and recall trials were recorded and summed.

As described in Lowenstein et al. (2003), Bag B objects belonged to the same semantic categories as those in Bag A. They were carefully selected on the basis of a prior study examining the type of intrusive errors made by several hundred AD patients compared to healthy elderly controls (Schram *et al.*, 1995). For example, among AD patients, the most frequently occurring intrusion for *ring* was a bracelet or other type of jewelry; therefore, a bracelet, an exemplar of the category jewelry was selected as a Bag B item. Similarly, the remaining items in Bag B are all exemplars of the categories to which Bag A items belong.

Further scores were derived from SIT performance to evaluate proactive and retroactive interference effects after controlling for memory performance, per se. A Proactive Interference Ratio (PIR) was calculated by dividing the score from Bag B recall by the average recall score of the three learning trials (reflecting episodic encoding and retrieval). A Retroactive Interference Ratio (RIR) was also calculated by dividing Bag A-Short Delay Recall score from the last recall of Bag A, before the introduction of Bag B, to determine any decrements in performance associated with the semantically related set of Bag B objects. Lower PIR scores and RIR scores would indicate greater proactive and retroactive interference, respectively. The Total Interference Ratio (TIR) was computed by summing the PIR and RIR ratios.

Clinical Dementia Rating

Participants were rated on the CDR scale (Hughes *et al.*, 1982; Morris *et al.*, 1988), without reference to the neuropsychological measures. All MYHAT interviewers have undergone CDR training and been certified by the Washington University online training module. Interviewers performed these ratings based on participants' self-reports, informant reports when available, and their own impressions of the participants' functional level, including, e.g., participants' understanding of and adherence to their prescribed medication regimens, knowledge of their own and family information, etc. Although the assessments were conducted by one interviewer,

the CDR ratings were carried out after the visit with review and discussion with at least one other interviewer. The rating was based on an assessment protocol composed of standardized questions, as well as observation, regarding the participant's daily functioning in the six areas of memory, orientation, judgment, home and hobbies, community affairs, and personal care. Each of the six areas was rated on a scale of 0 through 0.5, 1, 2, and 3, and a standard algorithm was used to generate a summary CDR rating of 0 (no dementia), 0.5 (possible dementia), 1.0 (mild dementia), 2.0 (moderate dementia), and 3.0 (severe dementia).

Statistical methods

Because all SIT variables were not normally distributed, to assess the association between each SIT variable and the CDR scores, we first dichotomized each SIT variable based on the 10^{th} percentile. Then, the association was examined using simple logistic regression (unadjusted) and multiple logistic regression (adjusted) models with the CDR global score as the dependent variable and the dichotomized SIT variable as the main independent variable. Age, gender, education and race were the adjusting confounders in the multiple logistic regression models. In these models, age was categorized into three groups: 65–74, 75–84, and ≥85 years old at baseline; educational levels were categorized into three groups: less than high school, high school graduate, and more than high school; and race was dichotomized into white and non-white groups. All interaction terms between the four demographic variables and all SIT variables were examined in the multiple logistic regression models.

Unadjusted association between dichotomous SIT scores and demographic variables as well as the association between dichotomous SIT scores and WRAT-3 Reading were examined using simple logistic regression only with participants with CDR = 0. In addition, Spearman correlation coefficient was used to investigate the rank correlation between each original continuous SIT score and education in years, age in years, and WRAT-3 Reading. Association between CDR global score and each demographic characteristic were assessed by simple logistic regression.

For participants with CDR = 0, the distributions of the SIT variables were assessed by mean, SD, minimum, maximum, 5^{th}, 7^{th}, 10^{th}, 25^{th}, 50^{th} (median), 75^{th}, and 90^{th}, 93^{rd}, and 95^{th} percentiles.

Of the 1982 participants who completed the full baseline assessment, 1959 had either normal cognitive functioning or mild deficits measured by the CDR scale. Among 1959 individuals, only 38 (1.9%) refused any component of the SIT. In the analyses, the sample size was restricted to the 1921 non-demented participants with complete data on all tests. Analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina) and Stata version 9 (StataCorp, College Station, Texas).

Results

The current report restricted to 1921 participants with complete SIT data and CDR global score < 1; of these, the majority (1393) individuals received CDR scores of 0 and 528 individuals received CDR scores of 0.5. Mean age was 77.51 (SD 7.38), with n=668 (34.8%) age 65–74, n=896 (46.6%) age 75–84, and n=357 (18.6%) age 85 years and older. Mean education in years was 12.87 (SD 2.41), with n=259 (13.5%) reporting having less than a high school education, n=868 (45.2%) were high school graduates, and n=794 (41.3%) reported greater than high school education. The number of males was 743 (38.7%) and n=1823 (94.9%) participants were self-reported as "white." The mean MMSE score was 27.04 (SD 2.29) with a range of 17 – 30.

Table 1 presents the summary of unadjusted and adjusted logistic regression models predicting a CDR rating of 0.5 from SIT variables, based on 10^{th} percentile cut-points. The simple logistic regression models show that the unadjusted association between CDR global score and SIT variables were significant for all ($p < 0.001$). The multiple logistic regression models present that all adjusted odds ratios (ORs) of the main predictor were significant except for the Total Interference Ratio. The ORs indicate increased odds of belonging to the CDR 0.5 group with worse test performance. For instance, there is an approximately a three times greater likelihood of receiving a CDR 0.5 rating with poor performance on the Combined Interference measure of Bag A + Bag B Recalls. Of note, the confidence intervals of the measures with significant effects are overlapping, indicating little reliable distinction between the ORs of the test variables.

The multiple logistic regression models only included significant interactions in the final models, and the odds ratios of the main effect were presented in Table 1. Interactions between the test variables and demographic characteristics were significant for the following: OME 3 Trial Recall × Age, PIR × Age, and TIR × Education. With regard to age, for OME 3 trials the association with CDR score was statistically significant in all 3 age groups although the strength of the association varied across age groups ($p \leq 0.001$); PIR was significantly associated with CDR only in those aged 65–74 ($p < 0.0001$). With respect to education, TIR was significantly associated with CDR only in those with at least high school education ($p = 0.01$). There were no interactions of any subtests with gender or race.

Associations between SIT and demographics were examined using simple logistic regression models in a sample of 1336 individuals with CDR=0 and complete data on the variables of interest. Associations between better performance on SIT measures and higher education were mostly significant (≥ HS vs. < HS: ORs from 0.32 to 0.59, all p-values < 0.05 except for SIT Bag A Short Delay Recall and RIR). Positive correlations between SIT performance and WRAT-3 Reading standard scores were small in magnitude with all significant associations (ORs from 0.96 to 0.98, $p < 0.05$) except for SIT Bag B Recall, RIR, and intrusion. SIT performance was more highly associated with younger age (≥ 75 vs. 65–74, ORs from 1.58 to 8.39, all p-values < 0.05). Women outperformed men on OME 3 Trial Recall, Bag B Recall, Bag A Recall, sum of Bag A & Bag B Recall and Bag A Delayed Recall (OR 0.60 to 0.71, $p < 0.05$). In addition, Spearman correlation was used to assess the rank correlation. Correlations between better performance on SIT measures and higher years of education were mostly significant (all p-values < 0.05 except for SIT Bag A Short Delay Recall, SIT Bag A Delayed Recall, and RIR) but uniformly small in magnitude (r from 0.06 to 0.11). Positive correlations between SIT performance and WRAT-3 Reading standard scores were similarly small in magnitude, with the following associations significant ($p < 0.01$): OME 3 Trial Recall ($r = 0.14$), SIT Bag B Recall ($r = 0.13$), SIT Bag A Short Delay Recall ($r = 0.09$), SIT Bag A and Bag B Recalls ($r = 0.13$) and SIT Bag A Delayed Recall ($r = 0.08$). SIT performance was more highly associated with younger age (r from −0.10 to −0.32, all p-values < 0.001).

Regarding associations between demographic characteristics and CDR score, participants with CDR 0.5 ($n = 528$) were older (75–84 vs. 65–74 and ≥ 85 vs. 65–74: OR (95% CI of OR) = 1.53 (1.21, 1.95) and 2.73 (2.05, 3.62), had less education (= HS vs < HS and > HS vs < HS: OR (95% CI of OR) = 0.57 (0.43, 0.77) and 0.55 (0.41, 0.74)), were more likely to be male (female vs. male: OR (95% CI of OR) = 0.72 (0.59, 0.89)) and more likely to be non-white (white vs. non-white: OR (95% CI of OR) = 0.53 (0.35, 0.80)) compared to participants with CDR 0.

Tables 2a–f present normative distributions of selected SIT variables within CDR = 0 participants in age bands of five years, from 65 – 99 years old.

Discussion

This study examined the distribution characteristics of a novel testing paradigm evaluating semantic interference and episodic memory in a large, population-based cohort of non-demented older adults. To our knowledge, this is the first description of use of the semantic interference model of assessing memory at the population level. Our results demonstrate concurrent validity of the test. Almost all specific measures of the SIT were strongly associated with independently rated CDR score; i.e., they significantly differentiated participants with rated normal functioning (CDR 0 global score) from those with mild cognitive difficulties affecting daily functioning (CDR 0.5). In addition, SIT indices were minimally affected by degree of educational attainment or estimated premorbid function. Better SIT performance was associated with younger age and being female, but with age showing a much stronger effect than gender. These associations are in line with other memory tests (Mitrushina *et al.*, 2005). Normative data stratified by age are provided.

The original Fuld OME (Fuld, 1981) was developed to assess several aspects of learning and retrieval in older adults, based on the selective reminding method introduced by Buschke (1973). The modification of the Fuld OME and addition of the SIT by Lowenstein et al. (2003) added the component of semantic interference to the assessment of episodic memory, with the goal of improved prediction of incipient dementia. The SIT capitalizes on the increased vulnerability observed in AD patients to competing information in the environment during learning (interference). In effect, the SIT functions as a “stress test” for this vulnerability by imposing an additional list of semantically-related objects to be learned, and this leads to depressed subsequent recall and recall errors (intrusions).

The SIT has many potential advantages. First, its conceptual novelty expands our current understanding of memory and aging by focusing on the dimension of relative vulnerability to semantic interference. It has been previously shown to discriminate between healthy older volunteers and patients with AD and mild cognitive impairment in clinical settings; we have now shown that it is also associated with independently scored rating of cognitively driven daily functioning (CDR) in a large, representative population-based cohort. Second, we have also shown that this relatively complex clinic-based test with non-standard stimuli, is feasible to administer in a large-scale epidemiological study in the homes of older participants in small towns. Notably, the refusal rate of any component of the SIT was very low (less than 2%). Third, the test has appeal related to its novel presentation, using objects inside mysterious black bags which individuals have to touch, see, name, and remember; a perhaps welcome alternative to the standard paper and pencil tasks which older adults may view as boring or even threatening in their similarity to school “tests.” Fourth, the SIT has potential utility for assessment of persons who may be illiterate or of low educational attainment. In contrast, performance on standard neuropsychological measures of verbal learning and memory tend to show relatively strong associations with educational attainment in healthy older adults (Mitrushina *et al.*, 2005). The SIT requires no reading, encoding of items is multi-modal (tactile, visual, and aural), and the objects to be encoded are commonly encountered in daily life. As we report currently, the influence of educational attainment and of reading ability (suggested as a proxy for quality of education, Manly *et al.*, 2002), on SIT performance is insufficiently large to be clinically significant. By comparison, Delis et al. (2000) reported a correlation of 0.46 between total recall trials on the California Verbal Learning Test – II, one of the more commonly used verbal memory tests, and vocabulary scores. Finally, the test conditions of the SIT are such that no translation and back-translation are required for adapting to different linguistic/cultural groups.

Comparison of the SIT scores from our population cohort (CDR 0) to those from 98 cognitively screened, healthy memory clinic controls reported in Lowenstein et al. (2004) reveals that the means and standard deviations are remarkably similar for all test variables. This further

supports the premise that the SIT transfers well from clinic to 'real-world' settings and is relatively resistant to the influence of different population characteristics (e.g., educational/cultural background, screened vs. unscreened health history, propensity to volunteer for research studies, etc.).

Strengths of the present study include the large size and representativeness of the cohort. The study also has some limitations. Since by design the MYHAT cohort excludes individuals with moderate to severe cognitive impairment, we cannot provide data on dementia or dementia subtypes such as AD. Since the data are cross-sectional at this stage, we cannot yet report whether SIT performance will predict future development of dementia. Its population-based design precludes the detailed clinical assessments of individuals and reliable informants that are standard in specialized memory disorder centers; however, those studies in turn suffer from selection bias. Finally, we observed no statistically reliable differences among specific semantic interference measures in the strength of their associations with CDR ratings in the present study. Nevertheless, it is perhaps suggestive that the variable with the highest OR was the Proactive Interference Ratio, as vulnerability to proactive interference was highly predictive of progression to dementia within three years among older adults with MCI in the Lowenstein et al. (2007) study. In clinical settings, difficulties with semantic interference can be observed in the absence of initial list learning performance. As such, the potential predictive validity of measures of semantic interference as measures of early cognitive dysfunction and progression of decline can only be addressed by the longitudinal follow-up of our current cohort.

In sum, we present initial validity data in a population-based cohort for the SIT, a novel paradigm evaluating semantic interference with the aim of increased sensitivity for mild cognitive changes associated with early dementia. Future analyses will investigate the utility of the SIT and its specific semantic interference measures in discriminating between individuals with normal cognition and MCI in a population-based setting, and its predictive validity for progression to dementia.

References

Backman L, Jones S, Berger AK, Laukka EJ, Small BJ. Cognitive impairment in preclinical Alzheimer's disease: a meta-analysis. Neuropsychology 2005;19:520–531. [PubMed: 16060827]

Buschke H. Selective reminding for analysis of memory and learning. Journal of Verbal Learning & Verbal Behavior 1973 Oct;12(5):543–550. 1973.

Buschke H, Sliwinski MJ, Kuslansky G, Lipton RB. Diagnosis of early dementia by the Double Memory Test: encoding specificity improves diagnostic sensitivity and specificity. Neurology 1997;48:989–997. [PubMed: 9109889]

Delis, DC.; Kramer, JH.; Kaplan, E.; Ober, BA. California Verbal Learning Test -II. San Antionio, TX: Psychological Corporation; 2000.

Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research 1975;12:189–198. [PubMed: 1202204]

Fuld, PA. Fuld Object-Memory Evaluation. Woodale, IL: Stoelting Company; 1981.

Ganguli M, Snitz B, Vander Bilt J, Chang C-CH. How much do depressive symptoms affect cognition at the population level ? The Monongahela-Youghiogheny Healthy Aging Team (MYHAT) study. Internal Journal of Geriatric Psychiatry. 2009

Hodges JR, Salmon DP, Butters N. Semantic memory impairment in Alzheimer's disease: failure of access or degraded knowledge? Neuropsychologia 1992;30:301–314. [PubMed: 1603295]

Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. British Journal of Psychiatry 1982;140:566–572. [PubMed: 7104545]

Loewenstein DA, Acevedo A, Agron J, Duara R. Vulnerability to proactive semantic interference and progression to dementia among older adults with mild cognitive impairment. Dementia and Geriatric Cognitive Disorders 2007;24:363–368. [PubMed: 17911981]

Loewenstein DA, Acevedo A, Luis C, Crum T, Barker WW, Duara R. Semantic interference deficits and the detection of mild Alzheimer's disease and mild cognitive impairment without dementia. Journal of the International Neuropsychological Society 2004;10:91–100. [PubMed: 14751011]

Loewenstein DA, et al. Semantic interference in mild Alzheimer disease: preliminary findings. American Journal of Geriatric Psychiatry 2003;11:252–255. [PubMed: 12611756]

Loewenstein DA, et al. The occurrence of different intrusive errors in patients with Alzheimer's disease, multiple cerebral infarctions, and major depression. Brain and Cognition 1991;16:104–117. [PubMed: 1854466]

Manly JJ, Jacobs DM, Touradji P, Small SA, Stern Y. Reading level attenuates differences in neuropsychological test performance between African American and White elders. Journal of the International Neuropsychological Society 2002;8:341–348. [erratum appears in J Int Neuropsychol Soc 2002 May;8(4):605]. [PubMed: 11939693]

Masur DM, Sliwinski M, Lipton RB, Blau AD, Crystal HA. Neuropsychological prediction of dementia and the absence of dementia in healthy elderly persons. Neurology 1994;44:1427–1432. [see comment]. [PubMed: 8058143]

Mitrushina, M.; Boone, KB.; Razani, J.; D'Elia, LF. Handbook of Normative Data for Neuropsychological Assessment. New York: Oxford University Press; 2005.

Morris JC, McKeel DW Jr, Fulling K, Torack RM, Berg L. Validation of clinical diagnostic criteria for Alzheimer's disease. Annals of Neurology 1988;24:17–22. [PubMed: 3415196]

Mungas D, Marshall SC, Weldon M, Haan M, Reed BR. Age and education correction of Mini-Mental State Examination for English and Spanish-speaking elderly. Neurology 1996;46:700–706. [PubMed: 8618670]

Prince M. Methodological issues for population-based research into dementia in developing countries. A position paper from the 10/66 Dementia Research Group. International Journal of Geriatric Psychiatry 2000;15:21–30. [PubMed: 10637401]

Schram L, Rubert M, Lowewenstein DA. A qualitative analyis of intrusive errors in Alzheimer's disease. Archives of Clinical Neuropsychology 1995;10:255–263. [PubMed: 14588692]

Table 1

Associations of OME/SIT test variables with Clinical Dementia Rating (N=1921):

	Unadjusted				Adjusted			
Test	**OR**	**95% CI for OR**		**P Value**	**OR**	**95% CI for OR**		**P Value**
OME 3 Trial Recall ≤ 17	4.60	3.49	6.05	<0.001	3.72	1.78	7.80	< 0.001
SIT Bag B Recall ≤ 4	3.10	2.42	3.96	<0.001	2.55	1.97	3.29	<0.001
SIT Bag A Short Delay Recall ≤ 2	3.08	2.35	4.03	<0.001	2.71	2.05	3.57	<0.001
SIT Bag A + Bag B Recalls ≤ 7	3.71	2.85	4.83	<0.001	3.10	2.36	4.08	<0.001
SIT Bag A Delayed Recall ≤ 4	3.97	3.02	5.22	<0.001	3.33	2.51	4.40	<0.001
Proactive Interference Ratio ≤ 0.572	2.06	1.53	2.79	<0.001	4.79	2.26	10.16	<0.001
Retroactive Interference Ratio ≤ 0.286	2.54	1.89	3.40	<0.001	2.29	1.69	3.09	<0.001
Total Interference Ratio ≤ 1.028	2.34	1.73	3.17	<0.001	0.95	0.48	1.87	0.880
Intrusions ≥ 3	2.64	2.00	3.48	<0.001	2.25	1.69	2.99	<0.001

Note.

Multiple logistic regression models with CDR=0.5 as outcome and OME/SIT variable as predictor, adjusted for age, education, gender, and race.

Cutoffs based on 10^{th} percentile of total distribution of the OME/SIT variables.

Non-white race, older age, and male gender are significantly associated with 0.5 CDR global score.

Significant interactions are Fuld OME 3 trials × Age, PIR × Age, and TIR × Education.

Int Psychogeriatr. Author manuscript; available in PMC 2011 August 1.

Table 2

Fuld OME and SIT score distributions among participants with CDR = 0

Table 2a. Age 65 – 69; CDR = 0 (n=308)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
OME 3 Trials (encoding)	24.3	2.9	15	19	20	20	22	25	26	28	28	28	30
SIT Bag B Immediate Recall (proactive interference)	7.2	1.5	2	5	5	5	6	7	8	9	9	9	10
SIT Bag A Short-delay Recall (retroactive interference)	6.1	2.0	0	2	3	3	5	6	7.5	8	9	9	10
SIT Bag A + Bag B Immediate Recall (combined interference)	13.3	2.7	6	9	9	9	11	13.5	15	17	17	18	20
SIT Bag A Delayed Recall	7.8	1.7	0	5	5	6	7	8	9	10	10	10	10
Proactive Interference Ratio	0.9	0.2	0.3	0.6	0.6	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.4
Retroactive Interference Ratio	0.7	0.2	0.0	0.3	0.4	0.4	0.6	0.7	0.9	1.0	1.0	1.0	1.3

Table 2b. Age 70 –74; CDR =0 (n=226)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
OME 3 Trials (encoding)	23.6	3.2	14	18	18	19	22	24	26	27	28	28	29
SIT Bag B Immediate Recall (proactive interference)	6.8	1.5	2	4	5	5	6	7	8	9	9	9	10
SIT Bag A Short-delay Recall (retroactive interference)	5.9	2.2	0	2	2	3	5	6	7	9	9	9	10
SIT Bag A + Bag B Immediate Recall (combined interference)	12.7	3.0	5	7	7	8	11	13	15	17	17	17	20
SIT Bag A Delayed Recall	7.4	1.9	0	4	4	5	7	8	9	9	10	10	10
Proactive Interference Ratio	0.9	0.2	0.3	0.6	0.7	0.7	0.8	0.9	1.0	1.1	1.1	1.1	1.3
Retroactive Interference Ratio	0.7	0.2	0.0	0.3	0.3	0.4	0.6	0.7	0.9	1.0	1.0	1.1	1.3

Table 2c. Age 75 –79; CDR = 0 (n=304)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
Fuld OME 3 Trials (encoding)	22.9	3.4	9	17	18	18	21	23	25	27	27	28	30
SIT Bag B Immediate Recall (proactive interference)	6.5	1.7	0	4	4	4	5	7	8	9	9	9	10
SIT Bag A Short-delay Recall (retroactive interference)	5.6	2.1	0	2	2	3	4	6	7	8	8	9	10

Table 2c. Age 75 –79; CDR = 0 (n=304)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
SIT Bag A + Bag B Immediate Recall (combined interference)	12.1	2.9	0	7	8	9	10	12.5	14	16	16	16	20
SIT Bag A Delayed Recall	7.3	1.7	0	4	5	5	6	7	9	9	10	10	10
Proactive Interference Ratio	0.9	0.2	0.0	0.5	0.5	0.6	0.8	0.9	1.0	1.1	1.1	1.2	1.7
Retroactive Interference Ratio	0.7	0.3	0.0	0.2	0.3	0.3	0.6	0.7	0.9	1.0	1.0	1.1	1.4

Table 2d. Age 80 – 84; CDR = 0 (n=343)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
OME 3 Trials (encoding)	22.3	3.6	7	16	17	18	20	23	25	26	27	28	30
SIT Bag B Immediate Recall (proactive interference)	6.1	1.7	0	3	3	4	5	6	7	8	8	9	10
SIT Bag A Short-delay Recall (retroactive interference)	5.2	2.1	0	1	2	2	4	5	7	8	8	8	10
SIT Bag A + Bag B Immediate Recall (combined interference)	11.3	3.1	0	6	7	7	9	11	13	15	16	16	18
SIT Bag A Delayed Recall	6.9	1.9	0	3	4	5	6	7	8	9	9	10	10
Proactive Interference Ratio	0.8	0.2	0.0	0.5	0.5	0.5	0.7	0.8	1.0	1.1	1.1	1.2	1.4
Retroactive Interference Ratio	0.7	0.3	0.0	0.2	0.3	0.3	0.5	0.7	0.8	1.0	1.0	1.0	1.3

Table 2e. Age 85–89; CDR = 0 (n=170)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
OME 3 Trials (encoding)	21.2	3.4	12	15	15	16	19	21	24	25	26	26	29
SIT Bag B Immediate Recall (proactive interference)	5.7	1.7	1	3	3	3.5	5	6	7	8	8	8	10
SIT Bag A Short-delay Recall (retroactive interference)	4.9	2	0	1	1	2	4	5	6	7	7	8	10
SIT Bag A + Bag B Immediate Recall (combined interference)	10.6	3.2	2	5	6	6	9	11	13	15	15	16	18
SIT Bag A Delayed Recall	6.4	1.9	0	4	4	4	5	7	8	9	9	9	10
Proactive Interference Ratio	0.8	0.2	0.2	0.5	0.5	0.5	0.7	0.8	1	1.1	1.1	1.2	1.4
Retroactive Interference Ratio	0.6	0.3	0	0.1	0.2	0.3	0.5	0.7	0.8	1	1	1	1.3

Table 2f. Age 90 – 99; CDR = 0 (n = 42)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
OME 3 Trials (encoding)	20.1	3.4	12	14	14	15	18	20	23	24	25	25	26

Table 2f. Age 90 – 99; CDR = 0 (n = 42)

Variable	Mean	SD	Min	5th %tile	7th %tile	10th %tile	25th %tile	50th %tile	75th %tile	90th %tile	93th %tile	95th %tile	Max
SIT Bag B Immediate Recall (proactive interference)	5.2	2.1	0	1	1	3	4	5	6	8	8	8	10
SIT Bag A Short-delay Recall (retroactive interference)	4.4	2	0	0	0	1	3	5	6	7	7	7	7
SIT Bag A + Bag B Immediate Recall (combined interference)	9.5	3.4	3	4	4	4	7	10	12	13	14	14	16
SIT Bag A Delayed Recall	5.9	1.8	1	3	3	4	5	6	7	8	8	8	10
Proactive Interference Ratio	0.8	0.3	0	0.3	0.3	0.5	0.7	0.8	0.9	1.1	1.2	1.2	1.3
Retroactive Interference Ratio	0.6	0.3	0	0	0	0.2	0.4	0.6	0.9	1	1	1	1.2