**Method**

**Participants**

The Memory and Aging Project (MAP) is a longitudinal study that began in 1997 with an ongoing enrollment (Bennett et al., 2005). The study was approved by the Institutional Review Board of Rush University Medical Center and funded by the National Institute on Aging. The broad aim of the study was to “identify factors associated with the maintenance of cognitive health despite the accumulation of AD and other pathology” (Bennett et al., 2012). Participant recruitment was focused on retirement communities in northeastern Illinois. Continuous care retirement communities, ranging from independent living to unskilled and skilled nursing care, were specifically targeted because these types of facilities enabled better rates of follow up. Frail elderly who might otherwise be unable to participate could still be visited for assessment and facility staff could be contact persons for participants and inform study coordinators if participants became ill or moved (Bennett et al., 2005). Participants were also encouraged to speak to family members about their involvement in the study. Because residents of continuing care facilities are more likely to be white and affluent, an effort was made to include residents of subsidized retirement homes, and recruit from local churches and social service agencies to ensure low-income and minority elderly were included. Individuals were required to be free from dementia at study enrollment, to participate in annual clinical evaluations, and agree to donation of their spinal cord, muscle and nerve tissues, and brain at the time of death. There were no other exclusion criteria and all clinical evaluations were all conducted as home visits. This enabled a more inclusive study sample where common conditions and multiple comorbidities are represented and minimized participant drop out due to health.

At the time of this analysis, 1290 women and 470 men had completed some portion of the MAP protocol. However, individuals who developed dementia over the course of the study period were excluded from this analysis. This resulted in a sample of 1,362 participants, 86% of whom identified as non-hispanic white, 7% as having Spanish, Hispanic, or Latino origin, 6% as Black or African-American, and the remaining 1% included individuals who identified as Native American, Indian, Asian or Pacific Islander and one individual for whom information on race/ethnicity was not available.

**Measures**

**Demographics**

Education and race and ethnicity were gathered from what was reported in the 1990 U.S. Census. Participants were additionally asked if they considered themselves of Spanish, Hispanic or Latino origin. Age was calculated from date of birth.

**Cognitive Performance Tests**

*Mental Status*

The Mini-Mental State Exam (MMSE) is a commonly used screening measure for mental status (Folstein, Folstein, & McHugh, 1975). Participants respond to items assessing orientation to time and place, attention, memory, working memory, and object naming.

Judgment of line orientation is a 15-item test of visual perception although considered here to be mental status because cognitively intact individuals typically perform near ceiling (Benton, Varney, & deS Hamsher, 1978). The task is for participants to judge the angle subtended by two lines by matching the item line angle to samples.

*Memory*

Seven tests of memory performance were administered. Logical Memory Ia and Logical Memory II are measures of immediate and delayed memory, respectively, from the Wechsler Memory Scale-Revised (Wechsler, 1987). For Logical Memory Ia the participant is read a short story and then asked upon conclusion of the story to recall as many details from as possible. For Logical Memory IIa participants are asked 30 minutes later to recall as many details of that same story as they can from memory. For both Logical Memory Ia and IIa performance is measured as the number of details recalled, with a possible score range of 0-25 for each.

Participants also completed a second story memory task, the East Boston Memory Test, from the East Boston studies of cognitive function (Albert et al., 1991; Wilson et al., 2002). A three sentence story is read to the participant and they are asked to recall as much of the story as possible for an immediate story recall score. Three minutes later, during which distracter tasks are completed, they are asked to recall the story again. The number of details recalled after the 3 minutes is the delayed story recall score. Both the immediate and delayed story recall scores have a possible range of 0-12.

The Word List Memory test measure from the CERAD set of neuropsychological performance tests was given (Morris et al., 1989). Participants are presented with a 10-word list and asked to immediately recall as many words as they could; they were given three trials with the words in a different order for each trial. The total number of words recalled out of 30 is the Word List Immediate recall score. A few minutes later the participant is asked to recall as many of the words as they can with the total number of words (out of 10) considered the Word List Delayed recall score. For Word List Recognition the participant must pick out each of the ten words shown previously from a set of four words. Performance is measured as the number of words correctly recognized (0-10).

*Language*

Complex Ideational Material is a test of verbal comprehension from the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1972). The test consists of eight questions to which the participant must answer either yes or no with one point given for each correct answer (range 0-8).

The Boston Naming Test is a measure of confrontation naming in which participants are shown line drawings of objects and asked to give the name (Kaplan, Goodglass, Weintraub, Segal, & van Loon-Vervoorn, 2001). The 15-item version from the CERAD neuropsychological test battery was given for a range of possible scores of 0-15 (Morris et al., 1989).

Category fluency is verbal fluency measure where participants were asked to generate as many words as possible belonging to a particular category in 1 minute. Participants are given two categories animals and fruits/vegetables. The sum of the total number of unique animal names and unique fruits/vegetables generated is the fluency score (Morris et al., 1989; Wilson et al., 2002).

*Executive Function*

Digits backwards is from the Digits Span subtest of Wechsler Memory Scale-Revised (Wechsler, 1987). Digits backwards is a measure working memory. Participants listen to a series of numbers of increasing length from 2 to 7 and then are asked to repeat the numbers backwards. A point is given for each number series correctly given for a range of 0-12.

Digit ordering is a working memory task where participants hear a series of numbers starting with 2 digits and increasing to 8 (Cooper & Sagar, 1993; Wilson et al., 2002). Participants are asked to repeat the series, in order, from the smallest number to the largest number. Each series is scored 0 or 1 for a possible range of 0 to 14.

*Attention*

Digits Span Forward is measure of attention from the Wechsler Memory Scale-Revised where participants listen to a series of numbers and are asked to repeat back the numbers just as they heard them (Wechsler, 1987). The number series length starts at two and increases to seven. Participants receive a point for each correctly repeated string for a possible score range of 0-12.

*Processing speed*

Symbol Digit Modalities Test was given as a measure of processing speed (Smith, 1984). Participants were shown a key of numbers from 1 to 9 and corresponding abstract symbols. They are then asked to call out the numbers that match the symbols shown one at a time as quickly as possible before the 90 second time limit is up.

Number Comparison was also given as a measure of processing speed (Ekstrom, French, Harman, & Dermen, 1976; Wilson et al., 2002). Participants are shown 48 pairs of numbers some of which are exactly the same and others that are different. The task is to judge whether number pairs are the same or different. Each response receives a score of 1 if correct. The total score is the sum of correct items minus the number of wrong answers including refused answers or those left blank for a possible score range of 0 to 48.

*Reasoning*

Standard progressive matrices is a 16-item test of reasoning (Raven, Court, & Raven, 1992). Participants are shown images that form a pattern with one element missing. The task is to choose the piece from a number of distracter options that completes the pattern.

*Semantic knowledge*

National Adult Reading Test is considered a test of semantic memory (Wilson et al., 2002). Participants are asked to read a list of words that increase in difficulty with the total score as the number of words correctly pronounced.

**Physical Functioning Measures**

*Pulmonary function*

Pulmonary function was tested using a hand-held spirometry (MicroPlus Spirometer MS03, MicroMedical Ltd.) which gives measures of forced expiratory volume (liters in one second), forced vital capacity (liters), and peak expiratory flow (liters/second). This device has been validated to American Thoracic Society standards and has been previously used in large epidemiological studies of respiratory function (Bennett et al., 2005). Measures of maximal inspiratory pressure (cm H2O) and maximal expiratory pressure (cm H2O) were taken using a hand-held device containing a pressure-sensitive transducer (MicroMouth Pressure Meter MP01; MicroMedical Ltd.). These are measures of respiratory muscle strength.

*Grip strength*

Grip strength was measured using the Jamar hydraulic hand dynamometer (Lafayette Instrument, Lafayette, Ind., USA) (Bennett et al., 2005; Buchman, Wilson, Bienias, & Bennett, 2005). Two trials of grip strength were obtained for each hand. A composite measure of grip strength was calculated from the average of the four trials.

*Walking Speed*

Gait speed was measured as the amount of time taken to walk 8 feet. Participants were instructed to walk at a normal pace and given two trials (Bennett et al., 2005).

**Covariates**

Self- report information about various health conditions was gathered via a structured questionnaire. Participants were asked if they had ever been told by a doctor, nurse or therapist that they have had a heart attack or coronary, coronary thrombosis, coronary occlusion, or myocardial infarction during the baseline interview and then asked if any of these events had occurred since the last assessment at subsequent interview. A score of 0 was assigned if none were ever reported and 1 if the participant ever responded yes to the question. Participants were asked about their history of smoking at the baseline interview as part of a structured questionnaire. Values were assigned from 0 (never smoked), 1 (former smoker), or 2 (current smoker). A diagnosis of diabetes was based on self-report and medication use (e.g., insulin). Participant’s height was measured (meters) as part of the baseline clinical examination.

*Dementia diagnosis*

Diagnoses of dementia and AD were made on the basis of all available information from clinical evaluation, self-report, and medication review following the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders association (NINCDS/ADRDA) (Bennett et al., 2005; McKhann et al., 1984). The diagnosis of vascular dementia was made following the National Institute of Neurological Disorders and Stroke/Association Internationale pour la Rechere et l’Enseignement en Neurosciences (NINDS/AIREN), although brain scans were not available (Román et al., 1993). A diagnosis of dementia with Lewy Bodies was adapted from the Report of the Consortium on DLB International Workshop (Bennett et al., 2005; McKeith, Perry, & Perry, 1999). A three step diagnostic process was followed. A computer algorithm assigned an education-adjusted impairment rating on the basis of 11 tests identified as commonly used in diagnosing AD. Then a board-certified clinical neuropsychologist reviewed the results of all of the cognitive tests, the computer-generated impairment rating, and other relevant information including education, occupation, sensory and motor deficits, and effort and subsequently made a clinical judgment about whether a diagnosis of cognitive impairment was appropriate. As a final step, participants were evaluation by a physician experienced in the evaluation of older persons for suspected dementia. A diagnosis of mild cognitive impairment was also made for individuals who the neuropsychologist judged to have cognitive impairment but did not meet accepted criteria for dementia by the clinician. Individuals not meeting criteria for dementia or mild cognitive impairment were categorized as having no cognitive impairment (Bennett et al., 2005) (Bennett et al., 2005). Other diagnoses included Parkinson’s disease and parkinsonism which was made according to clinical criteria put forth by the Core Assessment Program for Intracerebral Transplantation (CAPIT) (Langston et al., 1992).

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