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Social support and verbal interaction are differentially associated with cognitive function in midlife and older age

Megan L. Zuelsdorff, Ph.D.[3,6], **Rebecca L. Koscik, Ph.D.**[2,6], **Ozioma C. Okonkwo, Ph.D.**[2,3,4,6], **Paul E. Peppard, Ph.D.**[1,6], **Bruce P. Hermann, Ph.D.**[2,3,5,6], **Mark A. Sager, M.D.**[2,6], **Sterling C. Johnson, Ph.D.**[2,3,4,6], and **Corinne D. Engelman, Ph.D.**[1,2,3,6]

[1]Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, 610 Walnut St., Madison, WI 53726

[2]Wisconsin Alzheimer's Institute, University of Wisconsin School of Medicine and Public Health, 610 Walnut St., Madison, WI 53726

[3]Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave., Madison, WI 53792

[4]Geriatric Research Education and Clinical Center, William S. Middleton Memorial VA Hospital, 2500 Overlook Ter., Madison, WI 53705

[5]Department of Neurology, University of Wisconsin School of Medicine and Public Health, 1685 Highland Ave., Madison, WI 53705

[6]University of Wisconsin – Madison, Madison, WI 53706

Abstract

Social engagement is associated with healthy aging and preserved cognition. Two dimensions of engagement, verbal interactions and perceived support, likely impact cognition via distinct mechanistic pathways. We explored the cognitive benefit of each construct among enrollees (N=1,052, mean age=60.2 years) in the Wisconsin Registry for Alzheimer's Prevention (WRAP) study, who provide neuropsychological and sociobehavioral data at two-year intervals. Outcomes included six cognitive factor scores representing key domains of executive function and memory. Key predictors included self-reported perceived social support and weekly verbal interaction. Results indicated that after adjusting for lifestyle covariates, social support was positively associated with Speed and Flexibility, and that verbal interactions were associated with Verbal Learning and Memory. These findings suggest that support, which may buffer stress, and verbal interaction, an accessible, aging-friendly form of environmental enrichment, are uniquely

Corresponding Author: Megan Zuelsdorff, PhD, University of Wisconsin School of Medicine and Public Health, 610 Walnut St., 1007D WARF, Madison, WI 53726, mlzuelsd@wisc.edu.

Co-Author Information

Rebecca E. Koscik, PhD, 608-262-6953, rekoscik@wisc.edu

Ozioma C. Okonkwo, PhD, 608-265-4479, ozioma@medicine.wisc.edu

Paul E. Peppard, PhD, 608-262-2680, ppeppard@wisc.edu

Bruce P. Hermann, PhD, 608-263-5430, hermann@neurology.wisc.edu

Sterling C. Johnson, PhD, 608-262-9549, scj@medicine.wisc.edu

Corinne Engelman, PhD, 608-265-5491, corinne.engelman@wisc.edu

beneficial. Both are integral in the design of clinical and community interventions and programs that promote successful aging.

Keywords

Social networks; social activity; environmental enrichment; cognition

Introduction

Increasing prevalence of age-related cognitive dysfunction creates societal and individual burden; accordingly, much research has focused on risk factors for Alzheimer's disease (AD) and cognitive aging. However, consensus on truly modifiable risk or protective factors is elusive and there are still gaps in our knowledge, particularly concerning sociobehavioral ameliorative factors such as social engagement. Social engagement across the lifespan may be associated with better cognitive function and reduced risk for AD (Barnes, Mendes de Leon, Wilson, Bienias, & Evans, 2004; Bennett, Schneider, Tang, Arnold, & Wilson, 2006; Glei et al., 2005; James, Wilson, Barnes, & Bennett, 2011; Kuiper et al., 2015; Kuiper et al., 2016; Lee et al., 2007; Lee et al., 2013; Litwin & Stoeckel, 2016; Seeman, Lusignolo, Albert, & Berkman, 2001; Tomioka, Kurumatani, & Hosoi, 2016; Wang et al., 2013), but the mechanisms underlying this relationship are not well documented. Here, we consider two dimensions of the engagement construct, *social support* and *verbal interaction*; both may, through distinct pathways, protect cognitive health. Some studies of social networks and participation have explained the relationship through models of stress and coping. According to this psychologically and biologically plausible explanation, social support provides a "buffer" for stressful events (Aslund, Larm, Starrin, & Nilsson, 2014; Cohen & Wills, 1985; Paykel, 1994; Schoevers et al., 2000) and mitigates cognitively detrimental effects of stress such as inflammation (Kiecolt-Glaser et al., 2005; Kiecolt-Glaser et al., 2003; Lutgendorf et al., 1999; Miller, Rohleder, & Cole, 2009; Rohleder, 2014; Steptoe et al., 2003) and depressive symptomatology (Dautovich, Dzierzewski, & Gum, 2014; Dean, Kolody, & Wood, 1990; Glass, Kasl, & Berkman, 1997; Kahana, Kelley-Moore, & Kahana, 2012; Virtanen et al., 2015). Others have suggested an additional role for social interactions in stimulating brain networks (Barnes et al., 2004; Bassuk, Glass, & Berkman, 1999; Bennett et al., 2006). If this is true, conversational stimulation as a form of environmental enrichment benefits cognitive health via mechanisms, such as neurogenesis, that are conceptually and biologically distinct from stress-and-coping processes. However, few studies have attempted to *methodologically* explore this enrichment pathway (Hultsch, Hertzog, Small, & Dixon, 1999; James et al., 2012; Seeman et al., 2011; Ybarra et al., 2008; Ybarra & Winkielman, 2012). We focus here on subclinical levels of cognitive dysfunction during midlife and older age. Such research is relevant and useful in considering both healthy and ailing older populations, as maintenance and protection of cognitive ability at any age is desirable. Self-reported quality of life is higher if cognitive abilities remain intact (Missotten et al., 2008; Pan et al., 2015; Teng, Tassniyom, & Lu, 2012). Further, neuropathological processes responsible for eventual clinical presentation of AD are implicated in milder cognitive changes across the lifespan (Doherty et al., 2015; Salthouse, 2009). Prevention or delay of sublinical changes, therefore, is likely to delay AD onset as well.

Using data from the Wisconsin Registry for Alzheimer's Prevention (WRAP), we examined relationships between perceived social support, quantity of verbal interaction, and cognition. We hypothesized, based on theorized benefits of stress buffering and environmental enrichment, that greater levels of both perceived support and reported verbal interaction would be independently associated with better cognitive performance.

Design and Methods

Participants

Data were drawn from WRAP, a longitudinal study of cognitive function in adults enriched for a parental history of AD (Sager, Hermann, & La Rue, 2005). The original WRAP study design is described in detail elsewhere (La Rue et al., 2008). Briefly, the study is comprised of two subsamples: a parental history-positive and a parental history-negative group. Participants in the parental history-positive group, representing two-thirds of the total WRAP sample, have at least one biological parent with dementia due to AD. This was determined by review of medical records of the parent, including in some cases autopsy records, or by administering a dementia questionnaire to the adult child. Many in WRAP were recruited while accompanying a parent to an evaluative visit in a University of Wisconsin-Madison or satellite Memory Assessment Clinic. Others, including most parental history-negative participants, learned of the study via statewide educational presentations or word of mouth. The parental history-negative group consists of persons who do not have a first degree relative diagnosed with AD; to be eligible, they must have a mother who survived to age 75 and a father who survived to age 70. Most participants were between the age of 40 and 65 at enrollment, are English-speaking, and were cognitively intact at that time as determined by their scores on neuropsychological testing at the first study visit. Baseline enrollment began in late 2001 and is ongoing, with recent efforts targeted toward increasing the ethnic diversity of the sample. Participants come in approximately every two years for a full study visit. Due to the rolling enrollment design of WRAP, the number of evaluations (and accompanying data) for each participant varies depending on when they enrolled. The WRAP protocol for Visit 1 does not include social data; social engagement and other lifestyle questionnaires are currently completed by participants at Visit 2 and all subsequent visits. A novel verbal interaction questionnaire (Zuelsdorff et al., 2016) was introduced as a complement to the WRAP lifestyle measures in 2010.

Data for the current study thus came from Visits 2, 3, and 4, and only participants with complete social support and verbal interaction data from at least one of those visits were included in the analysis (N=1,052). Participants with a history of conditions that may influence cognitive function such as multiple sclerosis, Parkinson's disease, stroke, epilepsy, or meningitis were excluded. Participants who were determined by clinical consensus to have met diagnostic criteria for Mild Cognitive Impairment, AD, or another dementia at any follow-up WRAP study visit were also excluded. This study was conducted with the approval of the University of Wisconsin Health Sciences Institutional Review Board and all participants provided signed informed consent prior to enrollment.

Measures

WRAP visits are approximately three hours in duration. At each visit, participants complete questionnaires on health history, psychosocial and sociobehavioral factors, and lifestyle; a nurse collects a blood sample and clinical data including height, weight, and blood pressure; and a trained psychometrist administers a comprehensive battery of commonly used clinical neuropsychological tests, described in detail below. Additional details on the WRAP study protocol and sample characteristics are available in a recent WRAP publication (Clark et al., 2016).

Neuropsychological assessment—Key outcome variables included six cognitive factor scores from each WRAP visit, determined previously (Dowling, Hermann, La Rue, & Sager, 2010; Koscik et al., 2014) based on WRAP data. Briefly, factor analysis using promax rotation and maximum likelihood estimation (Grice, 2001) was used to reduce the set of cognitive measures to a smaller number of factors and obtain weights used to combine the measures within each factor. The resulting weighted factor scores were then standardized [~N (0,1)] into z-scores, using means and standard deviations obtained from the whole baseline sample. The six cognitive factors represent domains of episodic memory and executive function. These cognitive factors were Verbal Learning & Memory, Immediate Memory, Visual Learning & Memory, Story Recall, Speed & Flexibility, and Working Memory. Verbal Learning & Memory was derived from the Rey Auditory Verbal Learning Test (RAVLT), specifically RAVLT Learning Trials 3–5 and the RAVLT Delayed Recall Trial (Schmidt, 1996). Immediate Memory was also derived from the RAVLT, specifically from RAVLT Learning Trials 1–2. Visual Learning & Memory was derived from the three learning trials and delayed recall trial of the Brief Visuospatial Memory Test – Revised (Benedict, 1997). Story Recall is derived from the Logical Memory immediate and delayed recall subtests of the Weschler Memory Scale – Revised (Weschler, 1987). Speed & Flexibility is derived from time to completion on the Trailmaking Test A & B (Heaton, Miller, Taylor, & Grant, 2004), and number of items completed on the Stroop Neuropsychological Screening Test Color-Word Interference condition (Trenerry, Crosson, Deboe, & Leber, 1989). Working Memory is derived from number of correct items on the Digit Span Forward, Digit Span Backward, and Letter-Number Sequencing subtests of the Wechsler Adult Intelligence Scale-III (Wechsler, 1997).

Social support—Perceived social support was assessed via nine items taken from the Medical Outcomes Survey (Sherbourne & Stewart, 1991). Participants were asked how often different kinds of support were available to them if they needed it (e.g., “Someone you can count on to listen to you when you need to talk”). Response options ranged from 0 (none of the time) to 4 (all of the time) (Sherbourne & Stewart, 1991). Responses from all nine items were summed to create a support index score (possible range, 0–36). Prior to analyses, the support index score was standardized across all data points [~N (0, 1)].

Verbal interaction—A novel verbal interaction questionnaire was implemented in 2010 in order to explore our dual-pathways hypothesis. Reliability of the instrument is substantial, with weighted kappa values ranging from 0.49 to 0.79 (Zuelsdorff et al., 2016). Participants reported quantity of verbal interaction in seven distinct social domains (spouse/partner, other

family, friends, colleagues, club/hobbies, religious meeting attendance, and interactions with strangers) and one "other" inquiry designed to capture interactions that were not included in a previous domain. Responses, based on time per day or time per week depending on the domain in question, were on a six-point scale and ranged from a "none" response (e.g., "I don't have/talk with other family members") to four different time ranges between "Less than 30 minutes" and "Over two hours" (with write-in capability). To simplify analyses, assess the quantity of verbal interaction as a whole, and account for the possibility of substitution or tradeoff (for example, a decrease in time spent interacting with friends if time spent interacting with colleagues increased), a summed total time index score, using either midpoint of time range in a given response or written-in quantity, was created to represent the average number of minutes per week spent verbally interacting with others. The total time index score was standardized across all data points [~N (0, 1)].

In order to analytically distinguish the benefits of affect-neutral stimulation arising from conversation-related brain processes from the potential stress-mitigating or stress-generating effect of positive or negative social exchanges, a valence question inquiring on the overall *quality* of the interactions in question was included for each social domain ("How pleasant or unpleasant do you find these interactions to be most of the time?"). Response options for each ranged from −2 (very unpleasant) to 2 (very pleasant). Responses were weighted by quantity of interaction in the given domain and summed to create an important covariate, our overall *quality of interaction* index score.

***APOE* genotyping—**Because the presence of the APOE ε4 allele is one of the most well-established risk factors for AD and early cognitive decline (Scarabino, Gambina, Broggio, Pelliccia, & Corbo, 2016), and prevalence of the risk allele in our family history-enriched sample is high relative to the population as a whole, ε4 carrier status is included as a key covariate in all analyses. Genotyping for the two *APOE* single nucleotide polymorphisms that determine the ε2, ε3, and ε4 alleles, rs429358 and rs7412, was done previously by WRAP and has been described in detail (Johnson et al., 2011).

Other potential covariates—Several health and lifestyle covariates were considered. Participants were coded as never, ever, or current smokers and as abstinent, moderate, or heavy drinkers (abstinent=0 drinks in the past month, moderate=<1 or 1–2 drinks per day, heavy=3–5 or ≥6 drinks per day). Caffeine consumption was coded dichotomously; participants were categorized as heavy or not-heavy users of caffeine (heavy caffeine use = 3 or more caffeinated beverages per day). Height and weight were measured and body mass index (BMI) was calculated (kg/m^2). Self-reported physical activity was converted to metabolic equivalent of task (MET) hours per week. Partner status was dichotomous, with those reporting having a spousal or partner relationship considered partnered regardless of legal marital status.

Statistical analysis

Included participants had between one and three visits' worth of data available for analysis. Although there were too few participants with social data spanning three timepoints (N=3) to make a longitudinal analysis of cognitive change over time possible, a significant portion

of participants (N=410) did have data from two observations available, and in order to make use of that data, we conducted all analyses using mixed effects models in SAS, version 9.2 for Windows. To account for within-subject and within-sibling group correlations, random intercepts for participant and family were included in all models.

A base model was chosen based on established demographic and genetic risk factors. Health and lifestyle covariates were retained if they changed the sociobehavioral predictor-cognitive outcome relationship by ≥10%, independently improved the fit of the predictor-outcome regression model as measured by Akaike information criterion (AIC), *or* demonstrated a significant association at the $p<.05$ level with at least two cognitive outcome variables. Based on these criteria, BMI, alcohol consumption, and caffeine use were dropped. Ultimately, our six cognitive factor scores were regressed on our key predictor variables, social support and quantity of verbal interaction, in a set of nested models: (1) a base model controlling for age, gender, race, education, *APOE* ε4 carrier status, parental history of AD, and WRAP clinic site; (2) a model that added two lifestyle factors (smoking history and physical activity); and (3) a model that added an important social confounder, partner status. In the assessment of social support, set (3) represented our fullest model. In final assessments of verbal interaction quantity, however, we added (4) a model that included our valence control variable, quality of interaction. In consideration of possible non-linear relationships between key predictor variables and cognitive outcomes, contribution of squared terms for each sociobehavioral predictor was also assessed.

Potential multicollinearity was assessed with Pearson correlation analyses (not shown) of all variables included in the fullest models; further, tolerance values indicated that collinearity was not a concern.

Results

Participant characteristics from their earliest complete visit (representing a “baseline” for this cohort) are presented in Table 1. Participants ranged in age from 40 to 78 years old at the first included visit and a majority was female and partnered. Education levels for the sample were high; nearly two-thirds had completed a bachelor’s degree and over 40% had at least some postcollege education. Prestandardization social support scores were high, with a mean of 28.9 out of 36 possible points. Quantity of interaction data was winsorized at the 99^{th} percentile (81.3 hours per week of face-to-face verbal interaction) to account for improbability of self-reported quantities above that value. In Table 2, we present the adjusted associations of health and lifestyle covariates, as well as our quality of interaction control variable, with all six outcome measures; these models do not include our key social predictor variables. When models incorporating social support and total weekly quantity of verbal interaction were fitted, a squared term for verbal interaction showed a statistically significant association with at least one cognitive factor score. To ease interpretation and more precisely identify what levels of interaction were significantly related to performance, we divided quantity of interaction into quartiles and created indicator variables representing the following levels of weekly verbal interaction: Low (<9 hours/week), Moderate (9–15 hours/week), High (15–25 hours/week), and Very High (>25 hours/week). The “Low” group was used as a reference group in models incorporating these verbal interaction indicator

variables. In Table 3, we present the coefficients for social support index scores as well as moderate, high, and very high quartiles of verbal interaction in four nested models.

In a base model adjusting for key demographic and sampling characteristics only, higher social support index score was associated with higher Speed & Flexibility and Immediate Memory scores, $\beta=0.09$, $p<0.001$, and $\beta=0.07$, $p=0.01$, respectively; these relationships were attenuated but remained significant when two lifestyle factors, smoking status and physical activity, were added to the base model. While the relationship with Immediate Memory was attenuated to the point of non-significance when partner status was included, the relationship between social support and Speed & Flexibility remained significant, $\beta=0.07$, $p=0.01$.

Verbal interaction showed positive associations with both Speed & Flexibility and Verbal Learning & Memory in our base model, but these associations were seen only in a sub-range of reported quantity of interaction. The “high” quantity of interaction quartile, representing 15–25 hours of reported interaction per week, was the only quartile to demonstrate a relationship in both Speed & Flexibility, $\beta=0.12$, $p=0.04$, and Verbal Learning & Memory, $\beta=0.14$, $p=0.02$, domains. The relationship between high quantity of interaction and SF became non-significant when quality of interactions was controlled for, while the relationship between high quantity of interaction and Verbal Learning & Memory remained significant, $\beta=0.16$, $p=0.02$. A relationship between high quantity of interaction and Immediate Memory approached statistical significance, $\beta=0.16$, $p=0.05$; in fact, a non-significant trend wherein cognitive test performance peaked at moderate or high levels of verbal interaction, but declined at very high levels was seen across several cognitive domains (Figure 1).

Discussion

In this study, we examined the role of two dimensions of social activity, perceived social support and quantity of face-to-face verbal interaction, in cognitive test performance among a population of middle-aged and older adults at risk for AD. There was some support for our hypothesis that each social dimension would be positively associated with cognitive function independent of benefit from the other. In fact, social support and verbal interaction showed positive associations with distinct cognitive domains: Speed & Flexibility and Verbal Learning & Memory, respectively. Interestingly, the relationship between verbal interaction and Verbal Learning & Memory was quadratic rather than linear, with a diminishing of returns as reported interaction rose to very high levels.

The WRAP research group has reported a preliminary cross-sectional association between perceived availability of social support and SF in a subsample of parental history-positive WRAP participants (Zuelsdorff et al., 2013). The current study incorporates a much larger sample including persons both with and without a parental history of AD, and utilizes data from repeated visits for a large portion of participants. Crucially, this analysis replicates and expands upon the previous finding with the incorporation of novel verbal interaction data, including a quality-of-interaction covariate designed to control for positive versus negative valence of verbal interactions in each social domain. Our nested models demonstrate the importance of accounting for partner status in the assessment of social support and cognitive

benefit: attenuation of coefficients was seen in five of six cognitive domains with the inclusion of the variable. Of the two cognitive domains showing a significant association with social support in a model including demographics and lifestyle factors, Immediate Memory showed attenuation to the point of non-significance after adjusting for partner status.

The observed association between social support and Speed & Flexibility, a key component of executive function, is consistent with previous studies that specifically measured a support construct. Positive associations with global function (Gow, Mortensen, & Avlund; Pillemer & Holtzer, 2016; Seeman et al., 2001) and with executive function or processing speed in particular have been seen in populations of differing age, ethnicity, and nationality (Dickinson, Potter, Hybels, McQuoid, & Steffens, 2011; Gow et al.; Seeman et al., 2011; Sims, Levy, Mwendwa, Callender, & Campbell, 2011). Conversely, social isolation and social conflict have been associated with diminished executive function (Liao et al., 2014; Seeman et al., 2011), and depression potentially mediates such relationships (Gow et al.). Within this context, our findings provide additional evidence for the hypothesis that social support contributes to cognitive function via pathways of stress, buffering, and positive or negative affect.

Our original research question and motivation for measuring verbal interaction as directly as possible was driven by earlier social engagement research suggesting a separate beneficial role for conversation-related stimulation: observational studies of frequency of social contact (James et al., 2012; Seeman et al., 2011; Ybarra et al., 2008) and experimental studies showing immediate cognitive performance increases following social engagement with peers (Ybarra et al., 2008). Meta-analyses of previous work on social engagement and cognitive aging affirm that “structural” components of engagement including network size and participation frequency operate as lifestyle-based determinants of cognitive health trajectories (Kuiper et al., 2015; Kuiper et al., 2016). Finally, very recent study findings have provided additional evidence. In a study characterizing independent and joint benefits of social resources and all-type activity participation for later-life cognition, specifically for word recall, investigators concluded not only that each was cognitively beneficial, but that the *social component of activity participation* stood out as yielding the strongest positive influence (Litwin & Stoeckel, 2016). And, recent WRAP findings provide neuroimaging evidence for social interaction as environmental enrichment: in a study of occupational complexity and cognitive reserve, more complex work with *people*, but not with data or things, protected cognition in the face of hippocampal and whole brain atrophy (Boots et al., 2015).

Our discovery that the relationship between quantity of verbal interaction and cognitive test performance was parabolic rather than linear in shape, with lower outcome scores at the very low and very high ends of the interaction range, was borne out in greater detail with the quartile-based indicator variables. There are a few potential explanations for diminished test performance seen among those reporting the highest quantity of interpersonal interactions. First, very extensive interaction may introduce cognitive or emotional demand that outweighs the benefits seen for lower levels. Recent research exploring potential cognitively stimulating effects of grandparenting found that the relationship between days of childcare

and cognitive function is parabolic, suggesting that beneficial engagement may reach a critical threshold, with additional activity representing a cognitively detrimental stressor (Burn & Szoeke, 2015; Burn, Henderson, Ames, Dennerstein, & Szoeke, 2014). Reverse causality is another possibility, with people experiencing declines in cognition possibly spending increased time interacting with family members or other caregivers. Alternately, there may be unmeasured confounders in the group reporting very high levels of interaction. Comparing the highest quartile ("very high" interacters) to the third quartile ("high" interacters) revealed several modest differences between the two groups (data not shown). Those in the highest quartile were not only younger, but also more likely to be non-white, and less likely to have a parental history of AD than those in the third quartile (High). The education levels also varied between the two upper quartiles; in the Very High group, fewer participants reported having at least a college degree. While these factors were included as covariates in analytical models, and do not point irrefutably toward obvious additional confounding, the differences do raise the possibility that the Very High group is likely to be unique in other ways. For example, unmeasured confounders such as socioeconomic disadvantage could represent competing risk factors that mitigate the cognitive benefits of interaction. Finally, lower test scores at the highest levels of reported interaction could be due to differential misclassification, whereby a subgroup of individuals who have trouble performing on cognitive tests also have difficulty accurately and plausibly reporting the time spent in face-to-face interactions each week, perhaps due to unfamiliarity with, or anxiety related to, the research environment. This explanation seems especially worthy of consideration given the arguable implausibility of the upper range of reported time spent interacting with others.

Once all covariates were included, significant verbal interaction relationships were only seen in Verbal Learning & Memory, though the relationship with Immediate Memory also approached significance. Verbal Learning & Memory and Immediate Memory scores are determined by performance on a test of word recall (Lezak, Howieson, Loring, Hannay, & Fischer, 2004), and in that sense we echo others' findings (Litwin & Stoeckel, 2016). Interestingly, the relationship between verbal interaction and Speed & Flexibility was significant until our quality of interaction covariate was introduced to the model. While many more complex interactions are likely to require and promote executive functions (Ybarra et al., 2008; Ybarra & Winkielman, 2012), we believe this attenuation reaffirms the importance of relationship quality, stress, and affect in this domain of cognition. The null findings for other cognitive domains are difficult to fully explain, though there is evidence that some of those domains are quite strongly influenced by genetic risk factors (Darst et al., 2015).

In addition to the uncertainty regarding the non-linear relationship between our verbal interaction predictor and Verbal Learning & Memory, there are a few limitations related to this study. First, though repeated measures were available for approximately 40% of our study sample, additional within-subject data points are needed before we can assess the potentially bidirectional relationship between sociobehavioral factors and cognitive aging, and explore the impact of these factors on rates of change over time. Second, the WRAP sample may not be representative of the broader aging population: women and the highly educated are overrepresented, the sample was mostly white, and while all participants were

cognitively intact at baseline, WRAP by design oversamples for genetic vulnerability to earlier cognitive decline. Finally, the available measure of perceived social support cannot be conflated with amount of support actually received (Haber, Cohen, Lucas, & Baltes, 2007). Though our conceptual modeling for stress and coping processes places support as a moderator of stress and stress-related mood changes, our analytical models do not account for the potential role that stressful contexts and negative affect have been shown to play in the perception, and reporting, of available support (Cohen, Towbes, & Flocco, 1988).

Nonetheless, we believe this to be a strong, unique contribution to a nascent body of research establishing the pathways between social engagement and cognition. We hope that our findings will additionally be of interest to physicians guiding older patients in the "healthy aging" quest. While patients and their caregivers are often instructed in the benefit of staying socially engaged and cognitively active, traditional examples of such activities – forging new social relationships, joining groups or activities, puzzles or word games – can be unappealing, intimidating, or simply impossible for many adults. The addition of "everyday" activities such as casual conversation to the roster of beneficial activities may be perceived as more accessible, and offer more options to patients of varying personalities, abilities, and resources.

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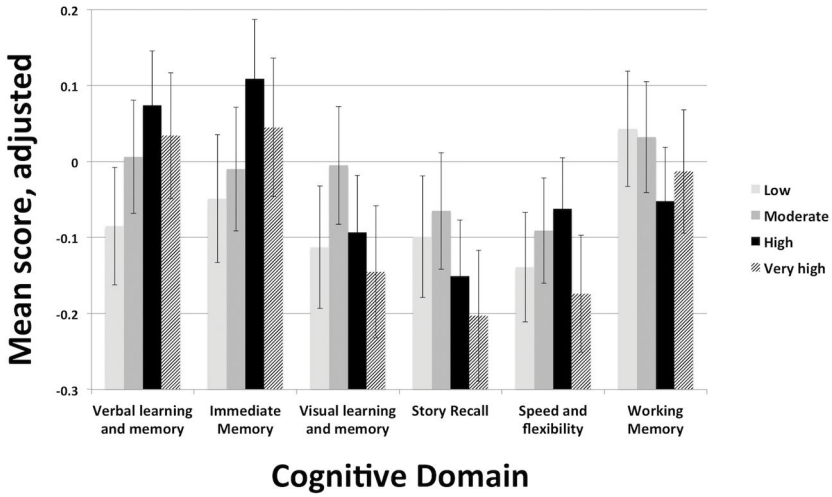

Figure 1. Cognitive factor scores by verbal interaction quartile

Note: Cognitive factor scores are adjusted for age, gender, race, education, *APOE* ε4 carrier status, parental history of AD, WRAP clinic site, physical activity, smoking, partner status, perceived social support, and quality of interaction

Table 1

Descriptive statistics for study participants (N=1052) at first sociobehavioral assessment.

Variable	Percent or M (SD)	Range
Age, years	60.2 (6.7)	40–78
Site		
Madison	72%	
La Crosse	22%	
Milwaukee	6%	
Gender, female	69%	
Race, non-white	5%	
Parental history of AD	72%	
Education		
High school/GED	9%	
Some college	28%	
College graduate	20%	
Postcollege	43%	
BMI, kg/m^2	29.0 (6.3)	17.1–57.6
APOE ε4 carrier	39%	
Smoking		
Never	57%	
Past	38%	
Current	5%	
Alcohol use		
Abstinent	20%	
Moderate	68%	
Heavy	12%	
Caffeine consumption, heavy	32%	
Physical activity, MET hrs/wk	17.7 (15.0)	0–81.3
Partner, yes	77%	
Support index	28.9 (6.8)	0–36
Quantity of interaction, hrs/wk *	19.7 (15.6)	0.25–81.3
Speed & Flexibility	0.05 (1.04)	−4.17–3.59
Immediate Memory	−0.04 (1.10)	−3.40–3.31
Working Memory	0.08 (1.01)	−2.54–3.30
Verbal Learning & Memory	0.02 (1.06)	−3.56–1.83
Visual Learning & Memory	0.03 (1.03)	−2.59–2.07
Story Recall	−0.08 (1.00)	−3.02–2.70

* Reported quantity of interaction was winsorized at the 99th %.

Table 2

Adjusted regression coefficients ± standard errors (p-values) for covariates by cognitive domain.

Covariates	Verbal Learning & Memory	Immediate Memory	Visual Learning & Memory	Story Recall	Speed & Flexibility	Working Memory
	β (se)	β (se)	β (se)	β (se)	β (se)	β (se)
Age	−0.03±0.004 (<.001)	−0.03±0.005 (<.001)	−0.03±0.005 (<.001)	−0.02±0.004 (<.001)	−0.07±0.004 (<.001)	−0.02±0.004 (<.001)
Female	0.75±0.06 (<.001)	0.64±0.07 (<.001)	0.29±0.06 (<.001)	0.26±0.06 (<.001)	0.33±0.06 (<.001)	−0.02±0.06 (.71)
Non-white	−0.21±0.19 (.27)	−0.13±0.20 (.52)	−0.05±0.19 (.79)	−0.21±0.19 (.27)	−0.49±0.18 (.007)	−0.35±0.19 (.07)
Education	0.17±0.03 (<.001)	0.10±0.03 (<.001)	0.14±0.03 (<.001)	0.20±0.03 (<.001)	0.08±0.03 (.006)	0.19±0.03 (<.001)
***APOE* ε4 carrier**	−0.05±0.06 (.45)	−0.06±0.07 (.35)	−0.10±0.06 (.14)	−0.11±0.06 (.09)	−0.12±0.07 (.05)	−0.08±0.06 (.20)
Parental history of AD	−0.04±0.07 (.54)	−0.05±0.07 (.53)	0.04±0.07 (.57)	−0.10±0.07 (.17)	0.07±0.07 (.29)	−0.03±0.07 (.70)
Site						
Madison	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
La Crosse	−0.09±0.08 (.24)	0.03±0.08 (.67)	−0.09±0.08 (.27)	−0.16±0.08 (.04)	−0.11±0.07 (.12)	−0.07±0.08 (.39)
Milwaukee	−0.05±0.18 (.79)	0.04±0.19 (.84)	−0.47±0.18 (.01)	−0.19±0.18 (.29)	−0.60±0.17 (<.001)	−0.32±0.18 (.08)
METs (10 hr/week)	−0.02±0.02 (.21)	0.002±0.02 (.93)	−0.04±0.02 (.05)	−0.01±0.02 (.63)	0.003±0.02 (.83)	−0.01±0.02 (.67)
Smoking status						
Never	(ref)	(ref)	(ref)	(ref)	(ref)	
Past	−0.01±0.06 (.84)	−0.08±0.06 (.24)	−0.13±0.06 (.03)	0.07±0.06 (.24)	−0.009±0.06 (.88)	0.13±0.06 (.04)
Current	−0.30±0.13 (.02)	−0.42±0.14 (.003)	−0.23±0.13 (.08)	−0.25±0.14 (.07)	−0.30±0.12 (.01)	0.07±0.13 (.61)
Partner	0.27±0.07 (<.001)	0.33±0.07 (<.001)	0.24±0.07 (<.001)	0.07±0.07 (.30)	0.16±0.06 (.01)	0.15±0.07 (.03)
Quality of interaction	−0.003±0.02 (.89)	−0.03±0.03 (.32)	−0.01±0.03 (.64)	−0.03±0.03 (.18)	0.06±0.02 (.008)	−0.03±0.02 (.16)

Note: Table S1 models include all covariates simultaneously but do not include key sociobehavioral predictor variables.

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Table 3

Regression coefficients ± standard errors (p-values) for social support and verbal interaction quantity by model and cognitive domain

	Verbal Learning & Memory	Immediate memory	Visual Learning & Memory	Story Recall	Speed & Flexibility	Working Memory
Model 1:Base demographic variables						
Social support index	0.05±0.03 (.06)	0.07±0.03 (.01)	0.04±0.03 (.12)	0.04±0.03 (.15)	0.09±0.02 (<.001)	0.05±0.02 (.06)
Verbal Interaction						
Moderate	0.10±0.06 (.10)	0.06±0.07 (.41)	0.13±0.07 (.06)	0.03±0.07 (.63)	0.07±0.06 (.19)	0.002±0.06 (.98)
High	0.14±0.06 (.02)	0.13±0.08 (.09)	0.02±0.07 (.79)	−0.04±0.07 (.52)	0.12±0.06 (.04)	−0.09±0.06 (.15)
Very high	0.08±0.06 (.22)	0.01±0.08 (.87)	−0.01±0.07 (.93)	−0.09±0.07 (.23)	0.08±0.06 (.20)	−0.07±0.06 (.30)
Model 2: Base + Lifestyle variables						
Social support index	0.04±0.03 (.14)	0.06±0.03 (.04)	0.03±0.03 (.24)	0.03±0.03 (.23)	0.08±0.02 (<.001)	0.04±0.03 (.13)
Verbal Interaction						
Moderate	0.10±0.06 (.10)	0.06±0.07 (.44)	0.13±0.07 (.06)	0.03±0.07 (.63)	0.08±0.06 (.15)	−0.002±0.06 (.98)
High	0.15±0.06 (.02)	0.14±0.08 (.06)	0.04±0.07 (.59)	−0.05±0.07 (.51)	0.14±0.06 (.02)	−0.09±0.06 (.13)
Very high	0.10±0.07 (.15)	0.03±0.08 (.73)	0.01±0.07 (.93)	−0.09±0.07 (.21)	0.09±0.06 (.14)	−0.07±0.06 (.31)
Model 3: Base + Lifestyle + Partner status						
Social support index	0.02±0.03 (.50)	0.03±0.03 (.29)	0.01±0.03 (.72)	0.03±0.03 (.31)	0.07±0.03 (.008)	0.03±0.03 (.33)
Verbal Interaction						
Moderate	0.07±0.06 (.22)	0.02±0.07 (.82)	0.10±0.07 (.17)	0.03±0.07 (.70)	0.07±0.06 (.22)	−0.02±0.06 (.77)
High	0.12±0.07 (.06)	0.10±0.08 (.19)	0.01±0.07 (.94)	−0.05±0.07 (.46)	0.12±0.06 (.04)	−0.12±0.06 (.08)
Very high	0.07±0.07 (.31)	−0.01±0.08 (.92)	−0.02±0.08 (.75)	−0.10±0.07 (.18)	0.08±0.06 (.19)	−0.08±0.07 (.21)
Model 4: Base + Lifestyle + Partner + Quality of Interaction						
Social support index	N/A	N/A	N/A	N/A	N/A	N/A
Verbal Interaction						
Moderate	0.09±0.06 (.15)	0.04±0.07 (.21)	0.11±0.07 (.12)	0.03±0.07 (.61)	0.05±0.06 (.40)	−0.01±0.06 (.84)
High	0.16±0.07 (.02)	0.16±0.08 (.05)	0.02±0.08 (.79)	−0.05±0.07 (.49)	0.08±0.06 (.22)	−0.09±0.07 (.15)
Very high	0.12±0.09 (.20)	0.09±0.11 (.37)	−0.03±0.10 (.75)	−0.10±0.10 (.29)	−0.03±0.08 (.68)	−0.06±0.09 (.52)

Note: Model 1 adjusts for age, gender, race, education, *APOE* ε4 carrier status, parental history of AD, and WRAP clinic site. Model 2 additionally adjusts for physical activity and smoking.