International Journal of Nursing
June 2015, Vol. 2, No. 1, pp. 48-55
ISSN 2373-7662 (Print) 2373-7670 (Online)

Published by American Research Institute for Policy Development
DOI: 10.15640/ijn.v2n1a5
URL: http://dx.doi.org/DOI: 10.15640/ijn.v2n1a5

Psychosocial Correlates of Cognitive Function in the Elderly: A Biobehavioral Approach

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Abstract

Objectives: Psychological stress, depression, and loneliness are associated with adverse cognitive health outcomes in a rapidly growing aging population. Prolonged activation of the HPA axis with elevated salivary cortisol is associated with poor cognitive function. This purpose of this pilot study was to examine correlates between psychological stress, depression, loneliness, and cognitive function from a biobehavioral perspective and enhance understanding of how salivary biomarkers are related to cognitive function in an elderly population. **Method:** Data were cross-sectionally collected from 71 community-dwelling elderly (mean age 86.4). Stress, depression, loneliness, and cognitive function were measured with standardized instruments, and saliva samples were collected for salivary cortisol and DHEA. **Results:** Stress and loneliness were significantly and negatively correlated with global cognitive function (r = -.25, r = -.30, both p = < .05) and executive function (r = -.26, r = -.40, both p< .05). Cortisol showed a significant negative correlation with executive function (r = -.30, p<.05), despite non-significant correlations with psychosocial variables. **Conclusion:** Loneliness, stress, and cortisol seem to be important biobehavioral variables on cognitive function in the elderly. Additional biobehavioral research is needed with more diverse study participants, longitudinal research designs, and other relevant biomarkers for cognitive functions. With increasing longevity, biobehavioral interactions and cognitive function will remain a significant area of research in the elderly and better understanding of such interactions may reduce adverse burdens in the aging population.

Introduction

The fastest growing subset of Americans is the elderly population, and it is believed that more than 11 million will experience a decline in cognitive function, including dementia or Alzheimer's disease (AD), in the coming years.Financial estimates associated with decreased cognitive function are expected to exceed $148 billion annually in direct and indirect costs (Alzheimer's Association, 2009).Empirical evidence, however, supports that neurogenesis and neuroplasticity are possible in the aging brain, and cognitive decline is not necessarily the inevitable outcome of old age (Struble& Sullivan, 2011). The remaining challenges are how to preserve the ability for the elderly to live independently and examine the factors that may influence cognitive decline in the elderly. The elderly are particularly at risk for experiencing psychological stress, depression, and loneliness, which are found to be negatively associated with cognitive function. Wilson et al. (2007a) followed a large population-based cohort for 5-12 years and found that chronic psychological stress was significantly associated with worsened cognitive function in old age. In another large population-based cohort, authors reported that stress was significantly associated with worse global cognitive function over a period of 10 years (Wilson et al., 2011). Similarly, authors of two longitudinal studies found significant correlations between higher depression and worse executive function in adults (Lampe, Sitskoorn & Heeren, 2004; Hinkelmann et al., 2009). A major gap in the literature exists, however, for the link between loneliness and cognitive function.

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In a 10-year follow up of community dwelling elders, Tilvis et al. (2004) reported that high loneliness was significantly associated with greater risk of cognitive decline at follow up. Similarly, Wilson et al. (2007b) found that lonely participants were twice as likely to experience cognitive decline at the 4-year follow-up. Biological mechanisms may underlie these associations between stress, depression, loneliness, and cognitive function. Prolonged activation of the hypothalamus-pituitary-adrenal (HPA) axis from psychological stress, depression, and loneliness leads to hypercortisolism, which is directly related to reduced dendritic branching, abnormal synapse formation, and neuronal death in areas of the brain known for their role in memory and executive function, the hippocampus and frontal cortex (Adam et al., 2006; Epel, 2009; Ferrari &Magri, 2008; Steptoe et al., 2004). Furthermore, chronic hypercortisolism may cause cellular damage and changes in the brain leading to neurodegenerative disease and/or alterations in cognitive function, including dementia and/or Alzheimer's disease (Epel, 2009). The purpose of this cross-sectional,pilot study was to examine associations of psychological stress, depression, loneliness, and salivary cortisol with cognitive function in the elderly population aged 65 years and over.It was hypothesized that (1) psychological stress, depression, and loneliness would correlate negatively with cognitive function, but positively with salivary cortisol, and (2) salivary cortisol would correlate negatively with cognitive function.

Methods

Study Design

Datawere collected once for all variables. Psychological stress, depression, loneliness, and cognitive function were measured with standardized instruments, and a saliva sample was collected for biological measures. Prior to data collection the study protocol was approved by the Committee for the Protection of Human Subjects at the University.

Subjects and Setting

Sample size was calculated using conservative values of effect size set at .5, power level set at .8, alpha was set at .05, and the correlation coefficient set to detect a moderate to strong Pearson's *r*. The estimated, minimum sample size was 60 participants. Inclusion criteria were: (1) $\geq$ 65 years of age, (2) the ability to read/write in English, and (3) no diagnosis of a neurodegenerative disease, such as dementia or AD. Exclusion criteria were: (1) inability to complete psychometric instruments as instructed, (2) inability to provide a saliva sample, and (3) currently taking hormone replacement therapy or corticosteroids.The setting was afaith-based, non-profit, Continuous Care Retirement Community that provides housing for residents with varying levels of physical and cognitive functioning and includesindependent living, assisted living, and long-term nursing care. Recruitment flyers were posted in the facility and included simple essential information about the study and contact information.When contacted, the study was explained in full detail to potential subjects and questionswere answered before obtaining written consent.Each participant received a gift card to the local grocery store in the amount of $20 upon completion of the study.

Measurement

Psychosocial and Cognitive Function

Psychological stress, depression, loneliness, and cognitive function data were collected using standardized reliable and validated instruments in the participant's individual apartment at thefacility. Data collection took approximately 30-40 minutes.Psychological stress was measured using the Perceived Stress Scale (PSS)to assess the degree to which situations in a person's life were appraised as stressful. The Likert style, 10-item instrument consists of easy to understand questions and has been psychometrically tested in various populations. The itemscores aresummed and a higher score indicates a higher perceived stress level with the possible score range of 0-40. The PSS is considered a reliable instrument in adults with a Cronbach's α of .86 and test-retest reliability of .85 (Cohen, Kamarck&Mermelstein, 1983). In this study, the Cronbach's α was .76. Depression was measured using the Geriatric Depression Scale (GDS). Designed specifically for use in the elderly, the instrument contains 15 items that are answered "yes" or "no," and a score of 0 -9 is considered "normal," 10 - 19 is "mildly depressed," and 20 - 30 is "severely depressed" (Yesavage et al., 1983).Cronbach's α was reported to be .81, with inter-rater reliability at .84 (Almeida & Almeida, 1999). In this study, the Cronbach's α was .71. Loneliness was measured with the Revised-University of California at Los Angeles (R-UCLA) to measure general feelings of social isolation and dissatisfaction with one's social interactions.

The 20-item,Likert style questionnaire contains 10 positively worded items and 10 negatively worded items. After reversing the negatively worded items, all items are summed and a total score is obtained ranging from 20 - 80. Higher scores indicate higher levels of loneliness. The instrument is considered reliable across various populations, with Cronbach's α ranging from .89 - .94, and test-retest reliability over a one-year period at .73 (Russell et al., 1980).In this study, the Cronbach's α was .83. Global cognitive function was measured using the Mini Mental State Examination (MMSE), an 11-item questionnairewhich is validated in the elderly population whether institutionalized or community dwelling. The MMSE includes simple tests and problems in the domains of orientation, registration, attention and calculation, recall, and language. Scores ≥ 24 are considered normal cognition, and those ≤ 23 correlate closely with dementia. The Cronbach's αis .96 (Folstein, Folstein,& McHugh, 1975). In this study, the Cronbach's α was .50. Executive function was measured with the CLOX I. Participants are first instructed to "draw a clock that says 1:45. On a blank sheet of paper, set the hands and numbers on the face so that a child could read them."Possible scores range from 0-15, and a higher score indicates better executive function. Tested in the elderly population, Cronbach's α for CLOX Iis .83 (Royall, Cordes,& Polk, 1998). In this study, the Cronbach's α was .86.

Saliva Sample Collection and Bioassay

The biomarker of cortisol was assessed from saliva,asthis non-invasive technique is practical and easy to use. Salivary cortisol measured by direct immunoassay reflects unbound, active cortisol fraction, and is highly correlated to serum cortisol (r = .81, p <.001; Gozansky et al., 2005). Saliva samples were collected on the same day aspsychological measurements between 1:00 p.m. and 5:00 p.m. to control for circadian rhythmicity. Each participant rinsed their mouth,waited five minutes,and collected saliva via passive drool into a small container. Most participants successfully provided approximately 2 mL of saliva within 10 – 20 minutes.Samples were transported in a secure cooler with ice pack tothe Biosciences Laboratory in the Center for Nursing Research.Salivary levels of cortisolwerebatch measured in duplicate using an enzyme immunoassay (EIA) kit. To evaluate precision of biological measures, coefficients of variability (CV) were calculated for biological measures. The intra-assay CV was calculated from the duplicates, whereas the inter-assay CV was calculated from CVs of different plates per manufacturer instructions. *A priori* criterion for inter-assay and intra-assay CV was set at ≤10%. Both intra-assay and inter-assay CVsmet *a priori* criterion.

Data Analysis

Data were verified to ensure data entry accuracy, stored into a secure, password-protected database, andanalyzed using SPSS version 21.0.All data were examined for sample distribution, and when data were deviated from the normal distribution, data were log transformed. For bivariate correlations, Pearson's product-moment correlation coefficient was used.*A priorip* value was set at .05.

Results

Individual Characteristics

The sample comprised of 71 elderly (Table 1). Participants ranged in age from 70-99 years (M = 86.4, SD = 6.35) and were predominately independently living and well-educated (40% with a baccalaureate degree or higher) Caucasian females who reported few medical problems. The most commonly reported medical conditions were osteoarthritis, hypertension, hypercholesterolemia, and hypothyroidism. Few participants reported depression, anxiety, diabetes, cardiovascular disease, or cancer, and only one reported end stage renal failure with weekly hemodialysis. Most participants reported using less than five prescription medications per day and many reported daily vitamin usage.

Descriptives of Psychosocial and Biologic Measures

Table 2 provides basic descriptive results for the psychometric instruments. All items on the five psychometric instruments were fully completed by all participants without missing data. Mean scores for the PSS and GDS were 13.06 (SD = 6.75) and 2.75 (SD = 2.24), respectively, indicating low overall perception of stress and depression. The mean score for the R-UCLA, however, was 35.14 (SD = 8.35), indicating a moderate level of loneliness. All participants except one scored within the normal range on the MMSE (M = 28.39, SD = 1.79), indicating adequate global cognitive function for most participants.About 40% of participants performed poorly on the CLOX I, and this was reflected with lower mean scores for CLOX I (M = 10.0, SD = 3.24). Most cortisol values were within the expected normal range for older adults (M = .23, SD = .24),except for the 22% that were lower, and the single highest cortisol value of 1.80 μg/dL.

Correlations between Psychosocial, Cognitive Function, and Biological Variable

Table 3 provides Pearson's *r*valuesto reflect associations between psychosocial, biological, and cognitive function variables. Correlation*r* values ranged from -.07 to.50. Depression was significantly correlated with loneliness, $r = .50$, $p < .001$, and stress, $r = .48$, $p < .001$, but was not significantly correlated with executive function or global cognitive function, $r = -.11$ and $-.07$, $p = .35$ and .56, respectively. Not surprisingly, stress, depression, and loneliness were positively correlated with each other, but onlystress and loneliness were significantly and negatively correlated with global cognitive function ($r = -.25$, $r = -.30$, both $p = < .05$) and executive function ($r = -.26$, $r = -.40$, both $p < .05$). For associations of the biological variable with psychosocial variables and cognitive function, a significant negative correlation was found between cortisol and executive function, $r = -.30$, $p = .02$.

Discussion

Psychosocial Variables and Cognitive Function

The hypothesis that psychosocial variables of stress, depression, and loneliness would correlate negatively with cognitive function was supported with significant negative correlations between both stress and loneliness with global cognitive function and executive function. The strongest correlation was found in an inverse relationship between loneliness and cognitive functions including global cognitive function and executive function. These findings are consistent withother studies in older adults,in which greater loneliness has been associated with cognitive deficits (Holmen et al., 1992; Tilvis et al., 2004; Wilson et al., 2007b). In a 10-year follow up,Tilvis et al. (2004) found that greaterloneliness was significantly associated with greater risk of cognitive decline at follow up in community dwelling elders.Similarly, ina large cross-sectional study,Holmen et al. (1992) found thatgreater loneliness was significantly associated with worse global cognitive function, and that participants living with a spouse, in a close relationship with another person, or actively engaged in activities with meaningful social contacts were less lonely.Wilson et al.(2007b) alsofound that lonely participants were twice as likely to experience cognitive decline over the 4-year follow-up, but frequent participation in social activities was significantly associated with decreased risk of cognitive decline.Participants in the current study had sufficient resources withample opportunities for social interactions in the retirement facility. Participants often spoke about their busy activity schedule and appeared to be highly satisfied with sufficient social support, but many also reported less frequent visits with family and close friends. Despite the external appearance of satisfaction with social relationships, there was variability in the levels of reported loneliness, high levels of which were negatively associated with cognitive functions.

Not surprisingly, a recent study with adult participants indicated that frequent visits with family were associated with decreased loneliness, whereas living aloneor in an environment without love or respect increased loneliness (Hacihasanoglu, Yildirim,&Karakurt,2012). With a large percentage of the participants in widowhood in the current study (68%), it raises the question that whether the weight of and satisfaction with social support the elderly perceives from non-family vs. family members differ and how this difference affects loneliness. The findings of a recent qualitative study suggest that despite strong non-kin ties, elderly people struggle with sadness and feelings of loneliness after the death of a spouse, siblings, or parents (Cloutier-Fisher, Kobayashi,& Smith, 2011). These findings support the potential differences in the intensity of loneliness from different types of social ties and sources of social supportin oldpopulations. More in-depth investigations on loneliness, in conjunction with the specifics of social support, may provide additional information to understand a decline in cognitive function and potential interventions to decrease loneliness. Stress was significantly and negatively correlated with global cognitive function and executive function, but the strength of the correlations was weaker than those with loneliness. These findings are consistent with published findings correlating chronic stress with decreasedglobal cognitive function and episodic memory (Wilson et al., 2005; Wilson et al.,2007a), but in contrast to another study that did not report similar findings (Jelicic et al., 2003). Wilson et al. (2007a) followed large population based cohort for 5 - 12 years and found that chronic psychological stress wassignificantly associated with increased cognitive decline in old age. In contrast, Jelicic et al. (2003) followed a considerably smaller cohort over a shorter period of three years and did not report similar correlations. The exact basis of the differences is not clear, but other factors, such as negative personality traits and chronic activation of the HPA axis with subsequent adverse effects in brain structures, may play a role.

Wang et al. (2009), in fact, reported that certain personality traits, such as high neuroticism and low extraversion, may intensify a person's stress response over the course of their lifetime and increase the risk for cognitive decline, suggesting the need for further research in this area. In contrast to loneliness and stress, depression was not significantly associated with cognitivefunction.This finding differs from others, in whichworse executive function was found in adultswith depression (Lampe, Sitskoorn,&Heeren, 2004; Hinkelmann et al., 2009). In these studies, however, the significant negative correlation between depression and executive function was evident only in participants diagnosed with major depression, but not healthy controls. Thus, the severity and duration of depression may influence its association with cognitive function.

Psychosocial Variables and Biological Response

It is widely documented that stress activates the HPA axis to increase cortisol secretion(Chrousos& Gold, 1992; Lupien et al., 2007). The hypothesis on positive correlations between psychosocial variables andcortisol was not supported. The positive correlation of higher stress, depression, and loneliness with cortisol in older adults is reported in other studies (Adam et al., 2006;Markopoulou et al., 2009; Schlotz et al., 2006;Steptoe et al., 2004). In community dwelling adults, salivary cortisol levels over three days weresignificantly positively correlated with stress, depression, and loneliness (Adam et al., 2006).Salivary cortisol assessed twice a week for three monthsalso showed a positive association with stress (Schlotz et al., 2006).However, in a cross-sectional study when saliva samples were collected immediately upon awakening, 30 minutes thereafter, and every two hours until bedtime, higher loneliness swas significantly associated with higher cortisol levels on awake but not at other times, indicating time-dependent variability in the strength of association between psychosocial variables and cortisol (Steptoe et al., 2004). In terms of saliva sample time, we collected all samples only once in the afternoon to accommodate the participants' schedule.It is possible thatthe timing of the sample and single collectionmay have affected the associations with cortisol in our study. The overall cortisol levels were lower than other reports and may be related to naturally declining levels associated with the diurnal pattern of the hormone. Our study participants were very old with the mean age over 86 years, and reduced variability with low cortisol levels may also have influenced its association with psychosocial variables.

Cognitive Function and Biological Variable

The hypothesis that cortisol would negatively correlate with cognitive function was partially supported. Cortisol showed negative correlations with executive function and global cognitive function, but only the correlationof cortisolwith executive function reached a statistical significance. The findings of cortisol and cognitive function aresimilar to previous findings (Beluche et al., 2009; Franz et al., 2011; Lee et al., 2007). In a 4-year follow up study, higher cortisolin the morning and throughout the day predicted worse executive function at follow-up but not for global cognitive function(Beluche et al., 2009).Also, in cross-sectional studies,executive function was significantly and positively associated with elevated cortisol throughout the day, but not global cognitive function(Franz et al., 2011; Lee et al., 2007). Although participants in other studies were far younger (50's) than our participants, cortisol consistently shows greater sensitivity for executive function than general cognitive function. Although reasons for this differential sensitivity of cortisol are not clear, the overall association of cortisol with cognitive function may be attributed to dysregulation of the HPA axis.Chronic exposure to elevated cortisol may increase neurotoxic effects in areas of the brain densely populated with glucocorticoid receptors, the hippocampus and pre-frontal cortex, thereby adversely affecting cognitive abilities (Sapolsky, Krey,& McEwen,1986).

Limitations

This study has several limitations. The cross-sectional research design limited the data analysis and interpretation to correlational associations between variables.The cohort was very homogenous and a majority of the participants were well-educated and economically comfortable Caucasian females withfew medical problems. Thus the findings of this studydo not adequately represent the general population. MMSE for general cognitive function showed a low Cronbach's α. Thus, the findings of this study should be interpreted with caution. Despite these limitations, we present several interesting insights on correlates of cognitive function in this very old elderly population, which can significantly contribute to the knowledge base of biobehavioral interactions in cognitive function.

Conclusion

Investigation on the relationships of psychosocial and biological variableswith cognitive function in an elderly population revealed that high stress and loneliness were significantly correlated with low global cognitive function and executive function. With increasing longevity, biobehavioral interactions and cognitive function will remain a significant area of research in the elderly. Future recommendations for research include,first, a need for diversifying the participants with diverse ethnicity, socioeconomic status, living environment, education, and age groups to better represent the general population. Secondly, other psychosocial and behavioral variablesneed to be examined for their relevance to overall or specific domains of cognitive function. In particular, loneliness seems to be a highly important and relevant factor for the aging population and a better understanding of this concept may provide more insight for potential future interventionsto improve cognitive health outcomes.Third, Longitudinal studies or randomized controlled experiments would allow assessment of trends over time and to determine the causal relationships between variables. Fourth, multiple samples over timewould allow more reliable biological responses for cumulative effects or a pattern over time. Lastly, measurement of variables should include careful consideration of reliability, accuracy, and sensitivity of psychometric measurements. Better understanding of biobehavioral contributions to cognitive function may reduce adverse burdens in the aging population.

Acknowledgements

This work was supported by grants awarded by Texas Nurses' Association District #9, and The Speros Martel Foundation.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Table 1: Characteristics of the Study Population (*N* = 71)

		N (%)	Mean	SD	Range
Age (yrs)		71	86.40	6.35	70 – 99
Gender	Males				
		16 (22.5%)			
	Females	55 (77.5%)			
Race					
	Caucasian	70 (98.6%)			
	Hispanic	1 (1.4%)			
Marital Status					
	Married	21 (29.6%)			
	Widowed	48 (67.6%)			
	Divorced	2 (2.8%)			
Education (yrs)		71	14.13	2.41	9 – 22
	<HS	3 (4.2%)			
	HS	27 (37.5%)			
	Associates	12 (18.1%)			
	Bachelors	22 (30.6%)			
	Graduate Education	7 (9.6%)			
Living Situation					
	Independent	66 (92.9%)			
	Assisted	4 (5.63%)			
	Extended Care	1 (1.4%)			
Time at Retirement Facility		71	55.3 mos (4.5 yrs)	57.7 mos (4.75 yrs)	.50 – 240 mos (.5 mos – 20 yrs)

Table 2: Descriptive data and Reliability of Instruments (*N* = 71)

	Possible Range	Score Range	Mean	SD	Cronbach α
Perceived Stress Scale	*0-40*	*0-28*	13.06	6.75	.76
Geriatric Depression Scale	0-15	0-8	2.75	2.24	.71
Revised-University of California at Los Angeles Loneliness Scale	20-80	22-64	35.14	8.35	.83
Mini Mental State Exam	0-30	23-30	28.39	1.79	.50
CLOX I	0-15	2-15	10.00	3.24	.86
Cortisol (μg/dL)	.09-1.55	.02-1.80	.23	.24	

Table 3: Correlation Coefficient for Psychosocial, Biological, and Cognitive Function Variables (*N* = 71)

	Stress	Depression	Loneliness	GCF	EF	Cortisol
Stress	1	.48**	.24*	-.25*	-.26*	-.12
Depression		1	.50**	-.07	-.11	.13
Loneliness			1	-.30*	-.40**	.02
GCF				1	.47**	-.20
EF					1	-.30*
Cortisol						1

Note. $^{**}p \leq .01$; $^{*}p \leq .05$ level; EF= executive function; GCF = global cognitive function