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Stress-related cognitive dysfunction in dementia caregivers

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SUMMARY

In a cross-sectional study, 31 dementia caregivers were compared to a group of 25 non-caregiving controls to evaluate whether the stress of being the primary caregiver of a person with dementia produces cognitive dysfunction. Cognitive differences were examined to evaluate the relationships between cognitive function and stress-related physiological and psychological measures to contribute information regarding its potential mechanism. The cognitive assessments were two measures of attention-executive function and one word-list memory task. Physiological and self-rated stress related measurements included cortisol, perceived stress, depression, self-efficacy, mindfulness, sleep quality, fatigue, and neuroticism. Caregivers performed worse than non-caregivers on the two attention tasks but not on the word-list memory test. There was no interaction of caregiver status and age on cognitive performance. The caregivers and non-caregivers differed in morning salivary cortisol and most of the self-rated stress related measures with the caregiver values reflecting greater stress. Of note, impaired sleep was the only potential mediator of the caregiver effect on cognitive performance in our small sample.

Keywords

dementia caregiver; chronic stress; cognition

INTRODUCTION

Alzheimer's disease (AD) and related dementias affect 4 million Americans and over 50% are cared for at home by family members or friends.¹ Older caregivers of relatives with any condition have worse psychological and physical health than non-caregivers.^{2, 3} More specifically, caregivers of persons with dementia (PWD) have greater self-rated stress, a higher incidence of depression, more physical symptoms, increased number of hospitalizations, and higher medication usage than non-caregivers.^{4–6} Older caregivers also have a higher mortality rate. Cognitive impairment in elder caregivers may impact their caregiving ability^{7, 8} and spouses of people with dementia, possibly independent of caregiving, have an increased incidence of dementia.⁹

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While acute stress has significant benefits including metabolic, immunologic and cognitive benefits, chronic stress is associated with impairments in health contributing to a broad range of diseases.^{10–12} “Stress” describes an event or condition that elicits a certain pattern of physiologic and behavioral responses with the brain being the critical interpreter of what is stressful.¹³ Physiologic responses to stress activate the hypothalamic-pituitary-adrenal axis and the locus coeruleus-norepinephrine-sympathetic nervous system pathways. From the human or non-human brain perspective, stress may cause cognitive decline, adverse effects in the hippocampus and prefrontal cortex, and contribute to neurodegenerative diseases either directly or through other stress mediators assessed by allostatic load.^{14–16}

Cognitive decline affecting speed, attention, and executive function occurs with stress and depression.^{17, 18} Negative effects of stress on cognitive function in aging have also been shown.^{18, 19} Cognitive tasks with a speed component, which is the case for many tests of attention and executive function, are also particularly sensitive to age.^{20, 21} However, the interaction between age and stress on cognitive function has not been well studied. Understanding the relationship of age and stress on cognitive function and the underlying cause of any stress-related cognitive changes independent of age would help physicians better understand the cognitive and daily functioning of dementia caregivers and potentially guide therapies that would help remediate these detrimental effects.

Cognitive function in dementia caregivers has been previously evaluated^{8, 22–24} even with a longitudinal study.⁶ However, only some of these studies used more than two cognitive assessments^{8, 23, 24}, which may contribute to understanding the mechanism of cognitive change. The preliminary explorations of potential mediators of this dementia caregiver effect on cognitive function has suggested several possibilities: depressed mood⁶, self-perceived distress²², hostility and metabolic risk factors.²⁴ Self-perceived sleep quality, however, has only partially been evaluated.^{22, 24} Additionally, neuroticism has not been included even though it correlates to dementia caregiver distress.²⁵ Although neuroticism is considered a personality trait, it is changeable with significant life events and has been shown to change with mind-body interventions.²⁶ The goal of this cross-sectional study was to evaluate the effect of dementia caregiving stress on cognitive function in older adults. The objectives were to determine: 1) which aspects of cognitive performance were affected by caregiver status and stress; 2) whether age interacted with the effect of stress on cognitive performance; and 3) which stress-related physiological and self-rated psychological measures may mediate the caregiver effect on cognitive performance.

METHODS

Participants

Participants were primary caregivers of a spouse or close relative with dementia or were control subjects. Participants were generally healthy, 45–85 years of age, and recruited from the Portland (Oregon) metropolitan area. Caregivers were recruited for a mindfulness meditation intervention study, the results of which have been reported.²⁷ The caregiver data reported here are pre-randomization baseline data. The controls were recruited to match the gender distribution and mean age of the caregivers. The study was approved by the OHSU Institutional Review Board, and all participants gave informed consent.

Exclusion criteria for both groups were:

1. score less than 25 on the Modified Telephone Interview for Cognitive Status²⁸;
- 2) significant medical or neurologic disease, such as major organ failure, insulin-dependent diabetes, alcoholism, or sleep disorder (e.g., sleep apnea), as determined by medical history records and interview;

2. significant, untreated depression, as assessed by Center for Epidemiologic Studies Depression Scale (CESD) score²⁹ greater than 16, medical history, and interview. Subjects with evidence of depression who were being treated with stable doses of serotonin reuptake inhibitors were not excluded;
3. use of certain medications known to affect CNS function or impact physiologic measures being collected for the intervention study (e.g., steroids or neuroleptics);
4. significant visual impairment (e.g., best-corrected visual acuity worse than 20/50 binocularly).

For the caregivers, the additional inclusion criteria were:

1. living with a close family member (spouse, sibling, or parent) PWD or providing more than 10 hours per week of care;
2. PWD diagnosed with progressive dementia;
3. agreeing to the intervention study protocol.

Measurements

One week before the lab visit, subjects were mailed the self-rated questionnaires so they could fill them out at their convenience (completion time < 60 minutes). Subjects who did not complete them at home could complete them during the lab visit. Questionnaires were reviewed for missing data and completed during the visit if necessary. Self-report questionnaires included stress, depression, fatigue, personality, self-efficacy, mindfulness, and sleep quality. The possible mediation measures were chosen because they are different between caregivers and controls, have been the subject of prior mediation analyses in this population, or were outcome measures of prior mind-body or caregiver intervention studies.

- *Self-rated Stress.* The Perceived Stress Scale (PSS)³⁰ was used as a measure of self-rated stress since its wide use will allow our results to be compared reliably to other studies.
- *Depression.* Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CESD).²⁹
- *Fatigue.* The SF-36 health-related quality of life Energy and Fatigue subscale³¹ (SF-36 Fatigue) was used. In addition to being a significant symptom among caregivers, this measure has changed with mind-body interventions in older adults.³²
- *Self-efficacy.* Self-efficacy was included because self-efficacy has been associated to anxiety (perceived stress) in caregivers undergoing a mindfulness intervention³³, depression in caregivers² and to pro-inflammatory cytokines in dementia caregivers.³⁴ The General Perceived Self-Efficacy Scale (GPSE), is a commonly used measure of self-efficacy³⁵
- *Mindfulness.* Two mindfulness questionnaires used in the intervention study assessed whether mindfulness is affected by caregiving and may mediate the caregiver effect on cognitive function: a measure of attention to the current moment, the Mindful Attention Awareness Scale (MAAS) (*mindfulness-current moment*); and Accept without Judgment subscale from the Kentucky Inventory of Mindfulness Skills (*mindfulness-non-judgmental*), a measure of how much the participant negatively criticizes their thoughts, feelings, experiences, or actions.³⁶ Each measure is a widely used and validated measure that corresponds to a factor from a factor analysis of mindfulness scales.³⁷

- *Sleep Quality.* Participants rated their overnight sleep quality using the Pittsburgh Sleep Quality Index (PSQI)³⁸, a highly reliable and widely used instrument to measure sleep quality during the previous month and to discriminate between good and poor sleepers. While there are objective sleep changes in dementia caregivers^{39, 40}, the PSQI has also demonstrated these changes.⁴⁰
- *Neuroticism.* Neuroticism was evaluated using the Neuroticism-Extraversion-Openness Five-Factor Inventory.⁴¹ Neuroticism has been shown to relate to caregiver distress in dementia caregivers.²⁵
- *Salivary cortisol.* Salivary cortisol was collected at home on awakening (cortisol am) and prior to sleep (cortisol pm) as performed in prior studies showing differences between dementia caregivers and controls.^{42, 43}

During the lab visit, inclusion and exclusion criteria were assessed, demographic information was collected, and cognitive tests were administered. Demographic data included gender, race, and, years of education. The subject's educational achievement level was assessed with the Wide Range Achievement Test (WRAT-3).⁴⁴ Additional data collected from caregivers were relationship to the PWD, the PWD diagnosis, and the activities of daily living subscale for the PWD.⁴⁵ The self-rated questionnaires were filled out at home. The cognitive tester, a research staff member who had observed doctoral level staff administering neuropsychological assessments and had over a hundred hours experience administering assessments before this study, was not blind to caregiver status.

Measures of cognitive function—Two tasks were chosen to focus on attention and executive function, domains thought to be most likely altered by stress, the Stroop Color and Word Test⁴⁶ and the Attention Network Task (ANT).⁴⁷ The Stroop Color and Word Test interference condition was used for analysis. The ANT is a computer-based attention task examining reaction times (RTs) on a flanker paradigm of 120 trials. Participants were instructed to push either a left or right button depending on the orientation of the central of the 5 chevrons presented at variable intervals. Stimuli were preceded half the time by a nonspecific cue (50% cue vs. 50% no cue). The direction of the 4 flanker chevrons presented simultaneously was in the same or different direction (50% congruent vs. 50% incongruent). The median RT to the hardest stimulus type (non-cued, incongruent) was used as the primary outcome measure of executive attention function on this task. In addition to the two attention-executive function tasks, the CERAD Word List Recall test⁴⁸ was used to evaluate participants' verbal memory. It consisted of 3 immediate recall trials of 10 words presented visually and read by the participants. The delayed recall trial was conducted 10 minutes following the last immediate trial and was used for the primary analysis. The cognitive assessment was limited to these three tasks to limit participant burden.

Analysis

The cognitive performance data used for analysis consisted of the Stroop conflict condition time, the ANT incongruent non-cued condition RT, and the correctly recalled words on the CERAD delayed recall. If the primary cognitive test measure was significantly different between groups, the other measures from the test (Stroop non-conflict condition and interference difference score, ANT cued and congruent conditions, and CERAD immediate recall) were also analyzed to ascertain the more specific cognitive component causing the stress-related decline. Other measures included were the demographic information, PSS, CESD-10, GPSE, the SF-36 Fatigue, PSQI, Neuroticism, mindfulness-current moment, mindfulness-non-judgmental, and salivary cortisol concentrations (am and pm).

Analyses were performed using Stata v11.0 (StataCorp LP, College Station, TX). Variables were inspected for normality, and Shapiro-Wilk testing was done. If the measure was not

normally distributed a transform was applied (log or square root). Initial group comparisons were done by t-test or, for gender, chi-square. Education and gender would be included in further analyses only if there were significant group differences. Cognitive function group differences were assessed using ANCOVA with age and age-squared, if significant, (the latter to allow for accelerated declines over the wide age range in this study) entered as covariates. The interaction between age and caregiving status was included in the ANCOVA. Since a separate analysis was performed for each of the 3 cognitive measures, a conservative overall Bonferroni correction was applied implying that any p value less than 0.017 ($0.05/3$) was considered significant and between 0.017 and 0.05 was considered borderline significant.

If the ANCOVA for cognitive function was significant for group, a simple mediation analysis was done. Given the small sample size and number of mediating factors being explored, only factors that were different in the two groups ($p < 0.05$ by ANCOVA) were used. The potential mediators were evaluated in a regression, only entering caregiver group, age, and the single mediator being evaluated. The potential mediators were the salivary cortisol and the self-rated questionnaires: PSS, CESD, SF-36 Fatigue, GPSE, PSQI, Neuroticism, mindfulness-current-moment and mindfulness-non-judgmental. Pearson's correlations were also calculated to describe the relationship between these variables.

RESULTS

The groups consisted of 31 dementia caregivers and 25 subjects who were not caregivers (controls). Groups were not different in terms of age, gender, or education (Table 1). Despite similar group mean age, age is entered into the analyses because of its known highly significant effect on the cognitive measures and the presence of significant simple correlations between age and the cognitive measures. Gender and education were not analyzed further because there were no a priori hypotheses about them concerning caregiving, and there were no significant effects of gender or education on the 3 cognitive measures after controlling for age in this small sample. Most of the participants were spouses, 23/31, and none of the caregiver offspring were men. In this small sample, the caregiving men were not significantly older than the women. For the same reasons as gender and education, no further analysis of relationship is done. Almost all data were obtained successfully – missing data (computer malfunction, lost forms, etc.) were simply omitted from the analyses. The diagnoses of the PWD were either Alzheimer's Disease or frontotemporal lobar degeneration. The mean (sd) Activities of Daily Living score was 7.0 (5.3).

The two groups were different in ANT performance ($p=0.006$), borderline different in the Stroop conflict condition time, ($p=0.03$) but not different on the CERAD delayed word-list memory task ($p=0.51$) (Table 2). Additional exploratory analysis was performed to determine if this caregiver status effect was related to an effect on simple processing speed. For the other three conditions on the ANT (cued-congruent, cued-noncongruent, and noncued-congruent), there was a significant effect of caregiving (all p 's < 0.05). The caregiving effect was not significant for the incongruent-congruent difference. However, for the Stroop task, there was no caregiving effect for the non-conflict condition, but there was an effect on the arithmetic difference between the conflict condition and the word-naming condition times ($p=0.03$). Word list was also further analyzed to look at the mean correct on the three immediate trials and the group differences were not significant, although borderline ($p=.06$).

Age and age-squared were significant covariates of the ANT performance (p 's < 0.05) However, there was no significant interaction between the age and caregiver effect. For the

Stroop, age as a covariate did not reach the significance level ($p=0.09$), but age-squared was significant ($p=0.03$). However, similar to the ANT, there was no significant interaction between age and caregiver status ($p=0.93$).

Most of the potential contributors or mediators of this caregiving effect were significantly different between the caregivers and controls ($p<0.05$) (Table 3a): awakening cortisol, PSS, CESD, SF-36 Fatigue, PSQI, Neuroticism, and mindfulness-non-judgmental. Self efficacy and mindfulness-current moment were not different between the two groups. The measures that were significantly different between the two groups (with uncorrected $p<0.05$) were highly correlated with each other (simple Pearson bivariate correlations in Table 3b). Further description of the analyses for Stroop and ANT follow. The verbal memory test is not described further since there was no significant group difference.

Awakening cortisol, PSS, CESD, Fatigue (SF-36), PSQI, NEO Neuroticism, and mindfulness-non-judgmental that had demonstrated group differences were entered into a simple mediation analysis taking each factor individually (Table 4). As can be seen in Table 4, entering only the PSQI had a significant impact on the p value for caregiver effect on ANT performance. A similar mediation analysis was also done for the Stroop task, even though the caregiver effect was only borderline significant. None of the potential mediators affected the significance of the caregiver effect on the Stroop other than the PSQI.

DISCUSSION

There was a significant effect of caregiver status on the incongruent flanker Attention Network Test (ANT) median reaction time after adjusting for age, even after a Bonferroni adjustment. There was no interaction between age and caregiver status on the reaction time. Finer analysis of ANT performance suggested that overall speed on this attention requiring task was the critical factor rather than the more specific executive function aspect as assessed by the incongruent-congruent RT difference. In addition, caregivers trended to perform worse on the Stroop Color-Word Test although this did not reach significance after Bonferroni adjustment. There was no caregiver effect on a word-list delayed recall task.

Most of the potential mediators, the self-rated measures and cortisol, were significantly different between caregivers and non-caregivers, and this is consistent with prior literature. Neuroticism and mindfulness-non-judgmental measures group differences have not been reported previously. While dementia caregiver neuroticism has been related to caregiver distress,²⁵ it has not been shown to be different than a control group. Mindfulness-non-judgmental showed group differences but other mindfulness measure based on attention to the current moment did not. We have observed the same pattern, changes in the mindfulness non-judgmental but not the mindfulness-current-moment measure, comparing veterans with and without post-traumatic stress disorder.⁴⁹

While other studies have reported differences in cognitive performance between caregivers of relatives with dementia and controls,^{6, 8, 22–24} only some directly compared the two groups using more than one measure of cognitive function.^{8, 23, 24} Our study observed a dementia caregiver status effect on speed, attention, and executive function in contrast to observing no effect on verbal memory. This differential effect is important since the pattern of cognitive deficits may give insight into the mechanism of the cognitive dysfunction. One study reported dementia caregiver changes in verbal memory, Auditory Verbal Learning Test, Stroop interference, and Letter Digit Coding Test although it did not report data from the Auditory Verbal Learning Test immediate delay.⁸

In addition, other studies of older caregivers, not specifically dementia caregivers, have had some similar observations. The large Nurses' Health Study observed a higher risk of low

performance of caregivers compared to noncaregivers on both the immediate and delayed recall components of the TICS 10-word list but no higher risk for low performance on the verbal fluency, immediate and delayed East Boston Memory Test, and Digit Span Backwards.²³ Palliative caregivers observed greater performance deficits using normative data in attention than memory tests.⁵⁰

In addition, despite cortisol and several self-rated psychological measures (CESD, Neuroticism, and Perceived Stress) being different in caregivers and controls and having significant correlations with each other, only sleep quality (PSQI) appeared to mediate the caregiver effect on cognitive function. While clearly exploratory in the case of Stroop effect, there were similarly no apparent mediators other than sleep quality. Of note, objectively measured and not just self-rated sleep quality has been demonstrated to be poorer in dementia caregivers compared to controls.^{40, 51, 52} One prior study evaluating mediators of a dementia caregiver effect on the Digit Symbol Test found that sleep disturbance, included as a composite distress measure component along with burden and affective questions, mediated the effect on cognitive change in caregivers.²² However, in a secondary analysis the sleep component, assessed by the Sleep Problems Questionnaire, a 4-question abridged version of the Sleep Disorders Questionnaire, did not appear to be a mediator. A later study by the same group also found no mediation of the cognitive function effect by the same sleep questionnaire.²⁴ The PSQI, a more widely used and current measure contains many more questions about sleep including daytime somnolence although it also includes some questions related to mood. Impaired sleep produces a relatively direct path to affect cognitive function since changes in alertness are known to produce changes in brain physiology as well as cognitive performance.^{53, 54}

The high correlation among many of these self-rated stress-related measures makes it difficult to make any definitive conclusions regarding depression. Some prior studies have observed a potential mediating effect of depression on cognitive function^{6, 8} but not others.²³ Further confounding the mediation analyses is depression, which is measured with questionnaires that often contain questions about sleep, and dementia care recipient cognitive status and behavior.⁵⁵ Although there is one report that depression may mediate the slowing of cognitive processing speed among caregivers,⁶ we did not observe any mediation of depression or morning cortisol.

There are other potential mediators of the caregiver effect on cognition. Two additional mediators of a longitudinal decline in dementia caregivers that we did not assess during our current study are hostility and metabolic risk.²⁴ Of note, in this longitudinal study these baseline measures were the same for caregivers and controls; the differences arose longitudinally. One study observed that hyperactivity in the care recipient and self-efficacy mediated the dementia caregiver effect on cognitive function.⁸ This study did not measure sleep quality and did not observe any baseline difference in depression between the two groups. A study of 16 older non-specific caregivers and 16 age-matched controls found psychological distress mediated the non-specific caregiver effect on cognitive function.⁵⁶ This global measure of distress included symptoms related to insomnia and severe depression.

The lack of caregiving status effect on verbal memory despite the effect on attention and executive function provides a speculative basis for explaining chronic caregiver stress-related cognitive change. This process may result in an increased longitudinal cognitive decline²⁴ and increased caregiver risk of dementia⁹, even if that higher risk is independent of caregiving per se.⁹ The neuropathology associated with dementia related to higher neuroticism, one measure of chronic stress, may be independent of the usual medial temporal Alzheimer pathology.⁵⁷ While depression, another psychological measure related

to stress, is known to increase the risk of dementia⁵⁸, its relationship to AD pathology is also less certain. The increased incidence of dementia associated with stress-related measures may be related to processes other than those related to amyloid.

There are several weaknesses to the study. Our preliminary findings in a small cross-sectional study need confirmation with future studies using a larger group and additional cognitive measures. A larger study with more power will better tease apart the stress-related psychological measures given their collinearity and the interactions such as with age and caregiving status. Covariance techniques can only partially account for the range in various functions over the wide age range. Different psychological constructs and additional biomarkers of stress may need be added into the assessment battery. Participants should include more men as well as under-represented populations. We did not control for education and gender in the analyses because of the lack of an effect on the cognitive measures in this small sample and lack of a priori hypotheses, even though education may correlate with stress in this population.⁵⁹ The small sample size also limited the ability to statistically explore the potential interactions of education, gender, and the relationship of the caregiver to the person with dementia to the cognitive measures. Dementia caregivers are difficult to recruit for extensive physiological and psychological studies since they already have very demanding time pressures. Therefore, dementia caregivers who volunteer to be participants in research may not be representative of all dementia caregivers. This is not an easily addressable issue, but the burden for study participation needs to be minimized and the potential gains to participants need to be increased (e.g., further classes, respite care, or monetary compensation) to broaden the profile of the recruited population. All cognitive testing was done in the research laboratory where dementia caregivers have lower perceived stress than at home in contrast to noncaregiver controls.⁶⁰ The cognitive tester was not blind to caregiving status. Of note the most significant group difference was for an automated computerized test and self-rated forms were filled out at home.

In summary, there are cognitive differences between caregivers and noncaregivers that involve timed and attention tasks more than delayed memory tasks. This study suggested perceived sleep quality was a mediator of this effect, although sleep as a mediator has not been consistent across prior studies. Whatever the mechanism, clinicians need to be aware of possible cognitive changes among caregivers since it may impact their ability to provide optimal care.⁷ This potential deleterious effect of caregiving highlights the pressing need for proper support and respite services to help caregivers cope with and reduce stress.

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Table 1

Demographics of caregivers and non-caregiver controls. *P* values are from ANOVA except for gender which is from chi-square.

Demographics	Dementia Caregivers	Controls	<i>p</i> -value
Number of subjects (# female, percent female)	31 (25, 80.6%)	25 (22, 88.0%)	0.46
Mean age (range, sd)	64.5 (46 – 81, 9.3)	66.5 (55–79, 7.6)	0.40
Mean Years of Education (sd)	16.4 (2.4)	16.4 (2.6)	0.95

Table 2

Cognitive performance on the three cognitive measures. Mean (Standard Deviation) and *p* value using ANCOVA. All three ANCOVAs had age, and age-squared if significant, entered as covariates.

Cognitive measure	Dementia Caregivers	Controls	<i>p</i> -value
Attention Network Test (ANT)(msec)	855 (123.0)	782 (118)	0.006
Stroop conflict condition time (sec)	224 (63.7)	202 (49)	0.03
CERAD Word-list (number of words)	6.8 (1.9)	7.1 (1.8)	0.51

Table 3a

Possible contributors/associations	Dementia Caregivers	Controls	<i>p</i> -value
Perceived Stress Scale (PSS) *	18.2 (7.0)	12.0 (6.8)	0.0016
Depression (CESD) **	15.8 (8.3)	12.5 (9.6)	0.0001
Fatigue (SF-36) **	9.5 (3.9)	13.4 (3.8)	0.0004
Sleep Quality (PSQI)	8.8 (3.2)	4.1 (1.9)	0.0001
Self-efficacy (GPSE)	30.5 (4.8)	32.1 (4.6)	0.24
Mindfulness – current moment	4.2 (0.7)	4.3 (0.7)	0.57
Mindfulness – non-judgmental **	21.8 (6.0)	27.4 (4.5)	0.0005
Neuroticism * (NEO)	19.1 (9.0)	12.8 (8.6)	0.01
Salivary cortisol (µg/dL, am) *	1.14 (.66)	0.66 (.40)	0.004
Salivary cortisol (µg/dL, pm)	0.35 (.48)	0.22 (.28)	0.35

Group differences in possible mediators of cognitive differences between caregivers and non-caregiver controls given as mean (std dev). *P* values are from ANOVA. Abbreviations and descriptions of measures are given in Methods section.

* is $p < 0.01$ and

** is $p < 0.001$

Table 3b

Zero-order correlations (r) between variables different in caregivers and controls

Possible mediators	CESD	Fatigue	Mindfulness	Neuroticism	Cortisol	PSQI
Perceived Stress (PSS)	.827***	-.665***	-.584***	.670***	.449**	.419**
Depression (CESD)		-.782***	-.500***	.528***	.425*	.562***
Fatigue (SF-36)			.355*	-.464***	-.239	-.507***
Mindfulness – non-judg.,				-.550***	-.147	-.401**
Neuroticism (NEO)					.444**	.265
Cortisol (am)						.271
Sleep Quality (PSQI)						

Zero-order correlations (r) between variables that were different in caregivers and controls.

* $p < 0.05$,
** $p < 0.005$,
*** $p < .0005$

Abbreviations and descriptions of measures are given in Methods section

Table 4

Potential mediation of the caregiving effect on ANT for the measures that were affected by caregiving

Possible mediators	Caregiver effect on ANT RT ^a	Caregiver effect on Stroop ^b
Perceived Stress Scale (PSS)	0.406 (.006)	.207 (.087)
Depression (CESD)	0.445 (.004)	.227 (.083)
Fatigue (SF-36)	0.494 (.001)	.217 (.089)
Sleep Quality (PSQI)	0.241 (.220)	.238 (.189)
Mindfulness – non-judgmental	0.388 (.013)	.254 (.037)
Neuroticism (NEO)	0.477 (.000)	.247 (.038)
Salivary cortisol (µg/dL, am)	0.478 (.007)	.333 (.035)

^a Mediator beta (*p* value); Effect on cognitive function without mediator beta .370, *p*=.006

^b Mediator beta (*p* value); Effect on cognitive function without mediator beta .240, *p*=.03

The caregiver effect from a regression on the ANT (left) and Stroop (right) for the potential mediators that were significantly different in the two groups from Table 3a. Sleep quality changed the *p* values for both and none of the others clearly did.