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Long-term caregiving is associated with impaired cardiovagal baroreflex

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ABSTRACT

Objective: Caregiving stress is associated with increased risk of cardiovascular disease (CVD). Inability to adequately regulate blood pressure is a possible underlying mechanism explaining this risk. We examined the relationship between length of caregiving and cardiovagal baroreflex sensitivity (cBRS) to better understand the link between caregiving and CVD risk.

Methods: A total of 146 elderly individuals (≥ 55 years) participated in this study, of whom 96 were providing in-home care to a spouse with dementia and 50 were healthy controls married to a non-demented spouse (i.e., non-caregivers). Among the caregivers, 56 were short-term caregivers (caring < 4 years) and 40 were long-term caregivers (caring ≥ 4 years). A multiple linear regression model, with contrast codes comparing short and long-term caregivers with non-caregivers was used to understand relationships between chronic caregiving and cBRS.

Results: After controlling for relevant demographic and health characteristics, mean ± SE log transformed cBRS for non-caregivers was 0.971 ± 0.029. Relative to non-caregivers, the long-term caregivers had significantly impaired cBRS (0.860 ± 0.033; $p = 0.013$). However, mean cBRS for short-term caregivers did not significant differ from non-caregivers (0.911 ± 0.028; $p = 0.144$).

Conclusion: These results suggest that long-term caregiving stress is associated with an impaired cBRS. Accumulation of stress from years of caregiving could result in worse cBRS function, which could be a mechanistic explanation for the correlation between caregiving stress and the increased risk of CVD.

1. Introduction

Caring for a spouse with dementia is often a burdensome life stressor with well-established links to psychological [1,2] and physical health morbidity [3,4]. Increased risk for cardiovascular disease (CVD) is believed to be one of the most likely health consequences resulting from the chronic stresses of caregiving. The link between caregiving stress and increased risk for coronary heart disease (CHD) [5,6],borderline hypertension [7], and other cardiovascular diseases [8] has been well documented in the literature.

Although the biological pathways from stress to CVD are not fully understood, one important mechanism could involve an impaired baroreflex function. The baroreflex is the negative feedback mechanism that plays a central role in acute as well as chronic regulation of blood pressure by modulating parasympathetic outflow to heart and sympathetic outflow to blood vessels. Increases in blood pressure will stretch mechanoreceptors embedded in the adventitia of the carotid sinuses and aortic arch, which will send action potentials via afferent fibers in the glossopharyngeal and vagus nerve to the nucleus tractus solitarius in the medulla. In turn, baroreflex-mediated reciprocal changes are triggered in efferent vagal and sympathetic activity. Vagal response is quick, which allows beat-to-beat heart rate adjustment [9]. Cardiovagal baroreflex sensitivity (cBRS) was used in this study to assess the parasympathetic (i.e. cardiac) limb of the baroreflex. Because parasympathetic nerve endings are concentrated in atria and AV node, they are particularly important for the regulation of heart rate and rhythm. CVDs are associated with decreased parasympathetic nervous system (PNS) regulation [10]. Notably, patients with recent myocardial

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Table 1
Demographic and health characteristics of the study participants.

Variables	Non-caregivers (N = 50)	Short-term caregivers (N = 56)	Long-term caregivers (N = 40)	F	χ^2	p
Age in years, mean ± SD	74.3 ± 5.9	72.9 ± 7.8	74.4 ± 8.2	0.63		0.53
Female, n (%)	36 (72.0)	43 (76.8)	31 (77.5)		0.46	0.79
Race					2.01	0.37
White Non-Hispanic, n (%)	40 (80.0)	50 (89.3)	35 (87.5)			
Other, n (%)	10 (20.0)	6 (10.7)	5 (12.5)			
Years of education, mean ± SD	15.8 ± 2.9	14.9 ± 3.1	15.3 ± 3.1	1.12		0.33
Body mass index, (kg/m^2) mean ± SD	26.0 ± 6.2	26.9 ± 4.8	25.8 ± 4.9	0.58		0.56
Taking anti-hypertensive meds, n (%)	26 (52.0)	30 (53.6)	23 (57.5)		0.28	0.87
Ever smoked, n (%)	20 (40.0)	28 (50.0)	15 (37.5)		1.79	0.41
CDC-recommended Exercise, n (%)	23 (46.0)	16 (28.1)	14 (34.2)		3.79	0.15
History of CVD, n (%)	3 (6.0)	8 (14.3)	8 (20.0)			0.13[a]
Resting heart rate, (BPM) mean ± SD	65.1 ± 9.6	67.7 ± 9.2	64.4 ± 9.5	1.69		0.19
Systolic blood pressure (mm Hg), mean ± SD	133.1 ± 16.3	132.4 ± 15.4	137.8 ± 16.1	1.47		0.23
Diastolic blood pressure (mm Hg), mean ± SD	72.3 ± 10.8	75.0 ± 8.3	77.5 ± 9.1	3.29		0.04

[a] Fisher's exact test.

infarction tend to have a lower cBRS and higher risk of developing fatal arrhythmias [11]. Even without history of cardiac events, middle aged people with cBRS lower then 3 ms/mm Hg have nine times greater risk of cardiac death compared to those with cBRS > 3 ms/mm Hg [12,13]. Given the studies that caregiving stress is associated with increased cardiovascular risk, a blunted cBRS may help explain higher risk of cardiovascular events in caregivers.

While caregiving is associated with increased psychological stress, the duration of exposure to the stress of caregiving may be associated with ever worsening cBRS. That is, the longer the individual is caregiving, the more blunted the cBRS becomes. Repeated exposure to stress has been shown to both accelerate atherosclerotic processes such as sympathetic reactivity [14,15], coagulation [16,17], and platelet activation [15] and induce frequent blood-pressure spikes [18] damaging the elastic fibers of the carotid arch and aortic sinus. These processes may reduce arterial compliance, thereby reducing distensability of the vessels and reducing the baroreceptors' ability to detect changes in blood pressure [19–21]. Additionally, functional magnetic resonance imaging (fMRI) studies have demonstrated that repeated SNS activation by chronic stress can reduce the sensitivity of supramedullary (cingulate cortex, insula, amygdala, and midbrain periaqueductal gray) control of the baroreflex [22]. Stress appears to dysregulate neural signals transmitted from these upper level brain structures to brainstem nuclei involved in autonomic cardiovascular control, thus blunting the cBRS. Therefore, it is reasonable to believe that long-term caregiver stress may lead to a blunted cBRS.

The aim of the current analysis was to evaluate the impact of the duration of stress exposure on cBRS function in three groups of elderly individuals: 1) long-term caregivers (≥ 4 years), 2) short-term caregivers (< 4 years), and 3) non-caregiver controls. We used 4-years as our cutoff for short vs long-term caregivers for two reasons: a) epidemiologic national sampling reports show that the average length of caregiving is 4.0 years [23], and b) we wished to remain consistent with our previous study examining the relation between length of caregiving and endothelial function in caregivers [24], where longer-term caregiving was associated with worsened endothelial function in this population. Because repeated exposure to stress has previously been shown to accelerate the atherosclerotic process, we hypothesized that long-term dementia caregivers will demonstrate the greatest cBRS blunting relative to short-term caregivers and non-caregivers. Because short-term caregivers have not experienced the extended years of stress accumulation like long-term caregivers, our second hypothesis was that short-term caregivers would show preliminary evidence of blunted cBRS function, compared to non-caregiver controls.

2. Methods

2.1. Study sample

One hundred forty-six elderly individuals participated in this study. These participants were enrolled between 2007 and 2012 into the University of California, San Diego (UCSD) “Alzheimer's Caregiver Study”. The study protocol was approved by the UCSD Institutional Review Board (IRB). Participants were recruited through referrals, the UCSD Alzheimer's Disease Research Center, support groups, senior care centers, and health fairs. Of these participants, 96 were providing care to a spouse with Alzheimer Disease (AD), and 50 were married to a non-demented, healthy spouse (i.e., non-caregivers). Among the caregiver sample, 56 had been providing care for fewer than 4 years (i.e., short-term caregivers), and 40 had been caring for ≥ 4 years (i.e., long-term caregivers). All participants provided formal written consent to participate in this study.

To be included in the study, caregivers were required to be providing in-home care to a spouse with dementia at the time of enrollment. Non-caregivers were required to be married to a healthy spouse free of any disease requiring care. All participants were required to be at least 55 years of age. Participants were asked to report all medications they were taking. These medications were reviewed and coded for whether or not they had anti-hypertensive properties (yes = 1, no = 0), since use of anti-hypertensives have been known to have effects on the cBRS. Participants were excluded if they were receiving current treatment for malignancies other than skin cancers or benign tumors, had severe chronic illnesses requiring ongoing medical treatment (e.g., heart failure, COPD, renal failure, or major psychiatric illnesses such as schizophrenia or bipolar disorder), used oral or parenteral steroids, had severe hypertension (> 200/120 mm Hg), or were receiving treatment with anti-coagulant or beta-blocking medications. A diagnosis of major depressive disorder or use of non-dihydropydirine calcium channel blockers were not exclusion criteria.

Demographic and health characteristics of the participants, by caregiving group, are presented in Table 1. Statistical comparisons of the non-caregivers, short-term caregivers, and long-term caregivers indicated these groups did not significantly differ on any demographic or health characteristics except diastolic blood pressure (F = 3.29, p = 0.04), whereby Tukey's HSD post-hoc tests indicated that long-term caregivers had significantly higher DBP compared to non-caregivers (p = 0.01). Normality tests revealed that BMI and cBRS values were significantly positively skewed (p = 0.001). Both variables were transformed using log transformation which resulted in an approximately normal distribution.

We categorized antihypertensive medications into classes and summarized the frequency of participants who were taking each type of