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A 5-year longitudinal study of the relationships between stress, coping, and immune cell β_2-adrenergic receptor sensitivity

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Abstract

Caring for a spouse with Alzheimer's disease (AD) is associated with overall health decline and impaired cardiovascular functioning. This morbidity may be related to the effects of caregiving stress and impaired coping on β_2-adrenergic receptors, which mediate hemodynamic and vascular responses and are important for peripheral blood mononuclear cell (PBMC) trafficking and cytokine production. This study investigated the longitudinal relationship between stress, personal mastery, and β_2-adrenergic receptor sensitivity assessed in vitro on PBMC. Over a 5-year study, 115 spousal AD caregivers completed annual assessments of caregiving stress, mastery, and PBMC β_2-adrenergic receptor sensitivity, as assessed by in vitro isoproterenol stimulation. Heightened caregiving stress was associated with decreased receptor sensitivity ($P = 0.009$) whereas greater sense of personal mastery was associated with increased receptor sensitivity ($P = 0.038$). These results suggest that increased stress may be associated with a desensitization of β_2-receptors, which may contribute to the development of illness among caregivers. However, increased mastery is associated with increased receptor sensitivity, and may therefore serve as a resource factor for improved health in this population.

Keywords

Personal Mastery; Overload; Health; Resource Factors

1. Introduction

A growing body of literature demonstrates detrimental health effects from caring for a loved-one with Alzheimer's disease (AD) (Shaw et al., 1997). For example, this care has been associated with increased likelihood of developing hypertension (Shaw et al., 1999), elevated sympathetic arousal (Irwin et al., 1997), increased risk for cardiovascular disease (Lee et al.,

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2003; Mausbach et al., In Press-b), and worsened immune system functioning (Kiecolt-Glaser et al., 1991; Kiecolt-Glaser et al., 1996; Kiecolt-Glaser et al., 1995; Kiecolt-Glaser et al., 2003). Each of these harmful effects provide potential mechanisms by which caregivers are at increased risk for mortality compared to non-caregivers (Schulz and Beach, 1999).

While the mechanisms associated with physical morbidity in caregivers are complex, a number of studies have examined the relationship between stress and peripheral blood mononuclear cell (PBMC) β_2-adrenergic receptor functioning (Dimsdale et al., 1994; Mausbach et al., In Press-a; Mills et al., 2004; Redwine et al., 2004). Among other functions, the β_2-adrenergic receptor mediates vascular smooth muscle relaxation (Fitzgerald and Goldfien, 2004), resulting in vasodilation. A number of authors have speculated that blunted β_2-adrenergic receptor sensitivity paired with unaffected or enhanced α-adrenergic sensitivity may contribute to the development of hypertension (Bertel et al., 1980; Cleophas and Kauw, 1994; de Champlain et al., 1989). Such an imbalance could potentially increase peripheral resistance resulting in elevated blood pressure. It is possible that a simultaneous desensitization of vascular alpha- and vascular beta-adrenergic receptors could leave blood pressure relatively unchanged, although alpha-adrenergic receptors are typically more resistant to desensitization and/or down-regulation than beta-adrenergic receptors, thus leaving this potential scenario not frequently observed (Zhao et al., 1996). Moreover, research suggests that, among the elderly, hypertension may exhibit a differential physiological profile. Specifically, previous research has found that aging tends to be associated with a profile of low cardiac output combined with heightened total peripheral resistance, as well as reduced beta-adrenergic sensitivity (Feldman et al., 1984; Kawamoto et al., 1989; Sowers, 1987).

In addition to playing a role in the development of vascular reactivity and hypertension, β_2-adrenergic receptors aid in the production of cytokines, which influence not only immune cell function but also other processes including glial cell proliferation (Giulian and Lachman, 1985) and neuron survival (Schwartz et al., 1991). Further, β_2-adrenergic receptors aid in the regulation of T-cell and natural killer cell functioning (Kohm and Sanders, 2001). β_2-adrenergic receptors play an important role in healthy immune system functioning and a blunting of the β_2-adrenergic receptors can result in both cardiovascular and immune system destabilization, potentially increasing caregivers' risk for a number of health consequences (Schulz and Beach, 1999; Shaw et al., 1997).

Desensitization of β_2-adrenergic receptors may occur by way of excessive activation of the autonomic nervous system via caregiving stress (Kohm and Sanders, 2001; Kühlwein et al., 2001). Indeed, Alzheimer caregivers, especially if they are distressed, are prone to exhibit exaggerated sympathetic arousal (Mausbach et al., 2005) and reduced β_2-adrenergic receptor sensitivity (Mausbach et al., In Press-a; Mills et al., 1997). Cross-sectional studies by Mills and colleagues (Mills et al., 2004; Mills et al., 1997) have demonstrated associations between stress, sympathoadrenomedullary (SAM) arousal, and β_2-adrenergic receptor sensitivity in AD caregivers. Previous research in other populations further confirms the link between increased SAM tone and decreased β_2-adrenergic receptor sensitivity and density (Bertel et al., 1980; Fraser et al., 1981; Sztajzel et al., 2006). As a whole, these data suggest the possibility that the stresses of caregiving may be associated with SAM hyperarousal and concomitant β_2-adrenergic receptor desensitization.

Although stress, particularly chronic stress such as seen in caregiving, may potentially impact vascular and immune system functioning, recent data suggest that positive coping factors may help maintain general well-being and possibly protect against deleterious effects of stress. For example, longitudinal studies among caregivers suggest that coping strategies are related to long-term mental and physical health benefits (Dimsdale et al., 1994; Goode et al., 1998; Hooker et al., 2002; Strang and Haughey, 1999). One coping factor receiving increased

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attention has been personal mastery. This construct represents an individual's belief that he/she can control the circumstances of his/her life (Pearlin and Schooler, 1978). Mastery likely exerts its benefits via initiation of positive behaviors in the face of environmental and psychological stressors. A greater sense of mastery has been associated with improved psychological (Boss et al., 1990; Hobfoll et al., 2003; Semple, 1992) and physical health (Lachman and Weaver, 1998), reduced risk for mortality (Penninx et al., 1997), and restored β_2-adrenergic receptor sensitivity (Mausbach et al., In Press-a). While these studies point to the importance of mastery in one's overall health, they are largely cross-sectional in nature. In addition to the study by Penninx (1997), one recent longitudinal study found hat mastery was associated with reduced longitudinal risk for disability among women (Penninx, 2000), while another found a positive effect of mastery on both mental and physical health outcomes in Alzheimer caregivers (Mausbach et al., In press-c). Longitudinal examination of the relations between stress, coping, and β_2-adrenergic sensitivity are therefore needed to illuminate the potential mechanisms underlying the development of health problems among elderly individuals under stress (e.g., cardiovascular disease) and to explore coping factors which may prevent such outcomes from manifesting.

The purpose of this study was to examine the longitudinal relations between stress, coping, and β_2-adrenergic receptor sensitivity in a sample of 115 spousal caregivers of individuals with Alzheimer's disease. Based on previous cross-sectional evidence showing a negative relationship between stress and β_2-adrenergic receptor sensitivity, we predicted that decreased receptor sensitivity would be associated with increased reports of stress over time. Alternatively, given our previous cross-sectional finding that higher levels of mastery are associated with increased β_2-adrenergic receptor sensitivity, we predicted a positive relationship between β_2-adrenergic receptor sensitivity and mastery over time.

2. Methods

2.1. Participants

Participants were 115 spousal caregivers of patients with AD who were enrolled in a study examining the psychobiological effects of stress. Caregivers were primarily elderly (mean age = 72.6 ± 8.8 years), female (68.7%), and Caucasian (92.2%). The duration that caregivers had been providing care when they enrolled ranged from 4 months to 15 years.

Inclusion/exclusion criteria included provision of in-home care to a spouse with a documented diagnosis of Alzheimer's disease, minimum age of 55 years, not taking β_2-adrenergic blocking medication, not using steroids, and not having severe hypertension as indicated by a blood pressure greater than 200/120 mm Hg.

2.2. Procedures

Our study protocol was approved by the UCSD Institutional Review Board (IRB). Prior to enrolling in the study, a research nurse met with study participants in their homes to obtain informed consent. Following consent, nurses conducted a structured interview with caregivers to obtain background and demographic characteristics and to assess both physical and psychological health. Following this interview, nurses obtained venous blood via a catheter in the participants' non-dominant forearm. Standard procedure for our blood draw was to draw blood approximately 14-minutes after the catheter was inserted. This assessment protocol was repeated every twelve months over a 5-year study period.

2.3. Measures

2.3.1. β-adrenergic receptors—β_2- adrenergic receptor sensitivity was determined on PBMC's (Mausbach et al., In Press-a; Mills et al., 1995; Mills et al., 2002). β_2-adrenergic

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receptor sensitivity on immune cells is considered a mirror of beta-activity on the vasculature (Fraser et al., 1981). PBMC's were suspended in cold Dulbecco's Modified Eagle's Medium (DMEH). Incubations in triplicate were begun by adding 0.1 ml of approximately 2×10^5 cold cells to 0.9 ml of 37°C DMEH containing 100 mmol/L isobutylmethylxanthine (IBMX) to inhibit cyclic nucleotide phosphodiesterase activity. Half of the tubes also contained 10 μM isoproterenol. Once the reactions were terminated, the tubes were frozen and later assayed for cyclic-AMP (Perkin Elmer, Boston, MA). Basal, non-stimulated cyclic-AMP was also determined. Isoproterenol, acting via the β-adrenergic receptor, typically causes an approximate three- to five-fold increase (over basal) in intracellular cyclic-AMP levels. The ratio of isoproterenol-stimulated cyclic AMP to basal non-stimulated cyclic AMP was taken as the index of β_2-adrenergic receptor sensitivity. We use the word “sensitivity” to denote how responsive the beta receptor is to stimulation with isoproterenol. Isoproterenol stimulation leads to activation of the beta-adrenergic receptor - Gs protein - adenylate cyclase complex. A sensitized or “coupled” receptor denotes that the beta receptor is coupled to the Gs protein which, upon stimulation, enables adenylate cyclase activation and cyclic AMP generation. A desensitized or uncoupled receptor cannot generate a cyclic AMP response.

2.3.2. Stress and mastery—Caregivers were administered 4 measures assessing multiple domains of caregiving stress. The first was the Pearlin Role Overload scale (Pearlin et al., 1990), which is a 4-item measure of overall subjective stress. Participants rate how much they agree with each of the 4-items (e.g., “You work hard but never seem to make any progress; “You have more things to do than you can handle”) on a 4-point scale with 1 = “Not at all” and 4 = “Completely”. A total score was created by summing the 4 items. Cronbach's alpha for the current sample was .77.

The second stress measure was the Pearlin Problem Behaviors scale (Pearlin et al., 1990), which assessed the number of care recipient problem behaviors (max = 13) the caregiver dealt with over the past week (e.g., “Try to dress the wrong way”; “Repeat questions or stories”). Responses ranged from 1 = “no days” to 4 = “5 or more days”. Scores were summed, and Cronbach's alpha was .74 for the present sample.

Care recipient dependency for activities of daily living (ADLs) was assessed using Pearlin's ADL scale (Pearlin et al., 1990). Caregivers rated how much their care recipients depended on them for each of 15 activities (e.g., eating, dressing, using the phone). Responses were given on a Likert scale ranging from 1 = “not at all” to 4 = “completely”. Cronbach's alpha for the current sample was .91.

A single-item assessed the average number of hours per day caregivers felt they were “on duty” during the past 6 months. Responses were as follows: 0 = None (0 hours per day); 1 = Little (1 to 6 hours per day); 2 = Some (7 to 12 hours per day); 3 = A lot (13 to 18 hours per day); 4 = Constant (19 to 24 hours per day).

Personal mastery was assessed using Pearlin's 7-tem Mastery scale (Pearlin and Schooler, 1978). Caregivers indicated the extent to which they agreed or disagreed with each item (e.g., “I can do just about anything I set my mind to do”), with 1 = “Strongly agree” to 4 = “Strongly disagree”. A total score was created by summing individual responses. Alpha reliability for this sample was .68.

2.3.3. Caregiver Depression—A trained research nurse administered the Hamilton Depression Rating Scale (HAM-D)(Hamilton, 1960) to all caregivers. The HAM-D consists of 17 items and is administered via a semi-structured interview. The scale is a valid and reliable measure of depressive symptoms (O'Hara and Rehm, 1983). Scores for the individual items

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range from 0 to 2 or 0 to 4, and a total depression score (maximum score = 54) is created by summing the scores for the 17 items.

2.3.4. Medical data—We collected additional medical information that was potentially related to β-adrenergic sensitivity. Systolic and diastolic blood pressure was obtained in triplicate by a trained research nurse using a Critikon Dinamap 8100 adult/pediatric noninvasive blood pressure monitor. Using the average of these blood pressure measurements, we calculated mean arterial pressure (MAP) as (2/3 * diastolic BP) + (1/3 * systolic BP). In addition, nurses interviewed the participants to obtain an interim medical history (IMED), as used in previous studies (Aschbacher et al., 2006; Mausbach et al., 2006a; Shaw et al., 1997). Participants rated whether or not they had experienced medical symptoms associated with 14 major systems during the past 6 months. Total number of "yes" responses is summed to create an overall health score, with scores ranging from 0-32.

2.4. Data analysis

Because caregiving stress is not confined to one domain, and because of potential problems resulting from multicollinearity between covariates in multilevel models (Shieh and Fouladi, 2003), we created a composite score of caregiving stress using principal components analysis of our four stress measures. This analysis indicated all four stress measures loaded on one factor and accounted for 58% of the total variance. This factor (hereafter "stress") was saved as a z-score for use in our primary analysis. Weights for the four individual factors were as follows: a) role overload = .186, b) problem behaviors = .339, c) ADLs = .368, and d) hours of care = .378. Change in β_2-adrenergic receptor sensitivity over time was evaluated using linear mixed-effects regression models. Because of skewness, β_2 receptor sensitivity values were $\log_{10}$ transformed. Time was entered as a linear variable with '0' corresponding to baseline scores. Models included main effects for time (years), sex, age, and time-varying values for mastery, stress, medical symptoms, and mean arterial pressure. To account for longitudinal within-subject correlations, our model included random intercepts and random slopes. We further tested the fit of including two-way interactions between time and time-varying scores for mastery and stress, but these interaction terms provided a worse model fit as per Akaike's Information Criteria (AIC), and were therefore dropped from our model.

3. Results

Baseline demographic and health characteristics of the sample are presented in Table 1. Over the course of the study, 5 assessments were made. Dropout information is as follows: Of the 115 participants enrolled in the study, 97 were assessed at the 1-year follow-up; 74 at the 2-year follow-up; 34 at the 3-year follow-up; and 11 at the 4-year follow-up.

3.1. Primary Analysis

Prior to conducting or primary analysis, we examined whether our primary outcome and our two primary predictor variables (i.e., stress and mastery) for significant within-person variability across time. Specifically, we conducted unconditional means models for mastery, stress, and beta-2 receptor sensitivity, respectively. For these analyses, we examined the significance of the "within person" variance to determine if within-person variation existed across time. Results indicated that all three variables exhibited significant within person variance (all p-values < .001). Examination of the within-person and between-person variance components indicated that for mastery, 36.7% of the total variability was within person; for stress, 51.4% was within person, and for receptor sensitivity, 97.1% was within person.

Results of the mixed-linear model analysis are presented in Table 2. As seen, β_2-adrenergic receptor sensitivity decreased significantly over the 5-year study period (t = -2.95, df = 41.68,

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$P = 0.005$). In addition to the effect of time, caregiver stress ($t = -2.64$, $df = 174.76$, $P = 0.009$) was negatively associated with receptor sensitivity. In contrast to the effects of stress, personal mastery had a positive relationship to receptor sensitivity ($t = 2.09$, $df = 153.40$, $P = 0.038$), whereby greater reports of mastery were associated with higher receptor sensitivity. As was expected, greater MAP was significantly related to reduced receptor sensitivity ($P = 0.046$). Because each of these covariates was time-varying, changes in β_2-adrenergic receptor sensitivity in any given year were associated with changes in these covariates. For example, during years when mastery was high and stress was low, participants would see notable increases in receptor sensitivity. Likewise, during years when mastery was low and stress was high, receptor sensitivity was considerably reduced.

3.2. Secondary Analyses

Given that changes in β_2-adrenergic receptor sensitivity differentially affect systolic (SBP) and diastolic (DBP) blood pressure, we conducted two post-hoc analyses to determine the relationship between time-varying values of systolic and diastolic pressure and β_2-adrenergic receptor sensitivity, and to determine if our stress and mastery variables remained significant while controlling for SBP and DBP, respectively. For these analyses, we replicated our primary analysis but replaced MAP with SBP and DBP, respectively. Results of these analyses indicated that SBP was not a significant predictor of β_2-adrenergic receptor sensitivity ($t = -1.16$, $df = 179.43$, $P = 0.246$). However, there was a significant relationship between DBP and β_2-adrenergic receptor sensitivity, whereby increased DBP was associated with reduced β_2-adrenergic receptor sensitivity ($t = -2.29$, $df = 180.74$, $P = 0.023$). In both of these analyses, stress and mastery remained significant predictors of β_2-adrenergic receptor sensitivity.

Because many caregivers suffer from elevated depressive symptoms, we conducted an additional analysis that included time-varying depressive symptoms (i.e., HAM-D scores) as a predictor of beta-2 adrenergic receptor sensitivity. Results of this model indicated that depressive symptoms were not significantly related to receptor sensitivity ($P = 0.622$). However, mastery remained a significant predictor ($P = 0.036$).

According to the Stress Process Model (Aneshensel et al., 1995; Pearlin et al., 1990), caregivers experience both primary objective (e.g., care recipient problem behaviors and memory loss) and subjective stressors (e.g., overload). These concepts have important conceptual differences that may differentially affect beta-2 adrenergic receptor sensitivity. Therefore, we conducted 2 additional analyses examining the association between receptor sensitivity and subjective stress (i.e., role overload z-score) and objective stressors (i.e., a component consisting of problem-behaviors, ADLs, and level of direct care provided), respectively. In these analyses, we retained all covariates described above. Results of the first analysis indicated that subjective stress (i.e., overload score) was not significantly associated with receptor sensitivity (coefficient = -0.05, $P = 0.168$), whereas mastery remained a significant predictor (coefficient = 0.01, $P = 0.035$). In the second analysis, both objective stress (coefficient = -0.06, $P = 0.01$) and mastery (coefficient = 0.01, $P = 0.03$) were both significantly associated with receptor sensitivity.

4. Discussion

Over a five-year longitudinal study, elderly dementia caregivers exhibited age-independent decreases in β_2-adrenergic receptor sensitivity. Furthermore, increases in caregiver stress and decreases in personal mastery were associated with reduced receptor sensitivity. These longitudinal findings are consistent with our previous cross-sectional study on the relations between stress, mastery, and β_2-adrenergic receptor sensitivity (Mausbach et al., In Press-a), and further strengthen a mechanistic understanding on how stress and mastery may each be associated with health-related outcomes (Mausbach et al., 2007; Mausbach et al., 2006b;

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Penninx et al., 1997; Shaw et al., 1997). Specifically, because declining β_2-adrenergic receptor sensitivity on immune cells is considered a mirror of beta-activity on the vasculature (Fraser et al., 1981), β_2-adrenergic receptor sensitivity may constitute a mechanism by which stress-related sympathetic hyperarousal is translated into impaired vascular responsivity, potentially contributing to the development of hypertension (Bertel et al., 1980). Also, because β_2-adrenergic receptors are important for PBMC trafficking and for cytokine production (Mills et al., 1999; Sanders and Straub, 2002), these results provide one possible mechanisms by which some caregivers are susceptible to illness (Schulz and Beach, 1999; Schulz et al., 1995; Shaw et al., 1997).

With regard to hypertension, healthy vascular functioning requires a synergistic balance between sympathetically-mediated vasoconstriction and vasodilation. Vascular tone is controlled by both local and hormonal mechanisms, with the latter governed primarily through the opposing effects of alpha-adrenergic (vasoconstrictive) and beta-adrenergic (vasodilating) receptors (Hjemdahl et al., 1979; Widmaier et al., 2006). When β_2-adrenergic receptors are desensitized, this would imply a corresponding decrease in the ability of blood vessels to vasodilate under stress (Fitzgerald and Goldfien, 2004). As the stresses of caring for a terminally ill spouse increase, decreases in beta-mediated vasodilation could potentially contribute to an increased risk of hypertension among caregivers. Indeed, we found that reduced β_2- adrenergic receptor sensitivity was associated with elevated blood pressure, and this relationship appeared more specific to diastolic blood pressure. Several other researchers have supported the notion that relative enhancement of alpha-adrenergic over beta receptor functioning is associated with sympathetic hyperarousal and hypertension among elderly individuals (Sowers, 1987; Supriano et al., 1999). Elderly hypertensives appear to exhibit significantly lower β_2-adrenergic receptor sensitivity relative to age-matched non-hypertensives (Kawamoto et al., 1989). The findings of the current study are consistent with previous research supporting a link between psychological stress, resiliency, blood pressure, and β_2-adrenergic receptor sensitivity (Mills et al., 2004).

The significant associations between β_2-adrenergic receptor sensitivity and both stress and mastery raise the question of whether interventions to increase mastery and reduce stress among caregivers might reverse down-regulation of β_2-adrenergic receptor sensitivity. Mastery, if conceptualized as a dynamic, changing factor in response to interactions with one's environment (i.e., to caregiving tasks), could be theoretically altered through psychosocial interventions. Indeed, previous literature suggests that psychosocial interventions for caregivers which include cognitive (e.g., altering negative thoughts/appraisals) and behavioral (e.g., increasing exposure to pleasurable stimuli) components indeed produce positive changes to one's sense of control (Coon et al., 2003). Whether or not such interventions would result in changes in physiology or ultimate cardiovascular outcomes is as yet unknown.

The current study expands upon previous research by demonstrating a significant relationship between objective caregiving stressors (e.g., care recipient problem behaviors and ADL dependencies) but not subjective stressors (i.e., role overload). These results may suggest that objective stressors play a more important role in health outcomes for caregivers, particularly beta receptor sensitivity, and targeting of these outcomes via interventions may be warranted. However, it should be noted that the coefficients for subjective (-0.05) and objective stressors (-0.06) were almost equivalent in relation to beta receptor sensitivity, suggesting greater error in subjective stress over the course of the study may have played a part in this difference. More research on these conceptual differences is therefore needed to determine the nature of these differences.

Several limitations are worthy of mention. Although the study demonstrated a relationship between β_2-adrenergic receptor sensitivity over time and stress and mastery as time-varying

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covariates, this should not be taken as a demonstration of causality. The constellation of results is consistent with a model in which stress produces receptor desensitization, but does not demonstrate so unequivocally.

Another limitation that needs mention is that we did not examine the effects of medication changes or drug/alcohol use on receptor sensitivity over the course of the study. Specifically, changes in these factors may explain changes in receptor sensitivity rather than the constructs of focus in this study (i.e., stress and mastery). Replication of the current findings while controlling for medication changes and both drug and alcohol use is therefore recommended.

A third limitation is that it is unknown whether the results of the current study may generalize to samples with significantly greater proportions of minorities, given that the functions of adrenergic receptors may differ by ethnicity (Ferdinand, 2006).

We also did not assess the relations between genetic variation and beta-2 adrenergic receptor function. Specific haplotypes for beta-2 receptors have been identified (Diatchenko et al 2006; Drysdale et al., 2000; Belfer et al., 2005], which have been associated with both psychological characteristics and physiologic characteristics (e.g., receptor expression and internalization). Thus, it may be that the association between mastery and receptor sensitivity is only present among those with genetic subtypes of Beta-2 adrenergic receptor function which are associated with both vulnerability to decreased feelings of mastery and reduced Beta-2 adrenergic receptor sensitivity in the setting of stress. More research examining this possibility is strongly recommended.

Finally, the extent to which β_2-adrenergic receptor sensitivity is related to downstream clinical indicators of vascular impairment remains unknown, and may be a potentially promising topic for future research in this area.

In sum, we found that β_2-adrenergic receptor sensitivity declined significantly over time in a sample of Alzheimer caregivers. Further, across the study, increased stress and reduced mastery were significantly associated with receptor sensitivity. Specifically, in years when stress was high and/or mastery was low, receptor sensitivity was significantly reduced in addition to the effect of time. Further, decreased β_2-adrenergic receptor sensitivity was associated with increased blood pressure, bolstering the notion that decreases in β_2-adrenergic receptor sensitivity may be associated with increased risk of developing hypertension or cardiovascular disease among caregivers. These are preliminary findings that need to be confirmed in prospective studies that examine the linkages between changes in β_2-adrenergic receptor sensitivity or overall SAM arousal with specific CVD disease outcomes, particularly hypertension. Nonetheless, the results are some of the first to demonstrate the relationship between stress, mastery, and adrenergic receptor functioning in a longitudinal study of elderly caregivers.

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Table 1

Baseline Characteristics of the Sample

Characteristic	
Age in years, M (SD)	72.6 (8.8)
Female, n (%)	79 (68.7)
Ethnicity, n (%)	
Caucasian	106 (92.2)
Non-Caucasian	9 (7.8)
Years caregiving, M (SD)	**6.0 (3.5)**
B_2-Adrenergic Receptor Sensitivity, M (SD)	4.5 (3.9)
IMED, M (SD)	6.1 (7.2)
MAP, M (SD)	88.0 (11.6)
Systolic Blood Pressure, M (SD)	131.1 (16.6)
Diastolic Blood Pressure, M (SD)	65.9 (11.0)
HAM-D Score	**4.4 (4.0)**
Overload, M (SD)	9.3 (3.3)
CR Problem Behaviors Score, M (SD)	26.9 (7.3)
CR ADL Score, M (SD)	36.8 (10.4)
CG Hours on Duty/Day, n (%)	
< 7	50 (43.5)
7-12	38 (33.0)
13-18	14 (12.2)
19-24	13 (11.3)
Mastery, M (SD)	19.1 (2.8)

IMED = Interim Medical History questionnaire; MAP = Mean Arterial Pressure; **HAM-D = Hamilton Depression scale;** CR = Care Recipient; CG = Caregiver

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Table 2

Parameter Estimates for Variables Predicting (log_{10}) Beta Receptor Sensitivity

Variable	Estimate	95% CI	P-value
Intercept	0.576	0.525, 0.627	<.001
Age	0.001	-0.004, 0.005	.748
Gender	0.028	-0.055, 0.112	.504
IMED	0.002	-0.004, 0.007	.511
MAP	-0.003	-0.006, -0.000	.046
Time (years)	-0.061	-0.102, -0.019	.005
Stress	-0.058	-0.100, -0.014	.009
Mastery	0.013	0.001, 0.025	.038

IMED = Interim Medical History questionnaire; MAP = Mean Arterial Pressure.