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Behavioral Symptoms of Dementia: A Dyadic Effect of Caregivers' Stress Process?

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Abstract

This study utilized multilevel modeling to evaluate a newly revised model wherein dementia caregivers' (CGs') stress process variables, perceived stress and emotional-behavioral responses, were posited as predictors of behavioral symptoms of dementia (BSD) within community-based dyads. Secondary analyses were conducted on data from a primary two-group (experimental and control) trial, in which experimental subjects received a home monitoring system for managing nighttime activity in persons with dementia (PWD). Models indicated that CGs' trajectories did not differ significantly between groups over time; however, the time by group interaction of BSD approached significance. Since BSD were not targeted, this indicated that the system may have indirectly lowered BSD. Additionally, CGs' perceived stress and emotional-behavioral responses predicted BSD, on average (across all occasions) and from occasion to occasion, with higher levels associated with worse BSD. These limited results provide some support for further research to investigate the nature of these relationships.

As the population continues to live longer, the incidence of dementia increases, with over 13 million individuals expected to have dementia by the year 2050 (Hebert et al., 2003). The large majority of those with dementia remain in the community (Czaja et al., 2000), with the assistance of informal caregivers (CGs) (Riggs, 2001). Informal caregiving for persons with dementia (PsWD) is considered uniquely challenging when compared to other caregiving situations, with greater stress and more problems associated with care duties (Ory et al., 1999).

Disruptive or disturbing behavioral symptoms of dementia (BSD) are understandably perceived as a problem, often the most difficult problem for those providing care, and in research, have thus generally been conceptualized as an important predictor of stress for informal CGs (Schulz & Martire, 2004). However, while the frequency and severity of BSD may certainly contribute to the CGs' perception of them as a problem or stressor, CGs' own characteristics may also influence these perceptions. Additionally, the relationship between BSD and CGs' stress process may be bi-directional; that is, CGs' stress may be as likely to influence BSD as the symptoms in PsWD are to cause CGs' stress (Sink et al., 2006). In systematic reviews, perceived stress and emotional or psychological responses have been correlated with BSD. However, reviewers have also cited scarce longitudinal evidence and lack of rigor, with a related inability to draw conclusions, particularly regarding the temporal or directional nature of these relationships (Ballard et al., 2000; Black & Almeida, 2004; Teri, 1997).

Since CGs in community-based dementia care dyads play a predominant role in managing environmental stimuli and providing for needs of PsWD, the intense role-related stress may impede their ability to provide the optimal caregiving environment for which they strive. For example, experts recommend that CGs adjust their own approaches, affect and demeanor in

order to positively enhance the caregiving environment, meet the needs of PsWD, and reduce BSD (Cohen-Mansfield, 2000; Hall, 1994; Kolanowski & Whall, 2000; Mittelman et al., 2004; Quayhagen et al., 2000; Smith et al., 2006). However, CGs with excessive stress and negative emotional-behavioral responses may not have adequate psycho-emotional resources to continually approach caregiving in the recommended manner. Negatively altered interactions or affect may be misinterpreted by PsWD, and BSD may increase (Sink et al., 2006). CGs' influence within dementia care dyads has been previously implicated when CGs' characteristics or caregiver-directed interventions have been linked to outcomes in PsWD (de Vugt et al., 2004; McClendon et al., 2004; Teri et al., 2005).

In this study, it is proposed that for dementia care dyads, the CGs are influential within the relationship. PsWD may react to cues from CGs based on their cognitively limited perceptions. Thus, BSD may be conceptualized, at least in part, as a function of the CGs' stress process. It is proposed that CGs' perceived stress and emotional-behavioral responses to stress may help explain levels of BSD in care recipients.

Secondary Analysis of BSD as a Potential Consequence of CGs' Stress Process

A monitoring system recently developed to assist CGs in management of nighttime awakenings in PsWD was tested in a two-group experimental trial (referred to as 'primary study' herein), using a repeated measures design to collect information on caregiver sleep, burden, worry, depression and mood within caregiving dyads longitudinally over a one-year period (N=53). The monitoring system was a newly developed technology that uses components similar to those of home security systems, a bed sensor, and bedside alerts for the CGs to track activities in PsWD during the night. The overall aim of the primary study was to test the efficacy of the monitoring system on CGs' outcomes, and on injuries or unattended exits in PsWD. The system had no mechanism to directly influence BSD (Rowe, et al. 2007; Rowe, et al. 2009).

The study reported herein is a secondary analysis of the data from the primary study to examine whether there was a relationship between CGs' stress process variables, perceived stress and emotional-behavioral responses, and simultaneously collected data on BSD. Additionally, the longitudinal nature of the primary study allowed analysis of trajectories for change over time within and across/between dyads, and analysis of experimental and control groups for a time by group interaction, for both CG perceived stress variables and BSD.

Theoretical Foundations

In previous work, the Stress-Health model (Schulz et al., 2004) regarding the effect of CGs' stress process on their own health was adopted and extended to reflect the influence of CGs within dementia care dyads. The detail regarding the extension of the Stress-Health model is reported elsewhere (Campbell, 2009). Briefly, in the extended "Consequences of Dementia Caregivers' Stress Process" model (seen in Figure 1), the consequences of CGs' stress are viewed more broadly than the previously described effect on CGs' health alone, and may include personal influences for the CG as well as dyadic influences on the PWD. In this model, BSD were conceptualized as an exemplar of a dyadic consequence of the CGs' stress process. To begin the process of testing the revised model, key concepts were identified. The CG' perceived stress was considered a major predictor of dyadic effects on PsWD, and it was thought that emotional-behavioral responses also had a role explaining influence of CGs' stress within the dyad. These CGs' stress process variables were included as predictors of BSD in a reduced model, "Dyadic Consequence of Caregivers' Stress: PWD Behavioral Symptoms" (seen in Figure 2), for testing in this study.

For purposes of this secondary analysis, behavioral symptoms were conceptualized as a 'communication' in response to stimulation from the environment, a situation or the care relationship; specifically, the CGs' verbal and non-verbal communication of their own perceptions of stress. For example, PsWD may be using BSD to try to communicate a need for attention or an intolerance of negative stimuli, including cues from the CGs. In order to reflect multiple ways that PsWD may be responding to the environment, including the care dyad relationship, a comprehensive measure of BSD was used. All 'non-cognitive' or 'neuro-psychiatric' behaviors reflecting perceptual, mood, behavioral and vegetative responses were collectively considered BSD (Donaldson et al., 1997, 1998; Finkel et al., 1996; Harwood et al., 2000; Smith & Buckwalter, 2005). The wide-ranging domains of the NeuroPsychiatric Inventory-Questionnaire (Kaufer et al., 2000) reflected this conceptualization of BSD, including an aggregate of symptom domains, such as: delusions/hallucinations, agitation/aggression, dysphoria/depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behaviors, nighttime behavioral disturbances, and appetite/eating disturbances (Kaufer et al., 2000).

Purpose and Aims

The overall purpose of this secondary analysis was to test the proposed reduced model, "Dyadic Effect of Dementia Caregivers' Stress: PWD Behavioral Symptoms" (see Figure 2). Patterns of change over time in the model's variables, and relationships among the variables, were examined using multilevel modeling. The specific aims and hypotheses were:

Specific Aim # 1—To describe patterns of change over time in model variables, including perceived stress, emotional-behavioral responses, and BSD, with consideration of modeled change over time a) within dyads (Level 1), and b) across dyads (Level 2), in general and according to experimental group, investigating for a time-by-group interaction.

Specific Aim # 2—To investigate the relationships between CGs' perceived stress, CGs' emotional-behavioral responses and BSD over time, both within and across dyads. More specifically, the following research questions were investigated:

- Are average BSD (across all data points; not time-varying) higher in dyads when levels of CGs' stress process variables are higher?
- On occasions (data points), when the population's estimated time-varying levels of CGs' current stress process variables were, on average, higher than usual, were care recipients' time-varying BSD higher, on average, as well?
- Given an occasion-to-occasion relationship in the population between CGs' current stress process variables and BSD in care recipients, are there differences among dyads in these relationships?

It was hypothesized that both perceived stress and emotional-behavioral responses in CGs would directly predict BSD, on *average* across all occasions and in *current* occasion-to-occasion analyses, and that these relationship would hold across dyads. It was further hypothesized that the system might moderate CGs' stress, and experimental dementia care dyads could have improvement (or less deterioration) over time on measures of CGs' stress process variables, as compared to controls. Since the system did not have any function that would directly influence BSD, it was hypothesized that system-related reductions in CGs' stress process variables could indirectly result in differences between groups in BSD; thus such group differences might provide some validation for the directional hypothesis in the model (Figure 2).

Methods

This secondary analysis utilized data collected in the primary study over 12 months, at baseline and months 2, 3, 4, 5, 6, 8, 10, & 12. Measures reflecting CGs' perceived stress/burden, depressive symptomatology, and mood/affect, as well as care recipients' BSD, were gathered simultaneously at each data point in the primary study (Rowe, et al., 2010; Rowe, et al., 2006).

Primary Study Methods

The primary study methods have been reported elsewhere and are summarized here (Rowe, et al., 2010; Rowe et al., 2006). A convenience purposive sample of community-dwelling dementia care dyads was recruited from 3 areas in north and central Florida, chosen to augment over-sampling of minorities. Dyads were recruited through advertisements, support groups, and dementia-appropriate clinics or organizations. Interested CGs made contact with researchers. To be eligible for the study, care recipients were required to have a medical diagnosis of dementia, and an English-speaking primary caregiver responsible for care, particularly at night. The CGs needed to have concern about nighttime activity of the PsWD, and could not have sleep conditions, medications, or cognitive/functional limitations that would limit response to system alerts (Rowe, et al., 2010; Rowe, et al., 2006).

Data points were not exactly equidistant for study participants. Progression to the month 2 data point for those in the experimental group followed a brief reliability phase; this was necessary to verify that sensors were manipulated appropriately to suit the dyad, that the system was functioning properly, and that CGs had mastered operation of the system. Due to scheduling issues, subsequent months were also not always exactly one month apart (Rowe, et al., 2006).

Approval was obtained from the university's Institutional Review Board (IRB) and CGs gave informed consent for themselves and the PWD in their care; PsWD indicated their assent for participation. CGs were prescreened by phone for preliminary inclusion criteria, and those qualifying were screened for cognition problems in the initial home visit, using the Mini-Mental State Exam (MMSE) (Folstein et al., 1975). One caregiver scored too low on the MMSE and did not enter the study. To reduce participant burden, instruments were entered into a user-friendly laptop interface by a technical consultant, allowing CGs to quickly complete them, and researchers carried back-up paper copies in case a computer failed. The MMSE was completed for PsWD early in the study to affirm the diagnosis of dementia; this was the only instrument that involved the PsWD directly, and was deferred if administration seemed inappropriate given the situation. Datasets never included personal or identifying information, and electronic storage/communications were through secure servers. Data outliers were checked for accuracy prior to analyses. In addition to IRB oversight, Data Safety Monitor Board (DSMB) reviews for adverse events were conducted, but did not trigger changes (Rowe, et al., 2010; Rowe, et al., 2006).

The first 4 dyads recruited were used in a preliminary reliability study, and were thus automatically recruited into the experimental group, since they already had the system in place. Subsequent experimental (with monitoring system) and control group (without system) assignment was random, allocated by a non-research staff member, for 45 of the dyads recruited. Two caregivers indicated willingness to participate only in the control group, and two voluntarily accepted control assignment due to incompatibility of the system with sleeping arrangements. The resulting groups were numerically and demographically similar. The primary reasons for withdrawal from the primary study were medical illness, death, or institutional placement (Rowe, et al., 2010; Rowe, et al., 2006).

Secondary Analysis Methods

Early in the primary study, the IRB approved changes to allow addition of an instrument to measure BSD. Subjects previously enrolled were re-consented and BSD were assessed at later data points; thus, only 37 subjects had baseline BSD data. Approximately 70% of the dyads completed the study. IRB approval was obtained after study completion for the secondary analyses. Of the 53 dyads in the primary study, 4 had only baseline data and were excluded from the secondary analysis, which focused on change trajectories over time.

In the secondary analysis' sample, demographics indicated that CGs were primarily Caucasian (78%) and female (82%), mostly wives (43%) and daughters (37%), and generally well-educated (33% college graduate or above). PsWD averaged age 80, were more often male (54%), and primarily had Alzheimer's type dementia (79%) with moderate cognitive impairment (MMSE average 14.67). There were no significant differences in demographic data according to experimental or control group.

Instruments

Instruments were available from the primary study that represented the model's predictor variables related to CGs' stress. A short version of the Zarit Burden Interview (ZBI) (Bedard et al., 2001) corresponded conceptually with perceived stress (B. G. Knight et al., 2000). Two instruments provided information related to the concept of emotional-behavioral responses: the Center for Epidemiological Studies-Depression (CES-D) (Radloff, 1977) and the Positive & Negative Affect Schedule (PANAS) (Watson et al., 1988) scale.

The ZBI (Zarit et al., 1985; Zarit et al., 1980) is considered valid and reliable, and the 22-item version is the instrument most often used to measure burden in dementia caregiving research. The short ZBI-Bedard (2001) was validated using 413 caregivers with factor analysis, change scores and item-total correlations to reduce the items to 12. Caregivers self-report aspects of burden on a scale from 0 (never) to 4 (nearly always), with a potential range of 0-48 (Bedard et al., 2001). The Cronbach's alpha for the sample in this secondary analysis was 0.89.

On the CES-D (Radloff, 1977), caregivers ranked the frequency of their depressive symptoms using a 4-point scale, with higher scores indicating worse symptomatology (maximum 60). The validity and reliability of the CES-D is widely supported; it has been utilized in dementia CGs, and a score of ≥ 16 has been established as clinically significant (Beekman et al., 1997; Gallicchio et al., 2002; Hooker et al., 2000; R. G. Knight et al., 1997; Radloff, 1977). Four items were originally worded to assess positive affect, with the intent of breaking tendencies toward negative responses (reverse-scored) (Radloff, 1977). This practice was later viewed as a violation of assessing the construct using 'positive' symptoms; only the 16 negative-item factor was validated (Schroevers et al., 2000). In the primary study, positive items were changed to reflect the opposite negative affect, presenting a less confusing instrument. For example, feeling *not as good* replaced *just as good* as others. The Cronbach's alpha in this secondary analysis was 0.92.

The PANAS (Watson et al., 1988) was used for CGs to rate relatively pure markers of affect (near zero loading on opposite factor) on a 5-point scale from 'very slightly or not at all' to 'extreme.' The PANAS is considered internally consistent and valid (Crawford & Henry, 2004; Denollet & De Vries, 2006). In the primary study, the number of items was reduced to 10, five each positive and negative, to decrease the burden of completing the tool in the sample of time-stressed dementia CGs (Kelly & Rowe, 2006). Items were chosen for their greater variability in a sample of community-dwelling older adults, and were compared to the full complement of choices for adequate reliability (Diehl, 2005). In this secondary analysis, only the negative items from the 'reduced' PANAS were used to reflect the model's

concept of emotional-behavioral responses, including 'distressed,' 'scared,' 'irritable,' 'nervous,' and 'jittery.' This scale was collected daily for 7 days at each data point, and was averaged for a weekly value if at least 3 days were ranked. The Cronbach's alpha for the instrument in this secondary analysis sample was 0.96.

Conceptually, each of these measures provided a unique representation of emotional-behavioral responses: the CES-D ranked mood/affect retrospectively over a month, and the modified PANAS reflected current rankings over 7 days at each data point. Nonetheless, the CES-D and negative portion of the PANAS were moderately correlated ($r=0.57$; $p=.000$ at baseline). Thus, while there was conceptual similarity in these measures in that they both represented emotional-behavioral responses, there was also unique contribution from each, both conceptually and statistically. The significant correlation of the measures allowed us to establish a composite score for emotional-behavioral responses by averaging Z-scores from both measures. This provided a more inclusive, comprehensive measure, and reduced the number of variables requiring estimation in examining model relationships.

The NPI-Q (Kaufer et al., 2000) was chosen to measure BSD (CGs behavior-related distress rankings were available, but were not used in this study). It is brief, requiring less completion time (Forester & Oxman, 2003). The NPI-Q uses the primary caregiver as an informant, allowing a more lengthy assessment window (1-month retrospective) in a natural setting than direct observation provides. The original directed-interview NPI (Cummings, 1997; Cummings et al., 1994) is established as reliable & valid, including test-retest reliability, inter-rater reliability, internal consistency, content and convergent validity. It is cited over 250 times in research literature, and is commonly used in clinical trials (Forester & Oxman, 2003; Lange et al., 2004). There is consensus that a score of 4 or greater reflects clinical significance (Lyketsos, 2007; Lyketsos et al., 2002; Schneider et al., 2001; Steinberg et al., 2004).

Developed as a self-administration version of the NPI for easy CG completion, the NPI-Q demonstrated convergent validity with the NPI using 60 care dyads; correlation on behaviors ranged from 0.71 to 0.93 for various domains and 0.91 for total scores. Caregivers endorse whether symptom domains occur using simple descriptions derived from the NPI interviews. For any domains endorsed, symptoms are ranked for severity on a scale from 1-3, with a maximum range of 36. Frequency was omitted to improve brevity on the NPI-Q, since severity is more closely related to distress in the caregiver (Forester & Oxman, 2003; Lange et al., 2004). While behavior domains on the NPI-Q may be considered independently or within established factors, it was the total score that was used in this study for a comprehensive, inclusive measure of BSD. The Cronbach's alpha for the behavioral scale in this secondary analysis sample was 0.82.

The MMSE (Folstein et al., 1975) was used for inclusion of CGs to rule out problems with cognition, and was also assessed in care recipients. The MMSE was originally established as a measure of cognitive impairment, with higher scores reflecting better cognition. The maximum score is 30. Despite some concerns, the MMSE remains widely accepted as a reliable and valid instrument for quick screening of cognitive impairment (Jones & Gallo, 2001). In this secondary analysis sample, the alpha was 0.82.

Statistical Analysis

All analyses used SPSS version 14; the alpha was set at 0.05. Univariate, bivariate, and preliminary trend analyses preceded the multilevel analyses.

Missing data—Due to a computer malfunction in the data collection interface, approximately 1-2 % of the potential NPI-Q behavior items were considered systematically

missing. When 3 of the items on the NPI-Q were endorsed, some subjects were mistakenly directed to the screen that assessed their distress related to behaviors, skipping the option to rate of the severity of BSD. This missingness influenced the sum scores for those subjects, and since it occurred within the score, it could not be addressed in modeling, as is possible with dropouts or skipped appointments. Consultations with an expert regarding missing data established that since the rate of missingness was low and the range of possible rankings narrow (1-3), complicated imputation techniques were considered inappropriate (Schafer, 2007). Furthermore, simple techniques commonly used were not appropriate. Averaging *across* dyads at a particular data point did not take into account the 9 correctly measured items in the *within*-person data at that point. Additionally, averaging the person's measures prior to and subsequent to missing data would have diminished the occasion-to-occasion change, and within-person trends over time were of interest in this study. Therefore, this missingness was remedied by calculating a mean of the items available *for that person at that data point* if at least 9 items were scored, and multiplying to return the value to scale (Fitzmaurice et al., 2004; Schafer, 2007; Schafer & Graham, 2002). This allowed use of the person's data that was available without skewing results with data imputed from sources in conflict with study aims.

Univariate and bivariate statistics—For each model variable, including CGs' perceived stress and emotional-behavioral responses, and behavioral symptoms in PsWD, univariate and bivariate statistics were assessed. Histograms were examined for normality. T-tests established the outcome of random assignment to groups for each model variable. Pearson correlations were used to establish relationships between variables over the study period. Means and standard deviations were calculated on each model variable (CGs' perceived stress and emotional-behavioral responses, and behavioral symptoms in PsWD) for the entire sample and according to experimental status, and were compared across all data points and using *t*-tests and graphs.

Preliminary trend analyses—Multilevel models for change over time must address the underlying change trends, with the simplest trend, linear, serving as the default. Preliminary inspection of individual *within-dyad* trends for model variables indicated substantial variability over the study period. The variation in direction and magnitude of change warranted within-dyad modeling, and suggested that change models should address both linear and quadratic trends. Orthogonal quadratic change functions were thus computed to avoid multi-collinearity between the linear and quadratic terms (using the residuals from a regression of the quadratic term on the linear term), to reflect the unique, independent contribution of quadratic change. As a result of the orthogonal computations, *all intercepts reported herein reflect the mid-point of the study*.

Multilevel Modeling—The repeated measures, missing data points, and unequal time distances for data points made multilevel modeling (MLM) a natural fit for these analyses. MLM techniques are versatile, and models can be estimated in a number of ways. Fixed effects represent population estimates, and random effects identify differences among the individuals in the aggregate. In this secondary analysis, measurements over time (Level 1) were nested within dyads (Level 2), with group status (experimental or control) representing an influential dyad-level factor (rather than a third level in the hierarchy). The use of repeated measures in longitudinal change studies may be considered a special case of multilevel modeling that can address clustering of data within persons (Cho, 2003), or in this case, within dyads. 'Days from baseline' was used to accommodate unequal time distances; however, 'month' of the study was used as the repeated term to structure the covariances, and for data point comparisons. More information regarding the specific modeling process is outlined in Table 1.

To address Aim #1, models were constructed to estimate population trajectories of change for all time-varying model variables, subsequently comparing average trajectories of the experimental and control groups.

For Aim #2, predictor models estimated the within-dyad and population's across-dyad (average) effect of CGs' stress process variables on BSD over time. CGs' predictors were meaned for the *average* effect over all occasions, and were centered for the *current* effect from occasion to occasion (see Table 2 for more information on interpretation). The model building process for hypothesized relationships in Aim # 2 used the accepted change model for BSD from Aim #1, but without consideration of the experimental group variable, as a baseline for comparison. In these analyses, it was the relationship between CGs' variables and BSD, regardless of treatment, which was of concern in assessing time-varying model relationships.

Results

Univariate and Bivariate Descriptives of Observed Raw Data

Sample means and standard deviations were calculated for all model variables across all data points, and are displayed in Table 3. The model variables were considered a family of related assessments; thus the significance of the *p* value was adjusted using the Bonferroni method ($3\ t\text{-tests}, 0.05 / 3 = 0.017$) to reflect the study alpha of 0.05. Accordingly, there were no significant differences according to experimental/control group at baseline for model variables. Additionally, *t*-tests describing experimental and control group differences at each data point are shown in Table 3, and observed raw scores for each of the model variables are graphed to visually compare means for experimental and control dyads at each data point in Figure 3. Lastly, all available data points for all dyads were aggregated, and there was a significant experimental group difference in means for each of the model variables (see last column in Table 3); however, these aggregate comparisons do not reflect change over time. Bivariate analysis showed that BSD were similarly correlated to perceived stress ($r=0.53$) and emotional-behavioral responses ($r=0.48$); for each of these CG variables, the positive correlation indicated that higher CGs' stress process variables were associated with worse BSD.

Aim #1: Modeling of Change over Time for each Model Variable

Caregivers' Stress Process Variables—To compare change over time in experimental and control CGs' variables, models with experimental group added were evaluated for improvement over previous models. For perceived stress, adding experimental group did improve the model fit criteria, and modeled perceptions of stress were significantly higher in the control group, worsening over the study period. However, the groups' differing modeled trajectories (similar to time*group interaction) were not significant. For emotional-behavioral responses, adding experimental group did not improve the model fit criteria; this meant that comparing the groups' modeled trajectories over time was inappropriate. Therefore, experimental and control groups' trajectories did not differ over time as hypothesized in Aim #1, for either CG variable.

BSD—Modeling BSD over time provided more information and is thus reported in more detail. First, the 'unconditional means model,' without consideration of time, indicated that 35 % of the unexplained variance was within PWD subjects ($17.29 + 32.27 = 49.56$; $17.29/49.56 = .35$), with the majority of variance between/across all PWD subjects. Secondly, neither linear nor quadratic trends over time described the entire sample adequately; thus, the default (linear) form of change over time was used in modeling. While the criteria for model fit were improved, linear change over time across dyads was non-

significant, indicating that the linear trend did not represent all subjects well. Lastly, adding experimental group did improve the model fit. The population's estimated mean for BSD including all data points was 9.084 (at mid-study; $p = 0.00$); experimental group differences approached significance, with control dyads averaging 3.19 points higher (at mid-study; $p = 0.056$). The differing change trajectories for experimental vs. control dyads as modeled linearly over time also approached significance ($p = 0.075$), with control dyads worsening, increasing approximately $+0.06$ per day from baseline ($p = 0.082$), and with experimental dyads stable (changing -0.003 —NS). Since larger numbers of parameters are more difficult to estimate, assessment of random effects, or within-dyad differences in slopes from population estimates, were not possible; the Level 1 within-dyad effect over time needed to be removed to allow the computer to settle on a solution for the estimates. The remaining random variability for BSD did support the use of predictors in further modeling.

Aim #2: Modeling Hypothesized Relationships

Adding both *average* and *current* levels of CGs' perceived stress and emotional-behavioral responses as predictors improved model fit criteria significantly and reduced unexplained variance, indicating that both CG variables were associated with BSD. For the first two research questions, estimation of fixed (population) effects included *average* (non time-varying) levels of predictors between/across dyads and *current* (time-varying from occasion to occasion) levels of predictors within dyads (see Table 2). Estimation of random effects (within-dyad differences from population estimates) in the last research question included only *current* levels of predictors, or occasion-to-occasion change. Modeling these CG stress process variables as predictor effects for BSD explained 33% of the previously unexplained variance between/across subjects, for perceived stress, and 27% for the emotional-behavioral responses. Additionally, again when modeled separately, perceived stress and emotional-behavioral responses explained 13% and 6% of the remaining variance within PWD subjects, respectively. Model-derived estimations of effects for each of the questions associated with Aim # 2 follow.

Are average BSD (across all data points; not time-varying) higher in dyads when levels of CGs' stress process variables are higher?—Both CGs' perceived stress and emotional-behavioral responses had a relationship with BSD in this study. At mid-study, for each point that the CG's *average* levels of perceived stress varied from the estimated population's typical, BSD differed by $+0.42$ ($p = 0.00$), on average. Additionally, when *average* levels of CGs' emotional-behavioral responses differed by 1 point from the estimated population's typical, BSD varied by $+3.57$ ($p = 0.00$), on average. When controlling for these *average* CG effects, perceived stress was substantially instrumental in explaining BSD, such that both the intercept and effects of time were non-significant, or negligible. On the other hand, when controlling for the CG's *average* emotional-behavioral effects, even though the effect of time was non-significant, the intercept remained significant (10.67; SE 0.73; $p = 0.00$). Thus, controlling for emotional-behavioral effects did not fully explain levels of BSD at mid-study.

On occasions (data points), when the population's estimated time-varying levels of CGs' current stress process variables averaged higher than usual, were care recipients' time-varying BSD higher, on average, as well?—For each point that the population's estimated time-varying levels of *current* CGs' perceived stress varied from the typical, levels of BSD changed by $+0.33$ ($p = 0.00$), on average. Additionally, for each point that the population's estimated time-varying levels of *current* CGs' emotional-behavioral responses varied from usual, BSD differed by $+2.14$ ($p = 0.00$), on average. Thus, both CGs' perceived stress and emotional-behavioral responses 'traveled together' with changes in BSD, either increasing or decreasing simultaneously. Though the magnitude of

the emotional-behavioral effects may seem high compared to that of perceived stress, recall that the emotional-behavioral responses variable was based on z-scores with a range constrained between $+1$ and -1 ; thus these values reflect a maximum possible change in BSD.

Given an occasion-to-occasion relationship in the population between CGs' current stress process variables and BSD in care recipients, are there differences among dyads in these relationships?—Models including CGs' stress process variables did explain further within-dyad variance in comparison to the baseline model. However, when random (within-dyad) time-varying effects of perceived stress and emotional-behavioral response were investigated, there were no significant differences identified. This indicates that these estimated time-varying relationship patterns generally held across dyads.

For Aims #1 and #2, the fixed (population) estimates are displayed in Table 4. Random effects (individual dyad differences) are omitted since they did not improve the models significantly. More detail about the modeling process is available from the corresponding author.

Discussion

Support of Proposed Theoretical Model

In general, there is evidence to support the relationships posited in the model, between CGs' stress process and BSD. Modeling the effect of CGs' stress process variables on BSD revealed that BSD increased when caregiver stress process variables were, on average, higher than usual (*current* levels). Also, in those dyads characterized by higher CGs' stress measurements, BSD were more severe (*average* levels) at mid-study.

In modeling change trajectories, analyses indicated that BSD worsened over time in the control group, and this effect approached significance. Particularly after the mid-point of the study, BSD were increasingly worse in control dyads, while BSD in experimental dyads stabilized across time. Importantly, this occurred even though the modest improvements in CGs' stress process variables over time were not significant. The primary study's intervention had the potential to influence CGs' stress process variables, but did not have properties to directly influence BSD. The lack of significant group differences in CGs' variables is counter-intuitive when attempting to reconcile results to the hypotheses in this study; i.e., it is unclear how BSD changes could approach significance over time without corresponding significant changes in CGs' stress process. It is possible that changes in disease occurred differently in the two groups, or that PsWD in experimental dyads received more sleep related to CGs' system alerts of their arising and subsequent encouragement to return to bed. However, another possible explanation is that very small improvements in CGs' stress (not significant) may have substantial impact within the dyad. In general, this evidence provides limited support for the directionality of the relationships in the model, from CGs' stress to BSD.

In this study, perceived stress seemed to have a greater impact on BSD than did emotional-behavioral responses, as evidenced by the intercept remaining significant when controlling for emotional-behavioral responses. In the proposed model, level of emotional-behavioral responses was thought to explain why perceived stress would influence BSD. It is not clear why emotional-behavioral responses did not have greater impact in this study.

Findings in Relation to Past Research

As in previous studies, BSD were a substantial issue in the care dyads in both groups in this study, remaining above the accepted level of clinical significance (>4) (Lyketsos, 2007) throughout the study. CGs in this study also had consistently high levels of perceived stress on the Short BDI-Bedard (Bedard et al., 2001; O'Rourke & Tuokko, 2003), and CES-D scores often approached 16, the cut-off for clinical depression risk (Radloff, 1977). In contrast, the weekly mean of scores on negative affect were under 1 on a scale of 0-5, possibly because these items were rated upon arising, before caregiving duties for the day were well under way.

Each of the CGs' stress process variables accounted for approximately one third of the variance in BSD that was unexplained in the baseline change model. These findings are in agreement with previous works that have proposed caregiver influence. In a population-based study of over 5000 dementia care dyads, CGs' depression and burden were among predictors of increased BSD (Sink et al., 2006), and one reviewer highlighted CGs' influence on BSD (Dunkin & Anderson-Hanley, 1998). In a prospective study of 96 dementia care dyads, CGs' role stress (negative attitude toward the care recipient) predicted worse social behaviors in PsWD, and CG factors explained 32% of variance in care recipient quality of life (Burgener & Twigg, 2002).

The relationship between the two caregiver variables, perceived stress and emotional-behavioral responses, is embedded within the Stress-Health model, which emerged from previous theory and research, and has extensive support from literature reviews (Goode et al., 1998; Pearlin et al., 1990; Pinquart & Sorensen, 2003a, 2003b, 2007; Schulz et al., 2001; Schulz & Martire, 2004; Vitaliano et al., 2003). Several researchers have presented evidence that may explain *why* CGs with a more intense stress process likely care for recipients with increased BSD. For example, previous quality of relationship (i.e., how 'communal' or reciprocal) predicted both depressive symptoms in CGs and frequency of harmful treatment of the care recipient (Williamson & Shaffer, 2001). Additionally, CGs with higher strain and distress were also higher in 'expressed emotion,' or criticism toward the care recipients (Tarrier et al., 2002). Longitudinally, CGs' high expressed emotion was predictive of increased negative behaviors over time (Vitaliano et al., 1993). A small body of research proposes that CGs' coping may have influence on PsWD: studies include those regarding CGs' 1) management strategies and their relationship with BSD (de Vugt et al., 2004), 2) cognitive decline and related increased BSD, possibly linked to the inability of CGs to provide an optimum care environment (de Vugt et al., 2006), and lastly, 3) ineffective coping and related low survival rates in PsWD (McClendon et al., 2004). This evidence indirectly connects the intensity of the stress process to BSD.

Strengths, Limitations, and Directions for Future Research

The use of MLM allowed change within dyads to be considered in analyses, with the potential of more precise estimates than is seen in traditional analyses. In MLM, dyads may "borrow strength" from the population when there is higher occasion-to-occasion variability within the dyad's measurements than exists in the sample. Furthermore, missing data points are accounted for efficiently. This emphasis on precision (over bias toward the sample) is the primary motivation to use MLM for model estimation (Schafer, 2007; Singer & Willett, 2003).

On the other hand, the secondary nature of the study meant a lack of control over data. Better statistical support of the reliability of the modified PANAS measure would improve confidence in that data from the primary study. While statistical analyses that established adequate reliability of the modified PANAS was reported in personal communication, the

statistical data itself was not available for reasons beyond the author's control. Additionally, covariates were limited to those available in the primary study. An example of a covariate that was not available in the primary study data is that of the quality of the pre-care relationship. Covariates such as gender, relationship, and race were equal in the study's groups; however, direct modeling of covariates could improve future estimates. Lastly, while measures collected in the primary study can be considered appropriate for stress process variables, it is not known whether they are the *best* measures. These issues may need to be clarified in future research.

Related to the outcome measure, this study utilized a comprehensive measure of BSD, which included behavioral, psychological, vegetative, and other symptoms. It would be useful for future analyses to include sub-scales of the behavioral domains. This might allow more clarity regarding the types of responses in PsWD affected by their CGs' stress process. Additionally, related to the predictors, the combined emotional-behavioral responses measure included current data from the PANAS recorded in the mornings over a week-long data point. While combining this with CES-D data was considered a more comprehensive, relevant measure, the retrospective CES-D data alone might have been more similar in nature to the other variables' measures. Future research may need to compare various measures would be useful.

Some researchers note concern about using CGs' proxy reports for BSD. Others acknowledge that using CGs as raters may be most logical, noting that CGs are intimately familiar with BSD exhibited, can report a wider time frame than direct observation can capture, and that CG reports have been correlated to direct observation (Cotter, et al., 2008; Davis et al., 1997). The Cohen-Mansfield Agitation Inventory, a common caregiver-report measure of BSD, was significantly correlated to formal CGs' direct observations of BSD (Cohen-Mansfield & Libin, 2004). These findings support the use of CGs' reports in community-based dyads. Nonetheless, future research with more objective measures should be considered. For example, videotaped observation of BSD, or Actigraphy to measure wandering or repetitive movements, could enhance measurement of BSD. Likewise, heart rate monitoring might substantiate subjective reports of perceived stress. While objective measures may strengthen the conclusions of the study, the use of MLM accommodated for minor variations in measurements over time, somewhat diminishing effects of self- and CG-report.

Lastly, the model's relationships were assessed with dyadic data that was collected simultaneously, and the relationships may be bi-directional. In these analyses, there was limited support for directionality proposed in the model herein, from CGs' stress to BSD. However, simultaneous assessment of model pathways across data points *within* dyads using more sophisticated multi-level mediation techniques may more effectively clarify these relationships.

In summary, further research may allow BSD to emerge as a viable consequence of CGs' stress process, leading to improved intervention strategies that target BSD through relieving CGs' stress, interrupting the cycle of negative dyadic effects and improving more distal outcomes (such as institutionalization) for these vulnerable dyads. Such research has practice protocol, societal, financial, and policy implications for dementia care. More importantly, development of a 'dyadic' approach, acknowledging the importance of attention to primary CGs' needs, may directly affect quality of life for millions of community-based dementia care dyads.

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Figure 1. Full “Consequences of Dementia Caregivers' Stress Process” Model adapted from Schultz & Martire's Stress-Health Model

Figure 2. Reduced "Dyadic Effect of Caregivers' Stress Process: PWD Behavioral Symptoms" Model with Key Variables and Relationships from the Full Model

Figure 3. Observed raw scores for each variable compared by occasion and according to experimental group (means and standard error bars)

Table 1
Estimation of Parameters for Multilevel Analyses

Model estimation	Maximum Likelihood	Computer uses an iterative procedure to determine the most probable estimates; i.e., examines within- and between-dyads variability and assigns more weight to sample means when subjects have high within-dyads variability, or have missing data points.
Steps in estimation	Unconditional means	Model without predictors to establish variance for further modeling, using intra-class correlations.
	Unconditional growth Or Change	Model with only time as a predictor, to establish whether there was enough variance within dyads to model level 2 factors.
	Unstructured conditional model	Modeled parameters assess for reduction in within-dyads variance, i.e., experimental group in change models & CGs' stress variables in predictor models.
	Structured models	Model including factors or predictors, and with the covariance structured.
Model comparisons (criteria used in model building steps)	-2 Log Likelihood	Used to evaluate subsequent improvement of models as compared to the baseline unconditional models.
	Pseudo- R^2	Assesses model's ability to explain variance, similar to the use of R^2 in traditional models. However, this value represents reduction of <i>explainable</i> variance; a fairly <i>small</i> change may mean a <i>large</i> pseudo- R^2 .
Structure of covariance	<i>Variance components</i>	Default in initial models, since unstructured models have a high number of parameters for estimation.
	Repeated variable	Final models structured with a repeated variable on a random statement: in this study, <i>Month</i> .
	Alternate covariate structures	Final models run with several covariance structures, for example <i>Autoregressive</i> , chosen based on expected longitudinal variances & correlations across elements.
	Akaike information criterion (AIC)	Criterion used to compare structured models with the default; this criterion balances complexity with parsimony in indicating the best model fit. The lowest AIC was considered the best fit of the data.

Note: Resources: Fitzmaurice et al., 2004; Singer, 1998; Singer & Willett, 2003

Table 2
Interpretation of CGs' Stress Process Predictor Variables in Aim #2 Analyses

	Level of Analysis	Variable and Meaning	Interpretation in relation to outcome of BSD	
FIXED	Level 2 Across or Between Dyads	<i>Average</i> levels perceived stress and emotional-behavioral responses (Predictors meaned)	Establishes dyads' mean levels of predictors. Dyads' means were then considered across dyads for the population effect; each dyad's contribution to the estimate was the same regardless of data point; a dyad's means are compared to the population's typical effect.	What is the extent to which CGs' general levels of stress process variables affect BSD, when compared across dyads? For example, are those dyads that are characterized with higher than average CGs' stress also likely to have more severe BSD in their care recipient? This effect reflected how CGs' stress process influenced BSD in general, not changing over time.
	Level 1 Within Dyads	<i>Current</i> levels perceived stress and emotional-behavioral responses (Predictors centered)	Establishes dyads' current deviation or variation from their own mean at each given data point. Dyad's current deviations considered across dyads for the population effect at each data point; each dyad's contributions to the estimate varied from one data point to another.	What is the extent to which CGs' current levels of stress process variables within dyads affect BSD within dyads? For example, on occasions (data points) when CGs' stress process variables were higher than the estimated population's typical, were care recipients' BSD higher, on average, as well? This effect reflected how caregivers' changing stress process influenced BSD over time.
RANDOM	Level 1 Within Dyads	<i>Current</i> levels perceived stress and emotional-behavioral responses (Predictors Centered)	Establishes dyads' current deviation or variation from their own mean at each given data point. Each dyad's trajectory of current deviations from their own mean was compared to population's typical trajectory.	Given a relationship between caregivers' stress process variables and BSD from occasion to occasion (over data points in study), are there differences among dyads in these predictor-outcome relationships or do the relationships generally hold across all dyads?

Table 3
Means, Standard Deviations, Differences, and t-tests by Experimental Group for Sample's Observed Raw Data across Study

Month of study (M)	Base-Line	M2	M3	M4	M5	M6	M8	M10	M12	All Months
Perceived stress (Short Zarit Burden Interview- Bedard)										
Mean	21.86	21.43	20.65	20.00	20.15	19.92	19.09	21.10	20.70	20.74
(SD)	(8.83)	(7.70)	(8.97)	(8.15)	(9.04)	(8.88)	(8.61)	(9.55)	(10.48)	(8.62)
Diff.	5.14	5.44	5.16	3.94	4.32	3.76	5.60	6.87	7.40	5.13
t-test	2.11	2.53	2.06	1.55	1.52	1.31	1.91	2.08	1.92	5.81
df	47	44	46	38	37	36	30	28	25	333.38
(p)	(.04)	(.02)	(.05)	(.13)	(.11)	(.14)	(.07)	(.05)	(.07)	(0.000)
$r^2=0.53$										
Emotional-behavioral responses (CES-D & NegPANAS combined*)										
Mean	.102	.011	.086	.058	.054	.048	.147	.069	.021	.002
(SD)	(.906)	(.942)	(.977)	(.908)	(.879)	(.866)	(.742)	(.932)	(.935)	(.90)
Diff.	0.34	0.48	0.27	0.56	0.36	0.23	0.54	0.52	0.55	0.415
t-test	1.33	1.87	0.98	2.01	1.31	.82	2.14	1.84	1.42	4.51
df	47	41.99	47	38	38	37	23.05	29	31	354.47
(p)	(.19)	(.07)	(.33)	(.06)	(.20)	(.42)	(.04)	(.08)	(.17)	(0.000)
$r^2=0.48$										
Behavioral Symptoms (Neuro-Psychiatric Inventory-Questionnaire-Behaviors)										
Mean	11.58	9.49	11.00	11.22	9.04	9.70	10.61	11.07	11.44	10.55
(SD)	(7.12)	(7.17)	(7.53)	(7.14)	(6.80)	(7.00)	(6.98)	(7.95)	(8.44)	(7.28)
Diff.	2.92	3.34	4.60	2.35	0.063	1.89	2.56	2.89	3.14	3.01
t-test	1.18	1.36	2.12	.98	.03	.82	1.04	1.53	1.65	3.72
df	32	31	43	34	34	35	30	27	20.5	293.98
(p)	(.25)	(.19)	(.04)	(.33)	(.98)	(.42)	(.31)	(.14)	(.11)	(0.000)

* combined z-scores from Center for Epidemiologic Study-Depression and negative portion of the Positive & Negative Affect Schedule.

r correlation with outcome, Behavioral Symptoms of Dementia, across all data points

Note: SD= standard deviation; Diff.= difference in means between control and experimental subjects.

Table 4
Estimated parameters for each variable modeled over time and by experimental status, then with CGs' stress process variables as predictor effects on BSD modeled

Model Variables	CGs' Perceived Stress		CGs' Emotional-Behavioral Responses		Behavioral Symptoms of Dementia	
Estimate		SE	Estimate	SE	Estimate	SE
Fixed Effects (across population)						
Intercept	18.56	1.54	0.0002	0.12	9.08	1.19
Linear time effect	0	0	0.00004	0.00	0	0
Quadratic time effect	0.00004	0.00	0.000005	2.21	n/a*	
Treatment effect at mid-study (control)	+5.03	2.12			+3.19	1.64
Linear time * Treatment group change per day from baseline (control)	+0.005	0.00			+0.006	0.00
(experimental)	+0.0002	0.00	n/a*		-0.003	0.00
Quadratic time * Treatment group change per day from baseline (control)	+0.00003	0.00				
(experimental)	0	0			n/a*	
Effects of perceived stress on BSD**						
			BSD intercept, controlling for perceived stress		1.86	2.01
			Effect of average perceived stress at mid-study		+0.42	0.09
			Effect of current perceived stress from occasion to occasion		+0.33	0.08
Effects of emotional-behavioral responses on BSD**						
			BSD intercept, controlling for emotional-behavioral responses		10.67	0.73
			Effect of average emotional-behavioral responses at mid-study		+3.57	0.91
			Effect of current emotional-behavioral responses from occasion to occasion		+2.14	0.61

Note: Bold= Significant; Bold Italics= approached significance; Intercepts reflect estimated population mean at the average number of days from baseline (mid-study)

* n/a= model was not improved, so parameters were not estimated

** Effects = change in estimated BSD per 1 unit change in predictor