# Cognitive Functioning under Stress: Evidence from Informal Caregivers of Palliative Patients

COREY S. MACKENZIE, Ph.D.,<sup>1,4</sup>\* MARILYN C. SMITH, Ph.D.,<sup>2</sup> LYNN HASHER, Ph.D.,<sup>2,3</sup> LARRY LEACH, Ph.D.,<sup>4</sup> and PEARL BEHL, Ph.D.<sup>2</sup>

## ABSTRACT

*Background*: Caring for a terminally ill family member can be extremely stressful, and stress is known to have a negative influence on aspects of cognition. In contrast to the well-known physical and mental health risks associated with caregiving, little is known about its impact on cognitive functioning.

*Objective*: The primary objective of this study was to explore cognition among caregivers of palliative family members with a battery of neuropsychological tests. A secondary objective was to examine changes in cognition following caregiving by retesting a subset of participants at least 6 months after the death of their care recipient.

*Method*: While caregiving, 27 participants completed an assessment battery measuring attention, learning, and memory, as well as intelligence, mood, and general health; 22 participants completed this battery again post-caregiving. We compared caregivers' cognitive performance to healthy normative samples.

*Results*: Participants who were caring for palliative relatives exhibited significant impairments in attention, including difficulty monitoring their performance and regulating their attentional resources. In contrast, participants' episodic and working memory performance was not impaired while caregiving. A mixed pattern of improvement and worsening of cognitive functioning was evident among caregivers retested after their family member's death.

*Conclusions*: In addition to the well-documented physical and mental health risks associated with caregiving, this study adds to a small body of literature demonstrating impaired cognitive functioning among family members providing end-of-life care. Secondary findings of both improvement and deterioration of cognition post caregiving provide tentative support for the possibility of reversing certain cognitive deficits by reducing caregiver stress.

## **INTRODUCTION**

Stress CAN HAVE DETRIMENTAL EFFECTS on both physical and mental health, as is evident in the substantial literature on the health and well-being of informal (i.e., unpaid) caregivers of individuals with dementia.<sup>1</sup> Such caregivers experience particularly high levels of stress, anxiety, and depression,<sup>2</sup> and are at increased risk for physical health problems<sup>3</sup> and even mortality<sup>4</sup> compared to noncaregivers. A much smaller but growing body of research is showing similar negative consequences associated with providing pallia-

<sup>&</sup>lt;sup>1</sup>Department of Counselling Psychology, OISE/University of Toronto, Toronto, Ontario, Canada.

<sup>&</sup>lt;sup>2</sup>Department of Psychology, University of Toronto, Toronto, Ontario, Canada.

<sup>&</sup>lt;sup>3</sup>The Rotman Research Institute of Baycrest Centre, Toronto, Ontario, Canada.

<sup>&</sup>lt;sup>4</sup>Department of Psychology, Baycrest Centre, Toronto, Ontario, Canada.

<sup>\*</sup>Current address: Department of Psychology, University of Manitoba, Winnipeg, Manitoba, Canada.

tive care for family members.<sup>5,6</sup> In contrast to the rich literature on the physical and mental health risks associated with caregiving, very little is known about the cognitive well-being of informal caregivers. The dearth of research examining cognition among this group of individuals is surprising considering that they are faced with important economic and legal decisions, as well as complex caregiving tasks, including understanding, remembering, and carrying out medical instructions.<sup>1,6–8</sup> The current study provides preliminary evidence concerning the cognitive consequences of being an informal caregiver for a dying spouse or parent.

Several literatures converge to suggest that caregiving will have negative effects on cognition. Acute and short-term stressors, such as continuous loud noise, heat, and sleep deprivation, are known to impair a wide range of cognitive abilities, ranging from attention to implicit and procedural learning.<sup>9</sup> Stress induced in college student and adult populations increases interference from irrelevant information, impairing selective attention and working memory.<sup>10–12</sup> Exposure to threat from a mild electric shock increases the speed with which people attempt verbal problems and also reduces their success in solving them.<sup>13</sup> Cognitive impairments are also associated with naturally occurring sources of stress. Everyday life events and daily stressors are associated with cognitive failures such as losing one's keys and forgetting to take medication.<sup>14</sup> Finally, individuals with chronically high levels of stress and burnout exhibit impairments in attention and episodic memory.<sup>15–17</sup>

Despite evidence that acute and chronic stress can impair fundamental cognitive abilities, there has been surprisingly little research investigating whether caregivers, who are known to experience both types of stress, are cognitively impaired. In the first of three studies we are aware of addressing this issue, 44 caregivers of spouses with dementia performed more poorly than 66 noncaregiver controls on a digit symbol test of complex attention and cognitive speed; a difference that was likely mediated by caregiver distress.<sup>18</sup> In a second study, more than 11,000 female caregivers of ill spouses from the Nurses' Health Study who completed a brief telephone assessment performed more poorly than noncaregivers on a general cognitive screen similar to the Mini Mental Status Examination, and on both immediate and delayed recall of a 10-item word list.<sup>19</sup> In a third study, 96 caregivers of spouses with dementia showed a significant decline in vocabulary over a 2-year period compared to 95 matched noncaregiver spouses, with greater decline among caregivers with hostility and metabolic risk factors.20

Thus, although research examining cognitive functioning among caregivers is just beginning to emerge, preliminary evidence suggests that this at-risk group has compromised cognition. Whereas the studies described above examined caregiver cognition using only cognitive screens and single cognitive measures, caregivers may experience difficulties in a variety of cognitive abilities that have previously been shown to be susceptible to stress, including attention, working memory, learning, and episodic memory. The present study provides a preliminary test, based on a small sample of family caregivers, of the hypothesis that they would exhibit attention and memory impairments when compared to age-matched normative samples on a battery of neuropsychological tests. We were also able to retest a subset of the initial group at least 6 months after the death of their care recipients to examine changes in cognition after cessation of the caregiving role.

#### **METHODS**

#### Participants and procedures

Participants were informal caregivers of terminally ill patients enrolled in a palliative care program associated with the Temmy Latner Centre for Palliative Care at the Mount Sinai Hospital in Toronto, Canada. The program enables dying individuals to be cared for at home by providing the support of a team of physicians and psychosocial workers who visit the patient regularly. A member of the palliative team gave caregivers an information sheet and asked if they were willing to participate in a study of the effects of stress on cognitive functioning. There was no obligation to participate, and members of the team were not informed as to which caregivers agreed to join the study. Consenting participants were competent English speakers with no known neurologic or incapacitating health problems. They received \$25 per session for their participation.

Twenty-seven participants completed the first testing session and 22 caregivers whose family members passed away at least 6 months earlier were retested. The average number of days between the first and second test sessions was 294.36 (standard deviation [SD] = 66.69) days, or roughly 9  $1/_2$  months. Demographic information for the entire sample of participants is shown in Table 1. Testing took place in participants' homes and lasted approximately 90 minutes. We selected common neuropsychological tests to measure cognitive functions that we hypothesized would

## COGNITIVE FUNCTIONING UNDER STRESS

Variable	n (%)
Mean (SD) age	58.78 (12.57)
Mean (SD) years of education	14.93 (3.99)
Gender	
Female	19 (70.4%)
Male	8 (29.6%)
Marital status	
Single	4 (14.8%)
Married or common-law	19 (70.4%)
Widowed	4 (14.8%)
Race/Ethnicity	
White	25 (92.6%)
Asian	1 (3.7%)
Pacific Islander	1 (3.7%)
Occupation	
Professional	8 (29.6%)
Nonprofessional	5 (18.5%)
Retired	14 (51.9%)
Primary language	
English	20 (74.1%)
Other	7 (25.9%)
Relationship to care recipient	· · · · ·
Spouse	16 (59.3%)
Child	11 (40.7%)
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be affected by chronic elevations in stress. Extensive normative data are available for the outcome measures, enabling us to compare standardized *z*-scores across each of the dependent variables.

#### Assessment battery

Ruff 2 & 7 Selective Attention Test. This test measures the speed and accuracy with which individuals can select relevant stimuli while ignoring distracters (selective attention). The participant completes 20 trials of a visual search and cancellation task by detecting and marking all occurrences of the target digits "2" and "7." In the 10 Automatic Detection trials, the target digits are embedded among letters of the alphabet, whereas in the 10 Controlled Search trials they are embedded among other digits. Support exists for both the reliability and validity of this test.<sup>21</sup> Normative data are available from 360 healthy volunteers from the western, central, and eastern United States. The normative sample is demographically similar to the 1980 census data and is stratified according to age, gender, and years of education.

*California Verbal Learning Test II (CVLT-II).* This test measures immediate and delayed recall and recognition for two lists of words: a primary List A and a secondary interference List B. Each list includes 16

words: 4 words from each of 4 semantic categories. The participant is presented with five trials of List A, followed by the interference List B, and then short-delay free-recall, and cued-recall of List A. After a 20minute delay the participant completes long-delay free-recall, cued-recall and yes/no recognition trials of the primary List A. The CVLT-II provides numerous parameters of learning and memory; we chose the following: trial one recall of List A, learning slope over the five trials, degree of vulnerability to proactive interference (detrimental effect of prior learning on retention of new material; List B minus trial one of List A) and retroactive interference (detrimental effect of new learning on recall of previously learned material; short-delayed free recall minus trial five of List A), delayed free recall of List A, and frequency of repetition errors in recall. We administered the alternative form for the second testing session to control for practice effects. A great deal of support exists for the validity and reliability of this test.<sup>22</sup> The normative sample for the CVLT-II consists of 1087 healthy adults who closely matched the 1999 U.S. census data with respect to race, geographical location, and education.

*Wechsler Memory Scale (WMS-III): Logical Memory subtest.* This subtest measures episodic memory for conceptually meaningful material. The participant listens to two paragraph-length short stories and recalls as much information as possible immediately following the presentation of each story and again following a 30-minute delay. The test manual provides strong support for the psychometric properties of the WMS-III subtests and indices used in this study.<sup>23</sup> Normative data for the WMS-III were provided by 1250 healthy, 1997 census-matched American men and women.

Wechsler Memory Scale (WMS-III): Working Memory index. This index measures working memory, which is defined as the ability to attend to information, manipulate it while holding it in memory, and formulate a response. The Working Memory Index consists of the Letter-Number Sequencing subtest and the Spatial Span subtest. Letter-Number Sequencing measures auditory working memory. After hearing a list of randomly presented numbers and letters the participant must first reorganize the numbers into ascending order and then the letters into alphabetical order. Spatial Span, which is the visual analogue of the Digit Span subtest, measures visual working memory. The participant watches an examiner tap blocks in sequences of increasing length and then repeats the sequence in the same order (forward span) and in the reverse order (backward span).

Wechsler Abbreviated Scale of Intelligence (WASI). The two-subscale version of the WASI provides a valid and reliable estimate of general intelligence based on normative data from 1255 healthy, 1999 census-matched Americans.<sup>24</sup> The Vocabulary subtest requires the participant to verbally define 38 words, measuring verbal knowledge and general information. The Matrix Reasoning subtest consists of four types of non-verbal reasoning tasks: pattern completion, classification, analogy and serial reasoning. The participant examines a matrix from which a section is missing and completes the matrix by choosing one of five response options.

*Beck Depression Inventory (BDI-II)*. This self-administered questionnaire consists of 21 items assessing the intensity of depression. Each item refers to a particular symptom of depression and includes four statements arranged in increasing severity. The participant selects one statement for each symptom that best describes the way they have been feeling during the past 2 weeks. This valid and reliable instrument is commonly used to assess depressive symptomatology.<sup>25</sup>

*State-Trait Anxiety Inventory (STAI)*. This 40-item questionnaire assesses current (state) and general (trait) levels of anxiety. The participant rates each statement on a 4-point rating scale ranging from never to almost always according to how they have been feeling over the past two weeks for the 20 state items, and in general for the 20 trait items. We used this questionnaire to measure participants' general tendencies regarding anxiety and to determine their state levels of anxiety at the retest period. The STAI is a valid measure of anxiety with moderate test-retest reliability.<sup>26</sup>

Health and background information. This questionnaire includes questions about basic demographic information, as well as: (1) self-rated health on a 4-point scale ranging from dissatisfied to satisfied, (2) current and past treatment for anxiety and depression, (3) caffeine and alcohol use, (4) current medications, and (5) the presence of risk factors for cognitive impairment, including head injury, diabetes, high blood pressure, and heart problems. Participants also indicated whether they were experiencing a list of health problems, including headache, depression, nervousness, sleep problems, poor appetite, and feeling run down. Participants completed the assessment battery in the following order: health and background information; CVLT-II learning and immediate recall trials; WMS- III Logical Memory immediate recall trial; Ruff 2 & 7 Selective Attention Test; WMS-III Working Memory Index; CVLT-II delayed recall trials; WMS-III Logical Memory delayed recall trial; WASI; and BDI-II. At the end of the second testing session participants completed the STAI prior to completing the BDI-II.

# Statistical analysis

We converted raw scores for all tests to age-corrected, normalized scores according to the respective test manuals. Unfortunately, not all tests utilized the same normalized test scores: Wechsler test scores are expressed as deviation intelligence quotients (M =100, SD = 15) whereas CVLT-II and Ruff 2 & 7 scores are expressed as z-scores (M = 0, SD = 1). In order to facilitate the analysis of patterns of performance across tests, we converted all normalized test scores to z-scores with 95% confidence intervals corrected for sample size.<sup>27</sup> z-Scores above zero reflected higher than average performance, whereas scores below zero reflected lower than average performance. We examined our primary hypothesis concerning cognitive impairment while caregiving using one-sample t-tests to determine whether standardized cognitive performance was significantly above or below the normative sample mean. We examined our secondary hypothesis concerning improvement in cognition when participants were no longer caregiving using paired t-tests comparing outcome measures at sessions one and two. We did not correct for multiple statistical tests because of statistical power limitations related to sample size, and because such corrections are considered unnecessary for hypothesis-driven a priori analyses.<sup>28-30</sup>

## RESULTS

#### CAREGIVING PERIOD

### Participant characteristics

As indicated in Table 1, caregivers in this study were predominantly female, most were spouses, and their average age was approximately 60. This sample of participants is demographically similar to others caregiver samples in the palliative care literature.<sup>8</sup> Participants in this study were relatively well-educated, with an average of nearly 15 years of education. In keeping with their education, the group's intelligence was slightly above average on the WASI (M = 106, SD = 12). Under normal circumstances, therefore, our

caregiver participants would be expected to perform at or somewhat above the norm on the cognitive tests used in this study.

Participants were also relatively physically healthy according to several indicators. Their self rated health, on a 4-point scale ranging from 1 (dissatisfied) to 4 (satisfied), was 3.31 (SD = 0.79). Of the 27 caregivers, 10 were taking no medications, the most medications any participant was taking was 4, and the average number was 1.58 (SD = 0.63). Their average score on a composite of health-related cognitive risk factors, including diabetes, high blood pressure, cancer, and thyroid problems, was 0.70 (SD = .95). Importantly, the key cognitive outcomes in Figure 1 were unrelated to the number of medications participants were taking (all ps > 0.25 and all rs < 0.25), and to the health-related cognitive risk factor composite (all ps > 0.44 and all rs < 0.16). Although participants were relatively physically healthy, the effects of caregiver stress were evident. More than half (n = 14) reported that they were run down, and the same number indicated having problems sleeping. Of the 27 caregivers, 20 reported having at least one of these two problems. As a group, caregivers' BOI-II scores fell in the mild to moderate range, with a total score of 12.04, and 5 participants were being treated for anxiety or depression.

#### Attention

*Ruff 2 & 7.* We began by examining whether caregivers experienced disruptions in their ability to attend to information; a process that has been shown to be vulnerable to the effects of stress in other populations.<sup>9–12,17,18</sup> As shown in Figure 1, which includes *z*-scores for key cognitive outcomes during caregiving (time 1), caregivers did, in fact, exhibit deficits in attention regulation. They were both faster and less accurate than expected. The mean Total Speed score was significantly above the norm, t(26) = 2.64, p = 0.01, whereas the mean Total Accuracy score was significantly below the norm, t(26) = -3.85, p = 0.001. We report the total scores for these indices because the findings were virtually identical for the automatic and controlled trials.

*CVLT-II*. Further evidence that caregivers were experiencing difficulty regulating attention comes from their performance learning a list of related words presented in random order. On the first recall trial, participants' performance was significantly lower than expected, t(26) = -2.02, p = 0.05. Furthermore, their learning slope was significantly lower than the normative sample, indicating that caregivers acquired fewer new items over the four subsequent learning tri-



**FIG. 1.** Mean *z*-scores ( $\pm$ 95% confidence interval [CI]) for 27 palliative caregivers during caregiving (Test 1) and 22 palliative caregivers at least 6 months after the death of care recipients (Test 2). High proactive and retroactive interference scores reflect low levels of interference, and vice versa. PI, Proactive Interference; RI, Retroactive Interference; LDFR, Long Delay Free Recall; LMII, Delayed Logical Memory; LNS, Letter Number Sequencing; S-Span, Spatial Span \*Significantly different from *z* = 0, *p* < 0.05.

als than their age-matched peers, t(26) = -2.24, p = 0.03. They were also significantly more likely to repeat already recalled items during the course of each recall trial, t(21) = 2.48, p = 0.02, providing further evidence of attentional dysregulation.

Data from the CVLT-II also indicate that the caregivers were experiencing difficulty switching attention from an initial learning task (the original List A) to a second task (the distracter List B). Specifically, high levels of proactive interference (indicated by negative z-scores in Figure 1) indicate that caregivers performed significantly poorer on distracter List B than on the first trial of the primary List A, presumably because of difficulty shifting attentional resources to the new list, t(26) = -2.02, p = 0.05. Then, because they learned List B poorly, it did not interfere with their ability to recall the original primary list after a short delay, resulting in a trend toward lower than expected levels of retroactive interference, t(26) = 1.76, p = 0.09.

In summary, data from the CVLT-II list learning test suggest that caregivers had difficulty: (1) attending to the contents of their own memory stores, making it difficult for them to acquire new items, (2) monitoring their memory performance, causing them to mistakenly recall the same items repeatedly, and (3) switching attention—or suppressing a strong but no longer relevant set of responses (primary List A) when they were required to learn a new set of responses (distracter List B).

*Episodic memory.* In contrast to caregivers' deficiencies on tasks requiring attentional regulation, their ability to retrieve CVLT-II List A items from episodic memory after 20 minutes was not significantly below the norm, t(26) = -0.78, p = 0.45. We note that delayed recall was likely aided by their poor learning of distracter List B (due to high levels of proactive interference), which resulted in lower than expected retroactive interference during memory recall. Episodic memory for the coherent stories from the Logical Memory subtest was also unimpaired, t(26) = 1.48, p = 0.15.

*Working memory.* Working memory scores were not significantly different from the mean of the normative sample. This was the case for both verbal working memory, t(26) = 1.13, p = 0.27, and spatial working memory, t(26) = -1.24, p = 0.22.

#### POST-CAREGIVING PERIOD

Five of the 27 caregivers initially assessed were not eligible for retesting because their palliative family member was still alive. We compared caregivers of surviving patients with those whose patients passed away on a variety of demographic and health variables measured during the first testing session using Analysis of variance with continuous variables and  $\chi^2$  analyses with dichotomous variables. There were no significant differences between these groups (all ps > 0.10).

#### Mood

Caregivers' self-rated level of depression, as measured by the BDI-II, improved from 12.00 at session one to 9.18 at session two, although this change only approached significance, t(21) = 1.90, p = 0.07. They also completed the STAI at the follow-up period. State anxiety levels (*z*-score M = 0.20, SD = 1.04) were slightly but not significantly elevated compared to the norm, whereas trait anxiety levels (*z*-score M = 0.61, SD = 1.22) were significantly elevated, t(21) = 2.36, p = 0.03. As expected, state and trait anxiety were correlated with one another, r(22) = 0.69, p < 0.01, and with the BDI-II total score, r(22) = 0.78; p < 0.001, and r(22) = 0.58; p < 0.05, respectively.

#### Attention

*Ruff 2 & 7.* Caregivers continued to exhibit an overall tendency to be faster than the normative sample, while also making more errors. The mean Total Speed score changed very little from the first testing session. There was, however, a significant improvement in accuracy, t(21) = 2.1, p = 0.04. So although caregivers continued to search for targets quickly, there was evidence of improvement in their accuracy 6 or more months after the cessation of their roles as caregivers, suggesting that attentional regulation is returning to normal.

*CVLT-II*. Although several indicators of attentional control on the list-learning task were returning to normal, improvements from time 1 to time 2 were not significant. This was true with respect to performance on the first trial of the primary word list, t(21) = -1.53, p = 0.14, and on subsequent learning across the five trials (i.e., learning slope), t(21) = -1.47, p = 0.16. Furthermore, as shown in Figure 1, we found a trend for low levels of retroactive interference to return to average levels at the second session, t(21) = 1.95, p = 0.06. As seen in the following section, however, an undesirable effect of interference returning to normal levels was poorer long-term episodic memory recall at the second test session.

*Episodic memory.* In contrast to their average longdelay free recall performance on the CVLT-II at the first test session, caregivers exhibited a trend toward deteriorating performance on this measure at session two, t(21) = 1.78, p = 0.09. Although their word-list recall performance deteriorated, participants showed very little change in their ability to recall meaningful information from stories on the WMS-III Logical Memory subtest, t(21) = -0.17, p = 0.86.

*Working memory.* Participants' performance on tests of verbal and spatial working memory also deteriorated when they were retested. Spatial working memory was significantly worse than at the first test session, t(21) = 2.43, p = 0.02, and verbal working memory was nearly significantly worse, t(21) = 1.90, p = 0.07.

In summary, the recovery pattern from the first to the second test session was not consistent across tests. Improvement was evident on tasks requiring monitoring and attentional regulation, whereas further deterioration was evident on a test of spatial working memory, and a mixed pattern was seen for episodic memory. Memory for structured, meaningful prose was preserved, while it deteriorated somewhat for a list of words that required participants to impose structure in order to perform well.

# DISCUSSION

The key finding from this study is that caregivers of palliative family members exhibited significant impairments in selective attention on the Ruff 2 & 7 test, as well as impairments in aspects of memory on the CVLT-II list-learning test that are mediated by attentional processes, including learning, performance monitoring, and switching between primary and secondary memory tasks. This finding is consistent with evidence of impaired attention during periods of chronic stress, including spouse caregivers who performed more poorly than matched noncaregivers on a digit symbol test of attention, working memory, and speeded visuomotor ability,<sup>18</sup> middle-aged female patients with chronic burnout syndrome who performed more poorly than healthy controls and the normative sample on a visual and auditory continuous performance test of attention,<sup>17</sup> and students with chronic daily hassles who performed more poorly than students with low levels of stress on a divided attention memory-scanning test.<sup>31</sup> Although these studies suggest

that care providers exhibit attentional deficits as a result of chronic stress, caregivers also necessarily experience short-term and acute stressors, which can also result in lapses of attention, narrowing of attention, and difficulty filtering out or inhibiting irrelevant information.<sup>9,10,12,32</sup> Interestingly, acute stress from the threat of an electric shock has been shown to increase speed and reduce accuracy among participants given a multiple-choice analogies test under the threat of mild electric shock for errors,<sup>13</sup> mirroring our findings of increased speed at the expense of accuracy on the Ruff 2 & 7 selective attention test. The acute and chronic stress literatures suggest that caregivers' attentional capacities may be doubly at risk from acutely stressful circumstances they encounter, and the longstanding stressful nature of caregiving.

At a practical, clinical level, deficits in caregivers' ability to regulate attention in order to ignore distraction and monitor performance could have potentially grave consequences. For example, palliative patients often have complex medication schedules, requiring caregivers to organize, coordinate, and administer multiple drugs in distracting environments and at various times during the day, reflecting the type of monitoring task that our participants experienced difficulty with. Impairments in the ability to attend to relevant information in distracting environments could also contribute to why family caregivers have been found to provide unreliable information about care recipients to health care professionals.8 In contrast to the attention dysregulation palliative caregivers exhibited across a variety of neuropsychological tests, their episodic and working memory was not significantly impaired during the caregiving period. The absence of delayed recall deficits on the CVLT-II word-list while providing care is at odds with the poor immediate and delayed word-list recall by 11,835 older females caring for ill husbands in the Nurses' Health Study.<sup>19</sup> This inconsistency may be the result of differences in statistical power given that delayed recall z-scores were below the mean in this study; a trend that may have reached statistical significance with a larger sample of participants. Another likely contributor to this inconsistency is that the list-learning task used in this study included distraction, whereas the list-learning task used in the Nurses' Health Study did not. Caregivers in our study had difficulty reallocating attentional resources to learn the secondary CVLT-II distracter list. As a result, it did not interfere with their ability to recall the original primary list, offering a delayed recall advantage that caregivers in the Nurses' Health Study did not have.

There are several other possible explanations for contradictory findings concerning episodic and working memory impairments while caregiving. First, stress-induced hormones, such as glucocorticoids, have been shown to enhance memory when they are present in moderate amounts following acute stress, and to impair memory when they are present in chronically higher doses.<sup>9</sup> This finding highlights the need to measure both

moderate amounts following acute stress, and to impair memory when they are present in chronically higher doses.<sup>9</sup> This finding highlights the need to measure both chronic and acute levels of stress in future caregiver cognition research. Second, episodic memory impairments appear to be more prominent among individuals who are both depressed and anxious than among individuals who only have symptoms of depression,<sup>33,34</sup> suggesting the need for accurate assessment of symptoms of stress, depression, and anxiety. Third, visual memory may be affected to a greater extent by chronic stress than verbal memory as a result of the detrimental effects of stress on the hippocampus, a key region of the brain responsible for memory, especially aspects of memory that are time-limited and spatial.<sup>16</sup> In support of this hypothesis, female patients with chronic burnout syndrome showed significant deficits in visuospatial episodic memory, but were unimpaired on a verbal list-learning task.<sup>17</sup> Future studies examining the impact of caregiver stress on memory should, therefore, include both verbal and nonverbal measures.

A secondary goal of this study was to explore the possibility of recovery of stress-related cognitive impairment by retesting 22 caregivers at least 6 months after the death of palliative patients. Our results were partially supportive of the recovery we expected to see. Participants who were no longer caregiving demonstrated improvement on tests requiring them to monitor their performance and regulate their attentional resources, although the extent of the improvement was only significant for selective attention accuracy on the Ruff 2 & 7 test. On the other hand, significant deterioration was evident on a test of spatial working memory and a trend toward deteriorating performance was seen on the CVLT-II test of delayed episodic memory for unrelated list words.

Improvement on certain tests and further deterioration on others suggests the possibility that multiple mechanisms of action are responsible for cognitive impairment in the face of caregiver stress. One limitation of the current study is that it did not examine why caregiving is associated with cognitive impairment. Several possibilities exist that will need to be examined in future research. Attention dysregulation among caregivers in this study is consistent with the view that stress-related intrusive thoughts compete for limited cognitive resources, thereby interfering with cognitive functioning.<sup>35–37</sup> This hypothesis would explain why caregivers' attentional capacity improved post-caregiving, when stress-related intrusive thoughts surely diminished. This view does not, however, explain why caregivers who were retested after the death of their relatives exhibited further deterioration on tests of episodic and working memory. These impairments are perhaps better explained by the negative influence of chronic stress and elevated trait anxiety on the hippocampus.<sup>15,16,38</sup> If our palliative caregivers did experience impaired hippocampal functioning as a result of their lengthy and stressful caregiving experiences, cognitive functions mediated by this structure may take much longer to return to normal, if they improve at all. A second limitation concerning this study is that its findings are based on a modest sample of 27 informal palliative caregivers who were compared to normative populations, which limits statistical power and generalizability. We note, however, that evidence of significant cognitive impairment with this modest sample suggests that cognitive deficits among caregivers are, if anything, likely underestimated in this study. It will be important to replicate our findings by comparing a larger and more diverse sample of caregivers to matched controls. A final limitation is that we did not assess caregiver stress directly, or the extent to which stress-related cognitive impairment may have been affected by factors such as the length of time spent caregiving, the amount of time devoted to other work and family responsibilities, or the extent to which caregivers attempted to manage stress using various professional and nonprofessional supports. In order to fully understand the cognitive risks associated with caregiving, future research in this neglected area should include a detailed examination of stress, physical and mental health, and factors that mediate their impact on cognition.

In conclusion, our findings add to a small body of evidence suggesting that while engaging in the highly stressful act of caring for a dying relative, informal caregivers exhibit cognitive deficits relative to healthy normative samples, and that attentional processes may be especially prone to stress-related impairment. Improvement in attentional regulation following caregiving suggests that at least certain cognitive impairments among highly stressed caregivers may be reversed by helping these individuals cope with stressful situations more effectively. Helping them to do so may improve their own health as well as the quality of care they provide.

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# REFERENCES

- Schulz R, Martire LM: Family caregiving of persons with dementia: Prevalence, health effects, and support strategies. Am J Geriatr Psychiatry 2004;12:240–249.
- Pinquart M, Sorensen S: Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. Psychol Aging 2003;18:250–267.
- Vitaliano PP, Zhang J, Scanlan JM: Is caregiving hazardous to one's physical health? A meta-analysis. Psychol Bull 2003;129:946–972.
- Christakis, NA, Allison, PD: Mortality after the hospitalization of a spouse. N Engl J Med 2006;354:719–730.
- Ferrario SR, Cardillo V, Vicario F, Balzarini E, Zotti AM: Advanced cancer at home: Caregiving and bereavement. Palliat Med 2004;18:129–136.
- Grunfeld E, Coyle D, Whelan T, Clinch J, Reyno L, Earle CC, Willan A, Viola R, Coristine M, Janz T, Glossop R: Family caregiver burden: Results from a longitudinal study of breast cancer patients and their principal caregivers. CMAJ 2004;170:1795–1801.
- Visser G, Klinkenberg M, van Groenou M, Willems DL, Knipscheer CPM, Deeg DJH: The end of life: Informal care for dying older people and its relationship to place of death. Palliat Med 2004;18:468–477.
- 8. McMillan SC: Interventions to facilitate family caregiving at the end of life. J Palliat Med 2005;8:S132–S139.
- 9. Mendl M: Performing under pressure: Stress and cognitive function. Appl Anim Behav Sci 1999;65:221–244.
- Braunstein-Bercovitz H: Does stress enhance or impair selective attention? The effects of stress and perceptual load on negative priming. Anx Stress Coping 2003;16: 345–357.
- Keinan G, Friedland N, Kahneman D, Roth D: The effect of stress on the suppression of erroneous competing responses. Anx Stress Coping 1999;12:455–476.
- Braunstein-Bercovitz H, Dimentman-Ashkenazi I, Lubow RE: Stress affects the selection of relevant from irrelevant stimuli. Emotion 2001;1:182–192.
- Keinan G: Decision making under stress: scanning of alternatives under controllable and uncontrollable threats. J Pers Soc Psychol 1987;52:639–644.
- Mahoney AM, Dalby JT, King MC: Cognitive failures and stress. Psychol Rep 1998;82:1432–1434.

- Bremner JD: Does stress damage the brain? Biol Psychiatry 1999;45:979–805.
- Lupien SJ, Fiocco A, Wan N, Maheu F, Lord C, Schramek T, Tu MT: Stress hormones and human memory function across the lifespan. Psychoneuroendocrinology 2005;30:225–242.
- Sandstrom A, Rhodin IN, Lundberg M, Olsson T, Nyberg L: Impaired cognitive performance in patients with chronic burnout syndrome. Biol Psychol 2005;69:271–79.
- Caswell LW, Vitaliano PP, Croyle KL, Scanlan JM, Zhang J, Daruwala A: Negative associations of chronic stress and cognitive performance in older adult spouse caregivers. Exp Aging Res 2003;29:303–318.
- Lee S, Kawachi I, Grodstein F: Does caregiving stress affect cognitive function in older women? J Nerv Ment Dis 2004;192:51–57.
- Vitaliano PP, Echeverria D, Yi J, Phillips PEM, Young J, Siegler IC: Psychophysiological mediators of caregiver stress and differential cognitive decline. Psychol Aging 2005;20:402–411.
- Ruff RM, Allen CC: *Ruff 2 & 7 Selective Attention Test. Professional Manual*. Odessa, FL: Psychological Assessment Resources Inc., 1995.
- Delis DC, Kramer JH, Kaplan E, Ober B: California Verbal Learning Test. Professional Manual, 2nd ed. San Antonio, TX: The Psychological Corporation, 2000.
- Wechsler D: WAIS-III, WMS-III Technical Manual. San Antonio, TX: Psychological Corporation (Harcourt Brace and Company), 1997.
- Wechsler D: Wechsler Abbreviated Scale of Intelligence Manual. San Antonio, TX: Psychological Corporation (Harcourt Brace and Company), 1999.
- Beck AT, Steer RA, Brown GK: *Manual for the Beck Depression Inventory*, 2nd ed. San Antonio, TX: The Psychological Corporation, 1996.
- Speilberger CD, Gorusch RL, Lushene RE: State Trait Anxiety Inventory Manual. Mountain View, CA: Consulting Psychologists Press, 1970.
- Cumming G, Finch S: Inference by eye: Confidence intervals and how to read pictures of data. Am Psychol 2005; 60:170–180.
- Perneger TV: What's wrong with Bonferroni adjustments. BMJ 1998;316:1236–1238.
- Rothman KJ: No adjustments are needed for multiple comparisons. Epidemiology 1990;1:43–46.
- Savitz DA, Olshan AF: Multiple comparisons and related issues in the interpretation of epidemiologic data. Am J Epidemiol 1995;142:904–908.
- Brand N, Hanson E, Godaert G: Chronic stress affects blood pressure and speed of short-term memory. Percept Mot Skills 2000;91:291–298.
- Skosnik PD, Chatterton RT, Swisher T, Park S: Modulation of attentional inhibition by norepinephrine and cortisol after psychological stress. Int J Psychophysiol 2000;36:59–68.
- Kizilbash AJ, Vanderploeg RD, Curtiss G: The effects of depression and anxiety on memory performance. Arch Clin Neuropsychology 2002;17:57–67.
- Airaksinen E, Larsson M, Lundberg I, Forsell Y: Cognitive functions in depressive disorders: evidence from a population-based study. Psychol Med 2004;34:83–91.

# MACKENZIE ET AL.

- 35. Sarason IG: Stress, anxiety, and cognitive interference: Reactions to tests. J Pers Soc Psychol 1984;46:929–938.
- Seibert PS, Ellis HC: Irrelevant thoughts, emotional mood states, and cognitive task performance. Mem Cognit 1991; 19:507–513.
- 37. Eysenck MW: *Anxiety: The Cognitive Perspective*. Hove, UK: Lawrence Erlbaum Associates, 1992.
- 38. Lovallo WR: Stress and Health: Biological and Psychological Interactions, 2nd ed. Thousand Oaks, CA: Sage, 2005.

Address reprint requests to: Corey S. Mackenzie, Ph.D. Department of Psychology University of Manitoba 190 Dysart Road Winnipeg, Manitoba, Canada R3T 2N2

E-mail: corey\_mackenzie@umanitoba.ca

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- 2. P. P. Vitaliano, J. Zhang, H. M. Young, L. W. Caswell, J. M. Scanlan, D. Echeverria. 2009. Depressed Mood Mediates Decline in Cognitive Processing Speed in Caregivers. *The Gerontologist* 49:1, 12-22. [CrossRef]