The Impact of Resilience Factors and Anxiety During Hospital Admission on Longitudinal Anxiety Among Dyads of Neurocritical Care Patients Without Major Cognitive Impairment and Their Family Caregivers

Emma E. Meyers[1,2,3,4], **Alex Presciutti**[5], **Kelly M. Shaffer**[6], **Melissa Gates**[4,7], **Ann Lin**[4,7], **Jonathan Rosand**[1,2,3], **Ana-Maria Vranceanu**[1,3,4,7,*]

[1]Henry and Allison McCance Center for Brain Health, Massachusetts General Hospital, 55 Fruit St., Wang Ambulatory Care Center 8th Floor, Suite 815 and 85, Boston, MA 021140, USA.

[2]Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Massachusetts General Hospital, Boston, MA 02114, USA.

[3]Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA.

[4]Integrated Brain Health Clinical and Research Program, Department of Psychiatry, Massachusetts General Hospital, 1 Bowdoin Square, 1st Floor, Suite 100, Boston, MA 02114, USA.

[5]Department of Psychology, University of Colorado Denver, Denver, CO 80217, USA.

[6]Center for Behavioral Health and Technology, University of Virginia School of Medicine, PO Box 801075, Charlottesville, VA 22902, USA.

[7]Department of Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA.

Abstract

Background/Objective: Anxiety is common in patients experiencing neurocritical illness and their family caregivers. Resilience factors like mindfulness and coping skills may be protective against symptoms of emotional distress, including anxiety. Less is known about the interplay of

anxiety symptoms and resilience factors between patients and caregivers. The purpose of this study is to examine the trajectory of anxiety symptoms among dyads of neurocritical care patients without major cognitive impairment and their family caregivers and to elucidate the relationship between resiliency (e.g., mindfulness and coping) and anxiety in these dyads.

Methods: Prospective, longitudinal study of adults admitted to the neurological intensive care unit (Neuro-ICU) and their caregivers. Dyads of patients ($N = 102$) and family caregivers ($N = 103$) completed self-report measures of mindfulness (Cognitive Affective Mindfulness Scale-Revised) and coping (Measure of Current Status-Part A) during Neuro-ICU hospitalization and anxiety symptoms (anxiety subscale of the Hospital Anxiety and Depression Scale) during hospitalization and at 3- and 6-month follow-up. We used actor–partner interdependence modeling to predict the effect of one's own baseline characteristics on one's own and one's partner's future anxiety symptoms.

Results: Rates of clinically significant anxiety symptoms were 40% for patients and 42% for caregivers at baseline. Of these, 20% of patients and 23% of caregivers showed moderate and severe symptoms. Approximately, one-third of patients and caregivers reported clinically significant anxiety symptoms at 3- and 6-month follow-ups, with more than 20% endorsing moderate or severe symptoms. Patients' own baseline mindfulness, coping, and anxiety symptoms were associated with lower anxiety symptoms at all time points ($ps < 0.001$)—this was also true for caregivers. For both patients and caregivers, one's own baseline mindfulness predicted their partner's anxiety symptoms 3 months later ($p = 0.008$), but not at 6-month follow-up.

Conclusions: Anxiety symptoms in Neuro-ICU patient–caregiver dyads are high through 6 months following admission. Mindfulness is interdependent and protective against anxiety in dyads at 3-month but not 6-month follow-up. Early, dyad-based interventions may prevent the development of chronic anxiety in patients without major cognitive impairment and caregivers.

Introduction

Admission to the neurological intensive care unit (Neuro-ICU) is often characterized by periods of uncertainty about survival and long-term prognosis, which is stressful for patients and their family caregivers (i.e., family or friends who provide the bulk of unpaid care). Unsurprisingly, rates of clinically significant anxiety symptoms are high among neurocritical care patients (20–43%) [1–3] and their caregivers (18–46%) [3–5]. Prospective studies of survivors of critical illness have demonstrated that anxiety rates remain elevated well beyond hospital admission [6, 7]. This is particularly concerning given that anxiety has been associated with greater risk of major adverse cardiovascular and cerebrovascular events and mortality in critically ill patients [8, 9]. In caregivers, chronic anxiety has been associated with caregiver strain and depression [4].

Resiliency, a multidimensional biopsychosocial construct defined as the ability to successfully adapt and recover from adversity or trauma [10], has been consistently linked to a variety of positive health outcomes [11–13]. Mindfulness and coping strategies are

two modifiable resilience factors. Mindfulness, or nonjudgmental awareness and focus on the present in the face of adversity [14], has been inversely associated with anxiety symptoms in a cross-sectional dyadic study of neurocritical care patients and their family caregivers during hospitalization [3, 13]. Mindfulness-based interventions have effectively improved stress, psychological symptoms, and quality of life for caregivers of patients with neurodegenerative disease [15, 16]. Coping strategies, defined as the cognitive, behavioral, and emotional skills that individuals draw on during times of stress, are also linked to positive psychological and physical health outcomes [17]. In medical populations, adults with chronic myofascial pain who rely on adaptive coping strategies such as emotion-centered coping have been found to experience less affective pain and depressive symptoms [18]. Couples undergoing unsuccessful treatment for infertility who use emotion-centered coping strategies have been shown to suffer less psychological distress in both individuals [18]. In Neuro-ICU patients and caregivers, poor coping strategies have been associated with increased global emotional distress and elevated psychiatric symptoms [13].

An increasing body of the literature acknowledges that patient and caregiver resiliency factors and symptoms are interdependent, with each individual's adjustment to medical illness impacting their partners' adjustment [19–21]. For example, in a cross-sectional study of Neuro-ICU patients and caregivers, depression symptoms have been shown to be interdependent between patients and caregivers, and high mindfulness in either the patient or caregiver has been associated with lower depression symptoms in both self and partner [3]. Accordingly, current guidelines recommend assessing patient and caregiver factors at the dyadic level (i.e., patient and caregiver together) [22, 23]. However, the longer-term trajectory of anxiety symptoms in Neuro-ICU survivors and their family caregivers, the impact of psychological resilience on that trajectory, and the nuanced role of the dyad in the development of chronic anxiety symptoms remain unclear.

The current study seeks to fill this gap by first examining the longitudinal trajectory of anxiety symptoms in neurocritical care patients and their caregivers and then exploring prospectively the synergistic relationship between resiliency factors and anxiety in patient–caregiver dyads. We hypothesize that for both patient and caregiver, anxiety symptoms will be predictive of one's own level of anxiety at the subsequent assessment, and that resiliency factors will be negatively associated with one's own anxiety symptoms across all time points. Further, we hypothesize that for both patients and caregivers, anxiety symptoms and resiliency factors will be interdependent, with one's own anxiety symptoms predicting a higher level of symptoms in their partner and one's own resilience being associated with lower levels of anxiety symptoms in their partner at follow-up.

Materials and Methods

Sample and Design

This is a prospective, longitudinal cohort study of adults admitted to the Neuro-ICU and their family caregivers at a large tertiary medical center in Boston, MA, between 2015 and 2016. The study was approved by the local institutional review board, and informed consent was obtained from all participants enrolled in the study. The full recruitment and enrollment protocol has been previously described [3]. The inclusion criteria for patients

were as follows: (1) adults aged 18 years or older, (2) English fluency and literacy, and (3) hospitalization to the Neuro-ICU within the past 2 weeks. Most patients were enrolled within 2 days of Neuro-ICU admission. Patients were excluded if they were deemed unable to provide consent due to cognitive impairment; had severe aphasia or cognitive impairment that prohibited full participation; had anticipated death; or did not have an family caregiver. Patients with cognitive impairments but who were still able to fill out questionnaires with assistance were included. Patients with transient aphasia or delirium who were asymptomatic at the time of consent were considered medically able to participate. Based on historic records from our Neuro-ICU, 70% of all admitted patients would be eligible for participation. All eligible patients were cleared for participation by the ICU team.

Family caregivers were eligible to participate if they met the following criteria: (1) adults aged 18 years or older, (2) English fluency and literacy, and (3) identification as a primary family caregiver for an eligible patient. As per criterion #3, only one caregiver who identified as the "primary family caregiver" was eligible for inclusion.

Patients and caregivers who consented to participation completed self-report measures on demographic information, psychosocial resilience, and psychiatric symptoms at the time of enrollment. At 3- and 6-month post-discharge, dyads were contacted via email to complete follow-up psychosocial measures using REDCap, a secure online data capture software [24].

Measures

Patient and Caregiver Demographics—During enrollment, patients and caregivers reported age, sex, ethnicity, race, marital status, education, employment status, and relationship to each other. Data were collected on admission diagnosis, need for intubation during hospital stay, and discharge location.

Anxiety Symptoms—Anxiety symptoms were measured via the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A) [25], a widely used and reliable measure among medical populations [26]. Patients reported the frequency of anxiety symptoms during the past week on a scale from 0 ("Not at all") to 3 ("Very much" or "Most of the time"). Seven items on the anxiety subscale are then summed (range 0–21), with higher scores representing greater anxiety symptoms. In our analysis, we considered scores ≥ 8 to be clinically significant mild, moderate, and severe anxiety symptoms [26] and used the higher cut-off of ≥ 11 to characterize clinically significant moderate or severe anxiety symptoms. Anxiety symptoms were measured during Neuro-ICU admission and at 3- and 6-month follow-up.

Resiliency Factors

Mindfulness: The extent to which individuals apply general concepts of mindfulness was measured via the Cognitive Affective Mindfulness Scale-Revised (CAMS-R) [27]. The scale's 12 items asking about engagement in mindfulness are scored on a scale from 1 ("rarely" or "not at all") to 4 ("almost" or "always"). Scores are then summed (range 12–48), with higher scores representing greater utilization of mindfulness techniques. The

CAMS-R is a reliable and valid scale that has been used in prior studies in neurocritical care populations [13, 28], as well as with other medical populations of patients and caregivers [29] It was administered during Neuro-ICU admission.

Coping: Coping skills were measured via the Measure of Current Status-Part A (MOCS-A) [30], in which 13 items assess confidence in skills related to relaxation and behavioral and cognitive responses to stressful thoughts or situations. Items are scored on a scale from 0 ("I cannot do this at all") to 4 ("I can do this extremely well"). The items are summed (range 0–52), and higher scores suggest better utilization of coping skills. The MOCS-A is a reliable and valid scale that has been used in prior studies in neurocritical care populations [13, 28] as well as with other medical populations of patients and caregivers [31]. It was administered during Neuro-ICU admission.

Statistical Analysis

We summarized participant characteristics with measures of central tendency (e.g., proportion, mean). Univariate tests (Pearson r, Chi-square, and paired sample t tests) between patient and caregiver variables were used as appropriate. Two-tailed tests were used to utilize to more conservatively identify statistical differences between participant characteristics. Statistical significance was determined with two-tailed tests and an -level of 0.05. Effect size was determined to be small, medium, or large based on Pearson r values of 0.10, 0.30, and 0.50 [32].

We used actor–partner interdependence modeling (APIM) to test impact of resilience and anxiety symptoms on individuals and their partners [33, 34]. This analysis models the contribution of one dyad member's predictors on his/her own outcome and simultaneously on his/her partner's outcome, while accounting for the correlation between dyad members' data. In the current study, an "actor effect" refers to the relationship between a person's baseline measures (resiliency factors and anxiety) with his/her own anxiety symptoms at follow-up. A "partner effect" refers to the relationship between a person's baseline measures (resiliency factors and anxiety) and his/her "partner's" (i.e., the other dyad member's) anxiety symptoms at follow-up. Contrast tests were used to determine whether patient and caregiver actor and partner effects were equivalent. If contrast tests yielded $p < 0.05$, patient and caregiver effects were considered significantly different and were interpreted separately. If contrast tests yielded $p > 0.05$, patient and caregiver effects were considered not significantly different and a pooled effect was interpreted.

In following recommendations from the Patient-Centered Outcomes Research Institute [35], we used multiple imputations with fully conditional specification to account for uncompleted measures [36] and created 40 imputed datasets. All analyses were performed using SPSS Version 24 [37].

Results

Participant Characteristics

Our prospective cohort consisted of 114 patient–caregiver dyads. Of these, 102 patients (89%) and 103 caregivers (90%) completed study measures and were included in the

present analysis. Excluded individuals signed informed consent but did not complete study measures. The included patients and caregivers are from 108 unique dyads, with 96 complete patient–caregiver dyads (i.e., completed study measures by both the patient and caregiver), six patients without caregivers, and six caregivers without patients represented. Rates of psychosocial measure completion were 94% at baseline, 77% at 3 months, and 71% at 6 months.

Table 1 summarizes demographic and medical characteristics. Both patients and caregivers were on average middle aged. The majority were white and completed some college education. There was a higher proportion of females to males and married/cohabitating individuals among the caregivers compared to patients. Cerebrovascular diseases, including ischemic and hemorrhagic stroke, were the most common neurological diagnoses, followed by intracranial tumors or other structural lesions. The most common patient–caregiver relationship was spouse/partners. Intubation was used as a proxy for disease severity. Seventy-six percent of patients were intubated at any point during their hospitalization; 22% of patients were intubated for a reason other than surgery. Indications for intubation included status epilepticus, neurological worsening leading to altered mental status, myasthenia gravis exacerbation, and hypercarbic respiratory failure unrelated to neurological injury.

Resiliency Factors and Anxiety Symptoms

Patient and caregiver resiliency factors and anxiety symptom severity are summarized in Table 2. There were no differences in mindfulness and coping scores between patients and caregivers ($t(1377) = -0.79$ and $t(653) = -0.27$, respectively, $p > 0.42$). Rates of clinically significant moderate or severe anxiety symptoms were high and were similar for patients and caregivers at baseline ($\chi^2(1) = 0.6$, $p = 0.49$). At 3- and 6-month follow-up, rates of clinically significant symptoms in patients slightly increased, while rates in caregivers slightly decreased. Overall, patients were more likely than caregivers to report moderate to severe anxiety symptoms at 3-month ($\chi^2(1) = 9.01$, $p < 0.001$) and 6-month follow-up ($\chi^2(1) = 9.82$, $p = 0.002$). Mean HADS-A score did not differ based on sex, age, race (white vs non-white), ethnicity (Hispanic vs. non-Hispanic), marital status, or education level (all $ps > 0.09$). There was no difference in mean HADS-A scores between patients with vascular, structural, or other types of diagnoses ($ps > 0.06$), between patients who were intubated and patients who were not intubated ($ps > 0.1$), and between family caregivers of intubated patients and non-intubated patients ($ps > 0.2$). Individuals with a self-reported prior mental health history had greater HADS-A scores ($M = 10.17$) than those without ($M = 6.62$; $t = -3.04$, $p = 0.002$) at baseline and at 6 months ($M = 8.99$ vs. $M = 6.01$; $t = -1.99$, $p = 0.047$).

Effects of Own Psychological Factors on Own Anxiety Symptoms (Actor Effects)

Bivariate Analysis—Bivariate correlations between resilience scores and anxiety symptoms are presented in Table 3. Within individuals, baseline anxiety symptoms were positively associated with symptoms at 3- and 6-month follow-up ($ps < 0.001$), and mindfulness and coping scores were negatively associated with severity of anxiety symptoms at both follow-up points ($ps < 0.05$). Effect sizes were mainly medium to large ($r > 0.3$) in both patients and caregivers.

Dyadic Analysis—Actor effects from APIM are presented in Table 4. For both patients and caregivers, severity of anxiety symptoms predicted the degree of symptoms at the subsequent time point (i.e., baseline to 3 months, 3 months to 6 months; $ps < 0.001$). The impact of baseline anxiety symptoms on symptoms at 3 months was greater in caregivers than patients ($\beta = 0.732$ and $\beta = 0.471$, respectively). Mindfulness and coping skills at baseline were associated with less severe anxiety symptoms at all time points.

Effects of Own Psychological Factors on Partner's Anxiety Symptoms (Partner Effects)

Bivariate Analysis—Bivariate correlations between patient and caregiver factors are presented in Table 3. Patient and caregiver anxiety symptoms were positively correlated at 3- and 6-month follow-up ($ps < 0.04$). Patient mindfulness was negatively correlated with caregiver anxiety at 3 months ($p < 0.001$). One's own coping skills were not correlated with one's partner's anxiety at any time point.

Dyadic Analysis—Partner effects from APIM are presented in Table 4. For both patients and caregivers, an individual's baseline mindfulness was associated with their partner's 3-month anxiety symptom severity ($p = 0.008$). No other partner effects were significant. Full details on APIM are presented in Fig. 1.

Discussion

In our cohort of Neuro-ICU patients and their family caregivers, initial rates of anxiety were high, with 40% of patients and 42% of caregivers endorsing clinically significant symptoms at the time of the patient's admission to the Neuro-ICU. Moderate to severe anxiety symptoms were present in 20% of patients and 23% of caregivers. These high rates of clinically significant symptoms remained relatively stable for patients and decreased slightly for caregivers. At 6 months after hospitalization, one in three patients and caregivers reported clinically significant anxiety symptoms.

The present findings are in line with previous cross-sectional work detailing high rates of clinically significant anxiety in the Neuro-ICU for both patients and caregivers [3]. As hypothesized, for both patients and caregivers, an individuals' elevated anxiety symptoms during Neuro-ICU admission were predictive of higher levels of chronic anxiety symptoms post-discharge. The chronicity of anxiety symptoms and the predictive relationship of baseline anxiety on follow-up anxiety have been observed in non-neurocritical care populations as well. In bariatric surgery patients, while preoperative depressive symptoms significantly decreased over time, preoperative anxiety symptoms remained stable through 24–36 month post-op. More so, preoperative anxiety symptoms significantly predicted 6–12-month and 24–36-month post-operative anxiety [38]. In survivors of acute myocardial infarction, anxiety scores at discharge and at 3-month follow-up were the sole predictors of anxiety at 18-month follow-up after adjusting for a number of demographic and lifestyle factors [39]. While the relationship between baseline and follow-up anxiety may seem obvious, maintaining elevated levels of anxiety symptoms beyond hospitalization is not trivial; rather, it is indicative of chronic anxiety that may have serious implications for survivors' and caregivers' quality of life and/or functional status. Clinically, the importance of chronic anxiety cannot be understated, as it has been associated with more adverse

cardiovascular and cerebrovascular events in other critical care patients [8, 9]. Emotional strain has been associated with increased morbidity and mortality for caregivers [40]. As the predictive nature of baseline anxiety on follow-up anxiety may certainly not be specific to neurocritical care populations, it is important that these symptoms are monitored and addressed across ICU and hospital settings.

Interestingly, baseline anxiety symptom levels were a stronger predictor of 3-month anxiety in caregivers than in patients, suggesting that caregivers' anxiety is particularly likely to maintain if endorsed during the patient's hospitalization. As emotional distress in caregivers can prevent them from delivering high-quality care [41], both dyad members may suffer if caregivers experience high levels of anxiety in the crucial early days of the recovery process. Regardless of dyad member, given the elevated risk of adverse cerebrovascular events associated with chronic anxiety [9], early intervention may thus be warranted to prevent further adverse events in an already vulnerable population.

Patients' and caregivers' levels of mindfulness and adaptive coping measured at the time of the patient's admission to the Neuro-ICU were associated with lower own anxiety symptoms—both concurrently at admission and prospectively over the 6 months following admission. These modifiable resilience factors have been tied to improved health outcomes in a number of medical populations [15–17]. In the Neuro-ICU, cross-sectional studies have demonstrated that greater mindfulness is associated with lower psychiatric symptoms in patients [3] and greater quality of life in their caregivers [42]. The present findings contribute longitudinal data to this growing evidence base in this population. Elucidating the protective qualities of mindfulness and adaptive coping may be particularly important in Neuro-ICU populations, as patients often face a lengthy recovery process, with deficits persisting well beyond discharge [43, 44]. Psychotherapeutic interventions that bolster these resilience factors to help patients and caregivers accept the chronic often uncertain nature of their deficits and engage in adaptive coping may lead to better adjustment post-Neuro-ICU stay. Of note, the benefits of mindfulness and adaptive coping on anxiety may not be specific to neurocritical care populations. In the absence of direct comparative evidence with other disease populations, the relative protectiveness of mindfulness and adaptive coping cannot be derived from our study. We suggest continued research efforts in examining the protective nature of mindfulness and adaptive coping in other medical populations, so as to identify specific populations that benefit from these resilience factors.

The dyadic modeling used in this analysis [34] examined how one individual's resilience or anxiety symptoms at hospitalization can not only impact their anxiety trajectory, but also the effects these factors can have on one's *partner's* anxiety. The previous cross-sectional research using APIM to look at resilience factors and psychological distress in Neuro-ICU patient–caregiver dyads demonstrated that for both patients and caregivers, higher levels of mindfulness in one dyad member are associated with lower levels of depressive symptoms in their partner at the time of hospital admission [3]. The present study builds upon these findings, showing that when a patient or caregiver endorsed greater mindfulness at Neuro-ICU admission, their partner reported lower anxiety symptoms 3 months later. The prospective partner effect of mindfulness on anxiety did not, however, extend to anxiety symptoms at 6 months. It is possible that heightened anxiety symptoms after 3

months may be more chronic and stable. Indeed, our analysis showed that 3-month anxiety was a stronger predictor of 6-month anxiety than baseline anxiety was of anxiety at 3 months. However, a more mindful partner may still be protective long term, as lower levels of anxiety at 3 months predict less future anxiety. These findings highlight the importance of dyadic modeling in critically ill patients and their caregivers by demonstrating interdependent protective factors (i.e., mindfulness-based practices) that can be utilized in early interventions. While APIM analysis reveals partner effects while controlling for actor effects and therefore produces a conservative estimate, further work is needed to replicate these results.

The present findings, in conjunction with a growing evidence on psychosocial factors in Neuro-ICU patients and caregivers [3, 13, 42], have important clinical implications. First, since those with clinically significant anxiety during the hospitalization are at high risk of developing chronic anxiety through 6 months, and mindfulness and adaptive coping at hospitalization are associated with less severe anxiety symptoms, an early intervention that starts in the hospital, continues through discharge, and teaches mindfulness-based practices and adaptive coping strategies may prevent the development of chronic anxiety in Neuro-ICU patients and their family caregivers. Second, since an individual's higher mindfulness early in the hospitalization is associated with lower anxiety in their partner at 3 months, the most promising interventions are likely dyad-based (i.e., patient and caregiver together). Qualitatively, patients and caregivers confirm experiencing high anxiety in the Neuro-ICU and express interest in participating in an early dyadic intervention aimed at preventing chronic emotional distress [45].

These findings contribute to a larger conversation taking place in the critical care literature about post-intensive care syndrome (PICS), a constellation of physical, cognitive, and psychiatric symptoms that persist after an ICU stay [46]. While characterizing PICS in the context of the neurological sequalae experienced by Neuro-ICU patients can be challenging, and this investigation looks at only one facet of this multidimensional condition, our findings are in line with rates of anxiety previously reported in the Neuro-ICU PICS literature [47]. Perhaps more significantly, the high rates of anxiety seen in caregivers in our study speaks to the concept of PICS-F, or the psychological ramifications of ICU hospitalization for the family members of the critically ill [46]. The role of psychological resilience factors and their interdependence between patients and caregivers suggests a potential avenue for prevention and treatment of PICS and PICS-F.

Our study is not without limitations. First, as only dyads in which patients had intact cognitive functioning were included, our findings cannot be generalized to all patient–caregiver dyads admitted to the Neuro-ICU, particularly the most severely impaired patients. Future inquiries should examine the trajectory of anxiety symptoms in caregivers of patients of worse cognitive status, after accounting for admission anxiety symptoms and resiliency factors. Next, although participants completed the self-report measures privately, there was still potential for positive response bias. Additionally, the present analysis includes limited clinical data on the patients' hospital course, including duration of and reason for intubation. Future studies should incorporate indication for and duration of intubation. Finally, our

sample was predominantly white (87%), and thus, our methods should be replicated in a larger, more racially diverse sample.

Conclusions

Neurocritical care patients and their family caregivers experienced high rates of anxiety during admission through 6 months. The severity of individuals' anxiety symptoms, as well as usage of mindfulness and adaptive coping strategies, was directly linked to one's own development of chronic anxiety post-discharge. Between dyad members, mindfulness-based practices had a protectively interdependent effect on the development of anxiety at 3 months. However, this effect is not present at 6-month follow-up. Early, dyadic-based interventions that teach mindfulness and adaptive coping strategies are needed to prevent the development of chronic anxiety in neurocritical care patients without major cognitive deficits and their family caregivers.
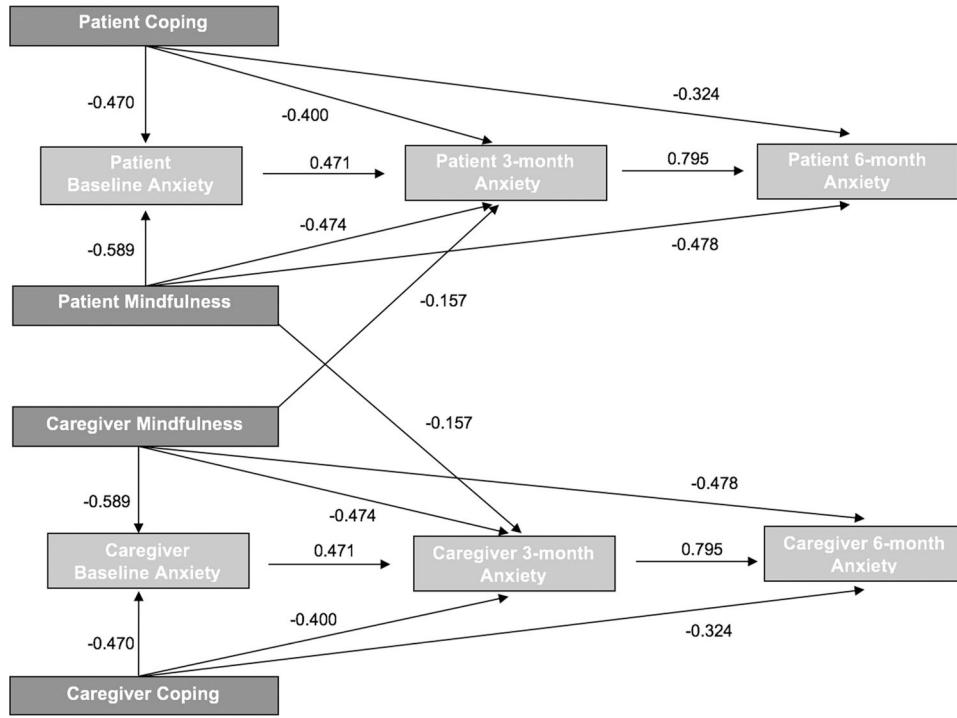
References

1. Campbell Burton CA, Murray J, Holmes J, Astin F, Greenwood D, Knapp P. Frequency of anxiety after stroke: a systematic review and meta-analysis of observational studies. Int J Stroke Off J Int Stroke Soc. 2013;8(7):545–59.

2. Cumming TB, Blomstrand C, Skoog I, Linden T. The high prevalence of anxiety disorders after stroke. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2016;24(2):154–60.

3. Shaffer KM, Riklin E, Jacobs JM, Rosand J, Vranceanu A-M. Mindfulness and coping are inversely related to psychiatric symptoms in patients and informal caregivers in the neuroscience ICU: implications for clinical care. Crit Care Med. 2016;44(11):2028–36. [PubMed: 27513536]

4. Denno MS, Gillard PJ, Graham GD, DiBonaventura MD, Goren A, Varon SF, et al. Anxiety and depression associated with caregiver burden in caregivers of stroke survivors with spasticity. Arch Phys Med Rehabil. 2013;94(9):1731–6. [PubMed: 23548544]

5. Hwang DY, Yagoda D, Perrey HM, Currier PF, Tehan TM, Guanci M, et al. Anxiety and depression symptoms among families of adult intensive care unit survivors immediately following brief length of stay. J Crit Care. 2014;29(2):278–82. [PubMed: 24411107]

6. Hatch R, Young D, Barber V, Griffiths J, Harrison DA, Watkinson P. Anxiety, depression and post traumatic stress disorder after critical illness: a UK-wide prospective cohort study. Crit Care Lond Engl. 2018;22(1):310.

7. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety symptoms in survivors of critical illness: a systematic review and meta-analysis. Gen Hosp Psychiatry. 2016;43:23–9. [PubMed: 27796253]

8. Roest AM, Martens EJ, Denollet J, de Jonge P. Prognostic association of anxiety post myocardial infarction with mortality and new cardiac events: a meta-analysis. Psychosom Med. 2010;72(6):563–9. [PubMed: 20410247]

9. Cserép Z, Balog P, Székely J, Treszl A, Kopp MS, Thayer JF, et al. Psychosocial factors and major adverse cardiac and cerebrovascular events after cardiac surgery. Interact CardioVasc Thorac Surg. 2010;11(5):567–72. [PubMed: 20805249]

10. American Psychological Association. The road to resilience. [Internet]. 2014; Washington, D.C. Available from: http://www.apa.org/helpcenter/road-resilience.aspx. Accessed Nov 2019.

11. Tugade MM, Fredrickson BL, Barrett LF. Psychological resilience and positive emotional granularity: examining the benefits of positive emotions on coping and health. J Pers. 2004;72(6):1161–90. [PubMed: 15509280]

12. Bonanno GA, Galea S, Bucciarelli A, Vlahov D. What predicts psychological resilience after disaster? The role of demographics, resources, and life stress. J Consult Clin Psychol. 2007;75(5):671–82. [PubMed: 17907849]

13. Shaffer KM, Riklin E, Jacobs JM, Rosand J, Vranceanu A-M. Psychosocial resiliency is associated with lower emotional distress among dyads of patients and their informal caregivers in the neuroscience intensive care unit. J Crit Care. 2016;36:154–9. [PubMed: 27546765]

14. Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol. 2003;84(4):822–48. [PubMed: 12703651]

15. Whitebird RR, Kreitzer M, Crain AL, Lewis BA, Hanson LR, Enstad CJ. Mindfulness-based stress reduction for family caregivers: a randomized controlled trial. The Gerontol. 2013;53(4):676–86.

16. Brown KW, Coogle CL, Wegelin J. A pilot randomized controlled trial of mindfulness-based stress reduction for caregivers of family members with dementia. Aging Ment Health. 2016;20(11):1157–66. [PubMed: 26211415]

17. Penley JA, Tomaka J, Wiebe JS. The association of coping to physical and psychological health outcomes: a meta-analytic review. J Behav Med. 2002;25(6):551–603. [PubMed: 12462958]

18. Austenfeld JL, Stanton AL. Coping through emotional approach: a new look at emotion, coping, and health-related outcomes. J Pers. 2004;72(6):1335–63. [PubMed: 15509285]

19. Lim J-W, Shon E-J, Paek M, Daly B. The dyadic effects of coping and resilience on psychological distress for cancer survivor couples. Support Care Cancer Off J Multinatl Assoc Support Care Cancer. 2014;22(12):3209–17.

20. Ben-Zur H, Gilbar O, Lev S. Coping with breast cancer: patient, spouse, and dyad models. Psychosom Med. 2001;63(1):32–9. [PubMed: 11211062]

21. Jacobs JM, Shaffer KM, Nipp RD, Fishbein JN, MacDonald J, El-Jawahri A, et al. Distress is interdependent in patients and caregivers with newly diagnosed incurable cancers. Ann Behav Med Publ Soc Behav Med. 2017;51(4):519–31.

22. Bakas T, Clark PC, Kelly-Hayes M, King RB, Lutz BJ, Miller EL, et al. Evidence for stroke family caregiver and dyad interventions: a statement for healthcare professionals from the American Heart Association and American Stroke Association. Stroke. 2014;45(9):2836–52. [PubMed: 25034718]

23. Savini S, Buck HG, Dickson VV, Simeone S, Pucciarelli G, Fida R, et al. Quality of life in stroke survivor-caregiver dyads: a new conceptual framework and longitudinal study protocol. J Adv Nurs. 2015;71(3):676–87. [PubMed: 25186274]

24. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377–81. [PubMed: 18929686]

25. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70. [PubMed: 6880820]

26. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69–77. [PubMed: 11832252]

27. Feldman G, Hayes A, Kumar S, Greeson J, Laurenceau J-P. Mindfulness and emotion regulation: the development and initial validation of the cognitive and affective mindfulness scale-revised (CAMS-R). J Psychopathol Behav Assess. 2006;29(3):177.

28. Shaffer KM, Jacobs JM, Coleman JN, Temel JS, Rosand J, Greer JA, et al. Anxiety and depressive symptoms among two seriously medically ill populations and their family caregivers: a comparison and clinical implications. Neurocrit Care. 2017;27(2):180–6. [PubMed: 28032249]

29. Marshall A, Guillien U, Mackley A, Sturtz W. Mindfulness training among parents with preterm neonates in the neonatal intensive care unit: a pilot study. PubMed—NCBI. Am J Perinatol [Internet]. 2019 [cited 2019 Sep 12]; Available from: https://www.ncbi.nlm.nih.gov/pubmed/?

term=Mindfulness+training+among+parents+with+preterm+neonates+in+the+neonatal+intensive +care+unit%3A+a+pilot+study. Accessed Nov 2019.

30. Carver CS. Measure of current status. [Internet]. 2006. Available from: http://www.psy.miami.edu/ faculty/ccarver/sclMOCS.html. Accessed Nov 2019.

31. Antoni M, Kazi A, Wimberly S, Sifre T, Urcuyo K, Phillips K, et al. How stress management improves quality of life after treatment for breast cancer. J Consult Clin Psychol. 2006;74(6):1143–52. [PubMed: 17154743]

32. Cohen J A power primer. Psychol Bull. 1992;112(1):155–9. [PubMed: 19565683]

33. Kenny D, Cook W. Partner effects in relationship research: conceptual issues, analytic difficulties, and illustrations. Personal Relationsh. 1999;6(4):433–48.

34. Kenny DA, Kashy DA, Cook WL. Dyadic data analysis. New York: Guilford Press; 2006. xix, 458. (Dyadic data analysis).

35. Li T, Hutfless S, Dickersin K, Scharfstein D, Neaton J, Hogan J, et al. Minimal standards in the prevention and handling of missing data in observational and experimental patient centered outcomes research [Internet]. Baltimore, MD: Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health; 2012 Mar p. 1–17. Available from: https://www.pcori.org/assets/Minimal-Standards-in-the-Prevention-and-Handling- of-Missing-Data-in-Observational-and-Experimental-Patient-Centered-Outcomes-Research1.pdf. Accessed Nov 2019.

36. van Buuren S Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res. 2007;16(3):219–42. [PubMed: 17621469]

37. Statistical Package for the Social Sciences. Armonk, NY: IBM Corporation; 2011. Accessed Nov 2019.

38. Zwann M, Enderle J, Wagner S, Mühlhans B, Ditzen B, Mitchell J, et al. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. PubMed—NCBI J Affect Disord. 2011;133(1–2):61–8.

39. Hanssen T, Nordrehaug J, Eide G, Bjelland I, Rokne B. Anxiety and depression after acute myocardial infarction: an 18-month follow-up study with repeated measures and comparison with a reference popula. PubMed—NCBI Eur J Cardiovasc Prev Rehabil. 2009;16(6):651–9.

40. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. JAMA. 1999;282(23):2215–9. [PubMed: 10605972]

41. Beach SR, Schulz R, Williamson GM, Miller LS, Weiner MF, Lance CE. Risk factors for potentially harmful informal caregiver behavior. J Am Geriatr Soc. 2005;53(2):255–61. [PubMed: 15673349]

42. Zale EL, Heinhuis TJ, Tehan T, Salgueiro D, Rosand J, Vranceanu A-M. Resiliency is independently associated with greater quality of life among informal caregivers to neuroscience intensive care unit patients. Gen Hosp Psychiatry. 2018;52:27–33. [PubMed: 29549820]

43. Mayer SA, Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, et al. Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. Neurology. 2002;59(11):1750–8. [PubMed: 12473764]

44. Hackett ML, Anderson CS. Health outcomes 1 year after subarachnoid hemorrhage an international population-based study. Neurology. 2000;55(5):658–62. [PubMed: 10980729]

45. mccurley JL, Funes CJ, Zale EL, Lin A, Jacobo M, Jacobs JM, et al. Preventing chronic emotional distress in stroke survivors and their informal caregivers. Neurocrit Care. 2019;30(3):581–9. [PubMed: 30421266]

46. Hwang D Is post-neurointensive care syndrome actually a thing? PubMed—NCBI. Neurocrit Care [Internet]. 2019 [cited 2019 Sep 12]; Available from: https://www.ncbi.nlm.nih.gov/pubmed/ 31420783. Accessed Nov 2019.

47. LaBuzetta J, Rosand J, Vranceanu A. Review: Post-Intensive Care Syndrome: Unique Challenges in the Neurointensive Care Unit. PubMed—NCBI. Neurocrit Care [Internet]. 2019 [cited 2019 Sep 12]; Available from: https://www.ncbi.nlm.nih.gov/pubmed/31486026. Accessed Nov 2019.

Fig. 1.
Actor–partner interdependence modeling (APIM) for resilience factors and anxiety symptoms at baseline, 3, and 6 months. Values represent standardized beta coefficients. Only significant paths shown

Table 1

Demographic and medical characteristics of Neuroscience ICU patients ($n = 102$) and their family caregivers ($n = 103$; patients and caregivers from 108 included dyads)

Demographic/medical characteristic	Patients n (%)	Caregivers n (%)	t or X²	df	p
Age (M[SD])	52 (17)	53 (14)	−0.471	92	0.64
Gender (female)	**48 (47)**	**65(63)**	**5.011**	**1**	**0.03**
Race/ethnicity (non-Hispanic white)	83 (81)	92 (89)	2.744	1	0.10
Education (some college or more)	76 (75)	82 (80)	0.556	1	0.46
Marital status (married/cohabitating)	**70 (69)**	**86 (83)**	**6.423**	**1**	**0.01**
Employment (full-time)	52 (51)	60 (58)	1.105	1	0.29
Diagnosis, n (%)[a]					
Cerebrovascular					
Stroke/Hemorrhage	38 (35)				
Brain aneurysm (unruptured)	3 (3)				
Other vascular	2 (2)				
Structural					
Tumor	32 (30)				
Lesion/brain mass	9 (8)				
Other					
Traumatic brain injury	5 (5)				
Seizure	4 (4)				
Other/> 1 diagnosis	11 (10)				
Not reported	4 (4)				
Intubated, anytime n (%)	78 (76)				
Intubated, other than post-op n (%)	22 (22)				
Days intubated *mean (range)*	3 (1–18)				
Discharge status, n (%)					
Discharge to home	69 (64)				
Discharge to rehabilitation facility	31 (29)				
Deceased at discharge	1 (1)				

Demographic/medical characteristic	Patients n (%)	Caregivers n (%)	t or X^2	df	p
Not reported	7 (6)				
Relationship to patient, n (%)					
Spouse/partner		71 (66)			
Parent		14 (13)			
Child		14 (13)			
Sibling		5 (5)			
Not reported		4 (4)			

[a]Diagnosis includes diagnoses of the six patients who did not complete measures but whose family caregivers were include ($n = 108$)

Table 2

Psychological characteristics of Neuroscience ICU patients and their family caregivers

Variable	Patients			Caregivers			Comparison		
	Mean	SD	Range	Mean	SD	Range	t	df	P
Continuous scores									
Mindfulness	36.09	7.37	18–48	36.81	7.43	20–48	− 0.79	1377	0.43
Coping	31.90	11.77	2–52	32.42	11.21	0–51	− 0.27	653	0.79
HADS-A Score									
Baseline	6.95	4.83	0–21	6.90	4.40	0–19	0.90	1402	0.37
3 months	6.24	5.16	0–21	6.47	4.94	0–19	0.05	697	0.96
6 months	6.37	5.73	0–21	6.17	4.72	0–20	0.52	576	0.61
% with mild, moderate, or severe clinically significant anxiety symptoms (HADS-A $\geq$ 8)		*n (%)*			*n (%)*		**X2**	*df*	*p*
Baseline		41 (40)			43 (42)		2.64	1	0.11
3 months		(40)			**37 (36)**		**6.91**	**1**	**0.009**
6 months		**37 (36)**			**33 (32)**		**8.76**	**1**	**0.003**
% with moderate-severe clinically significant anxiety symptoms (HADS-A $\geq$ 11)		*n (%)*			*n (%)*		**X2**	*df*	*p*
Baseline		20 (20)			24 (23)		0.6	1	0.49
3 months		**22 (22)**			**21 (20)**		**9.01**	**1**	**< 0.001**
6 months		**23 (23)**			**21 (20)**		**9.82**	**1**	**0.002**

HADS-A Hospital Anxiety and Depression Scale-anxiety subscale

Table 3

Bivariate correlations of psychological resilience factors and anxiety symptoms for Neuroscience ICU patients and their family caregivers

Variable	1	2	3	4	5	6	7	8	9	10
1. Patient baseline Anxiety symptoms	1									
2. Patient 3-month anxiety symptoms	0.508 **	1								
3. Patient 6-month anxiety symptoms	0.509 **	0.786 **	1							
4. Patient coping	− 0.372 **	− 0.373 **	− 0.284 *	1						
5. Patient mindfulness	− 0.575 **	− 0.479 **	− 0.505 **	0.625 *	1					
6. Caregiver baseline anxiety symptoms	0.215	0.280 *	0.253 *	− 0.100	− 0.211	1				
7. Caregiver 3-month anxiety symptoms	0.221	0.345 **	0.308 *	− 0.123	− 0.256 *	0.731 **	1			
8. Caregiver 6-month anxiety symptoms	0.167	0.278 *	0.268 *	− 0.069	− 0.154	0.662 **	0.815 **	1		
9. Caregiver coping	− 0.086	− 0.146	− 0.177	0.100	0.135	− 0.568 **	− 0.418 **	− 0.398 **	1	
10. Caregiver mindfulness	− 0.116	− 0.168	− 0.179	0.091	0.106	− 0.618 **	− 0.460 **	− 0.453 **	0.796 **	1

*
$p < 0.05$

**
$p < 0.001$

Anxiety symptoms = Hospital Anxiety and Depression Scale, anxiety subscale; Mindfulness = Cognitive and Affective Mindfulness Scale-Revised; Coping = Measure of Current Status-A

Table 4

Actor-partner interdependence models on effect of own psychological resilience factors and anxiety symptoms on own and partner's symptoms

	Actor effects				Partner effects			
	Unstandardized		Standardized		Unstandardized		Standardized	
	B	95% CI	p	β	B	95% CI	p	β
Prior anxiety symptoms								
Baseline → 3 m *								
Patient	**0.517**	**0.282** to **0.751**	**<0.001**	**0.471**	0.204	−0.017 to 0.427	0.071	0.124
Caregiver	**0.802**	**0.592** to **1.012**	**<0.001**	**0.732**	0.187	−0.097 to 0.231	0.426	0.061
3 months → 6 months	**0.826**	**0.731** to **0.922**	**<0.001**	**0.795**	0.022	−0.075 to 0.118	0.569	0.021
Mindfulness								
Baseline anxiety symptoms	**−0.368**	**−0.439** to **−0.297**	**<0.001**	**−0.589**	−0.060	−0.131 to 0.010	0.093	−0.097
3-month anxiety symptoms	**−0.325**	**−0.408** to **−0.242**	**<0.001**	**−0.474**	**−0.107**	**−0.189** to **−0.025**	**0.008**	**−0.157**
6-month anxiety symptoms	**−0.340**	**−0.427** to **−0.252**	**<0.001**	**−0.478**	−0.081	−0.168–0.006	0.072	−0.114
Coping								
Baseline anxiety symptoms	**−0.191**	**−0.241** to **−0.141**	**<0.001**	**−0.470**	−0.018	−0.068 to 0.033	0.507	−0.044
3-month anxiety symptoms	**−0.178**	**−0.234** to **−0.121**	**<0.001**	**−0.400**	−0.040	−0.096 to 0.016	0.170	−0.091
6-month anxiety symptoms	**−0.150**	**−0.211** to **−0.089**	**<0.001**	**−0.324**	−0.043	−0.104 to 0.019	0.186	−0.093

Bold = significant effect with $p < 0.05$

*
All contrast tests $p > 0.05$, except for patient and caregiver prior anxiety symptoms from baseline to 3 months, where $p = 0.018$ and so patient and caregiver effects are interpreted separately