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Correlates of Skin Conductance Reactivity to Stroke-Related Trauma Reminders During Hospitalization for Stroke

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Abstract

Objective: Although several risk factors for stroke-induced posttraumatic stress disorder (PTSD) have been identified, objective risk measures that can be detected in the acute aftermath of these events are needed. This study is the first to collect an objective measure of psychophysiological arousal—skin conductance (SC) reactivity to a trauma interview—in patients after stroke or transient ischemic attack (TIA) and investigate correlates of SC reactivity.

Methods: Mobile SC measurement during a resting baseline and standardized trauma interview was performed in-hospital in 98 individuals following stroke/TIA. We examined associations between several stroke-induced PTSD risk factors (sociodemographic, psychosocial, and medical characteristics) and SC reactivity to a trauma interview involving a free-response recalling of the stroke/TIA event.

Results: Of the sociodemographic, psychosocial, medical characteristics examined as correlates to SC reactivity to recalling the stroke/TIA event, 2 factors reflecting aspects of prior and in-hospital experience were significantly associated with this indicator of sympathetic nervous system activation. A greater cumulative trauma burden was significantly associated with greater SC reactivity ($r = .23$, $P = .04$). Additionally, individuals administered benzodiazepines in-hospital had significantly greater SC reactivity to recalling the stroke/TIA event ($M = 1.51$, $SD = 1.52$) than those who were not ($M = 0.76$, $SD = 1.16$; $P = .01$). Greater cumulative trauma burden remained significantly associated with greater SC reactivity when adjusting for age and in-hospital benzodiazepine administration (β=0.22, $P = .04$).

Conclusion: This study demonstrated that SC reactivity was related to both behavioral and psychological risk factors for PTSD after a stroke/TIA event. Additionally, we demonstrated the feasibility of a low-cost, mobile measurement of SC that can be conducted in-hospital in a novel patient population: individuals with a medical trauma. With this measure, we were able to identify those individuals with the greatest trauma-related sympathetic nervous system reactivity in the days following a medical trauma. Future research is needed to determine whether SC reactivity may be leveraged in the development of brief, noninvasive screening measures for enhancing PTSD risk prediction.

Keywords

Posttraumatic stress disorder, psychophysiology, skin conductance, stroke, transient ischemic attack, medically induced PTSD, benzodiazepine, PTSD screening

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Introduction

Strokes are life-threatening emergencies and a leading cause of death and long-term disability. In the United States, someone has a stroke every 40 s; every 4 min, someone dies of stroke, and the resultant yearly economic impact is estimated at $49.8 billion.[1] The effects of a stroke can be long-lasting and may result in physical (e.g., aphasia and paralysis), functional (e.g., loss of independence), and cognitive impairment (e.g., memory and attention deficits).[1] Although once thought to be brief and relatively benign episodes of temporary stroke-like symptoms, transient ischemic

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attacks (TIAs) have been increasingly recognized as clinical events that—like strokes—result from ischemia and can produce enduring brain injury.[2]

Stroke-Induced Posttraumatic Stress Disorder

The symptoms experienced during a stroke or TIA typically onset suddenly and can be terrifying, often involving numbness, weakness or paralysis of limbs, confusion, and difficulty speaking.[3] Given the unexpected and uncontrollable onset of symptoms—and the uncertainty about bodily control and recovery of function that may persist—sudden and catastrophic medical events like stroke/TIA can trigger the development of posttraumatic stress disorder (PTSD).[4,5] Meta-analytic evidence indicates that nearly 1 in 4 stroke/TIA survivors report elevated PTSD symptoms within 1 to 12 months following their stroke/TIA event, with 11% exhibiting symptoms more than 1 year after the event.[6] PTSD symptoms after stroke/TIA can negatively impact not only emotional health but also physical health. Indeed, individuals who develop PTSD following a stroke have greater risk of stroke recurrence and disability.[7,8] However, despite the relatively high prevalence of stroke-induced PTSD symptoms and their adverse outcomes, screening procedures for PTSD risk (or other adverse mental health outcomes) after stroke/TIA have yet to be widely acknowledged or implemented.[9]

Objective Measures of Psychophysiological Reactivity and PTSD Risk

Although several risk factors for stroke-induced PTSD have been identified, many rely on self-report, and there remains a need for multimodal approaches to risk factor analysis that include objective and subjective measures. Research has identified heightened psychophysiological reactivity as measured by skin conductance (SC) as an objective measure of sympathetic nervous system activation.[10] Heightened SC reactivity has been observed in individuals with PTSD[11-13] and is associated with a greater degree of trauma exposure,[14] suggesting that heightened SC response may reflect the impact of trauma exposure on the autonomic nervous system. In addition to their associations with trauma and PTSD status and severity, SC measures may be leveraged to predict which individuals are at elevated risk for developing PTSD following trauma exposure. Indeed, in-hospital mobile assessment showed that heightened SC reactivity while recalling the traumatic event in the acute period (0-3 days) following a nonmedical trauma (eg, motor vehicle accident) predicted both higher total PTSD symptom levels 6 months after trauma and a more chronic PTSD symptom trajectory over the first year after trauma.[15] This finding suggests heightened SC reactivity to trauma reminders may also be a predisposing psychophysiological phenotype for PTSD symptom development.

Although psychophysiological measures have traditionally been collected in the research laboratory, requiring substantial equipment and burden on participants, recently developed mobile assessments are a brief, low-cost, and noninvasive option that enable SC measurement in naturalistic settings, enhancing the utility of this biomarker.[15] Despite its promise, research examining mobile SC as an objective risk factor for PTSD in stroke/TIA patients is lacking. It is currently unknown how psychophysiological reactivity manifests in patients following a medical trauma. Furthermore, the extent to which various risk factors for stroke-induced PTSD relate to sympathetic nervous system activation after a stroke/TIA event has not been investigated. Early identification of individuals who may be at risk of developing PTSD symptoms after stroke/TIA has the potential to inform screening and prevention efforts aimed at promoting patients' mental and physical health.

Risk Factors for Stroke-Induced PTSD

Sociodemographic Factors. Growing research has identified younger age as a predictor of stroke-induced PTSD.[7,16] These findings parallel those from studies of cardiac disease-induced PTSD, which have found higher PTSD symptom levels in younger (vs older) individuals.[6,17-20] Additionally, female gender has long been associated with greater risk for PTSD following nonmedical traumas, but research in stroke patients has been mixed. Some,[19,21,22] but not all,[7] studies have found a link between female gender and greater risk of PTSD symptoms following a stroke after adjusting for factors like age and stroke severity. Educational attainment may also index risk for the development of stroke-induced PTSD, with 1 study identifying an association between lower educational attainment and greater stroke-induced PTSD risk.[21]

Medical Factors. Of the few studies that examined stroke severity as a medical-related predictor of PTSD, some,[23,24] but not all,[21] have linked greater stroke severity and related disability to stroke-induced PTSD. Additionally, certain medications administered during hospitalization for cardiovascular events may impact risk for subsequent PTSD.[25] Recent research demonstrated that individuals administered benzodiazepines in-hospital following acute coronary syndrome (ACS) were nearly 4 times more likely to develop PTSD in response to ACS than those not given benzodiazepines.[26] Benzodiazepines are commonly prescribed on demand during hospitalization following a medical trauma[27]; understanding their impact on stroke-induced PTSD may have important implications for in-hospital PTSD risk screening.

Psychosocial Factors. Greater cumulative lifetime trauma burden is a robust predictor of PTSD in nonmedical trauma samples,[28] and greater exposure to stressful events before a myocardial infarction has been associated with onset of

PTSD symptoms in response to the event.[29,30] PTSD symptoms due to a prior traumatic event have also been linked to greater risk of developing PTSD in stroke[19] and other cardiovascular patients.[31] As in the broader literature on PTSD due to nonmedical traumas,[32] greater perceived threat during the stroke/TIA traumatic event has emerged as a risk factor for subsequent PTSD as well,[21] which mirrors findings in other cardiovascular patient populations.[33,34] Early posttraumatic stress symptoms that onset in the initial (<1 month) period following a trauma (i.e., acute stress symptoms) have also been linked to later PTSD development.[35] However, there is substantial heterogeneity in the course of posttraumatic stress symptoms, and an individual's adaptation in the acute aftermath of trauma does not always accurately predict subsequent trauma-related distress.[35] Nevertheless, acute stress symptoms also have relevance to physical health outcomes.[36] Further, in patients evaluated for ACS, greater acute stress symptoms due to suspected ACS—measured days after evaluation—predicted greater risk of 30-day hospital readmission.[37]

Aims of the Current Study

In this initial cross-sectional study of mobile SC assessment in a medical trauma sample, we examined how psychophysiological responses to recalling the stroke/TIA event—measured in-hospital during a standardized trauma interview—manifested in Spanish and English-speaking patients in the acute aftermath of stroke/TIA. In addition, we investigated the extent to which these psychophysiological responses related to a variety of risk factors for stroke-induced PTSD. We hypothesized that individuals who were at greater risk of stroke-induced PTSD based on sociodemographic, psychosocial, and medical factors identified in previous research would exhibit greater SC reactivity to the trauma interview.

Method

Participants and Procedure

Participants were enrolled in the Reactions to Acute Care and Hospitalization for Suspected Stroke (REACH Stroke) study after evaluation for stroke or TIA at the New York-Presbyterian/Columbia University Irving Medical Center, an academic medical center serving a densely populated, urban area in Manhattan, NY. REACH Stroke is a prospective observational cohort study examining risk for—and consequences of—developing PTSD symptoms after stroke/TIA. The study began in 2015; study inclusion criteria were as follows: age ≥18 years, fluent in English or Spanish, and suspected diagnosis of stroke or TIA per the treating neurologist. Individuals with severe stroke symptoms (National Institutes of Health [NIH] Stroke Scale score >14,[38] in addition to significant aphasia, dysarthria, or cognitive impairment), terminal noncardiac medical comorbidities, or severe mental illness, as well as those not available for follow-up visits, were not eligible for the study. Eligible patients were given information about the study, and they provided written informed consent prior to participation. All study protocols were approved by the Columbia University Irving Medical Center Institutional Review Board.

Participant sociodemographics were collected at enrollment, and data on medical characteristics (eg, history of stroke, comorbid illness), medication, and stroke/TIA severity were extracted from participants' medical records. During hospitalization for the stroke/TIA event, highly trained research assistants fluent in English and/or Spanish assessed participants' lifetime trauma exposure, PTSD symptoms due to prior trauma, perceived threat during the stroke/TIA event, and acute stress symptoms due to stroke/TIA. Between August 2017 and June 2019, participants were also invited to complete the PhenX Toolkit Baseline and Trauma Challenge Psychophysiology protocol (for protocol details, see https://www.phenxtoolkit.org/protocols/view/630901) during hospitalization as part of a psychophysiology substudy. As described in SC Reactivity to Recalling the Stroke/TIA Event section, this protocol is brief and consists of SC measurement during a resting baseline period and standardized trauma interview in which participants answer questions about a traumatic event. Study assessments were conducted in English or Spanish, depending on participant preference. We translated the PhenX Toolkit protocol into Spanish for this study.

Measures

Sociodemographics. Age, gender (male, female), race/ethnicity (Hispanic, Non-Hispanic Black, Non-Hispanic White, other), and educational attainment (less than high school/some high school, high school degree, trade school/some college, college graduate, graduate school) were self-reported.

Medical Characteristics and In-hospital Medication. Study neurologists, blinded to PTSD status, categorized the index event as stroke, TIA, or other. The "other" group included individuals who presented to the emergency room with stroke/TIA symptoms and were later diagnosed with another neurological disorder (i.e., stroke mimics[39,40]). Stroke severity was indexed using the NIH Stroke Scale[38]; scores for the 11 items were extracted from patients' medical charts and summed to create a total score ranging from 0 to 42. History of a variety of medical conditions was documented in participants' medical charts, including prior history of stroke/TIA. As a measure of medical comorbidity, the Charlson Comorbidity Index was calculated.[41] In-hospital administration of benzodiazepines was extracted from patients' medical charts.

Psychosocial Factors

Cumulative Trauma Burden. Lifetime exposure to 16 types of traumatic events, in addition to any other very stressful event not specified (not including the stroke/TIA event that resulted in hospitalization), was assessed with the Life Events

Table 1. Participant Characteristics for Individuals Who Completed the Psychophysiology Substudy, $N = 98$.

Characteristic	% (*n*)	*M* (*SD*)	Range	Valid *N*
Sociodemographic factors				
Age, years		60.38 (16.49)	19-87	98
Gender, %				98
Male	44.9 (44)			
Female	55.1 (54)			
Race/ethnicity, %				98
Hispanic	39.8 (39)			
Non-Hispanic White	20.4 (20)			
Non-Hispanic Black	33.7 (33)			
Non-Hispanic other	6.1 (6)			
Educational attainment, %				98
Less than or some HS	22.4 (22)			
HS graduate	21.4 (21)			
Trade school/some college	17.3 (17)			
College graduate	22.4 (22)			
Graduate school	16.3 (16)			
Medical factors				
Index event category, %				98
Stroke	85.7 (84)			
TIA	4.1 (4)			
Other	10.2 (10)			
NIH Stroke Scale score		3.20 (3.02)	0-20	88
Prior stroke/TIA history, %	15.9 (14)			88
Charlson Comorbidity Index		1.16 (1.43)	0-7	98
In-hospital administration of benzodiazepines, %	29.6 (29)			97
Psychosocial factors				
Cumulative lifetime trauma burden		2.97 (2.61)	0-13	98
Past month PTSD total symptoms due to prior trauma		9.42 (10.89)	0-49	73
Peritraumatic threat perceptions for stroke/TIA		8.78 (6.39)	0-21	80
Acute stress symptoms due to stroke/TIA		22.96 (8.47)	14-55	90

Abbreviations: HS, high school; M, mean; PTSD, posttraumatic stress disorder; SD, standard deviation; TIA, transient ischemic attack.

Checklist (LEC-5).[42] A cumulative trauma burden variable was calculated that reflected the total number of types of traumatic events experienced by participants in their lifetime.

Prior PTSD Symptoms. PTSD symptoms due to participants' most distressing prior trauma were assessed with the PTSD checklist for *DSM-5* (PCL-5),[43] a reliable and valid measure of PTSD symptoms.[44,45] Participants indicated how bothered they were by each of the 20 symptoms that make up the *DSM-5* PTSD diagnostic criteria in the past month on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). Responses were summed to create a total PTSD symptom severity score.

Perceived Life Threat. Participants reported on their level of perceived threat during the stroke/TIA event with a 7-item measure.[46] Items (eg, "I was afraid" and "I felt helpless") assessed participants' experience when their "stroke or mini-stroke symptoms started." Responses were rated on a 4-point Likert scale ranging from 1 (not at all) to 4 (extremely) and were summed to create a threat perceptions total score. This measure has been found to have good internal consistency and test–retest reliability.[46]

Acute Stress Symptoms. Acute stress symptoms of reexperiencing, avoidance, and arousal (but not dissociation, as in prior research[20,37]) due to the stroke/TIA event that were experienced since coming to the hospital were rated on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely) using 14 items from the Acute Stress Disorder Scale, a measure with strong psychometric properties.[47] Responses were summed to create a total score.

SC Reactivity to Recalling the Stroke/TIA Event. SC was measured at the participant's bedside in-hospital using the eSense SC system (Mindfield Biosystems, Inc., Berlin, Germany) on an iPad, as in previous research.[11,15] This brief (<15 min) SC measurement protocol was conducted by trained research coordinators. The protocol consisted of a 2-min resting baseline followed by a standardized trauma interview in which participants were asked 15 questions related to the stroke/TIA experience (e.g., Where were you when you had the stroke/TIA event?; Did you have any

injuries?; During the stroke/TIA event, how helpless did you feel?). Prior to the resting baseline, research coordinators attached electrodes with Velcro to the middle phalanges of the index and middle finger of the participant's nondominant hand; electrodes were coated with isotonic paste to increase signal quality and guarantee suitable contact with skin. SC levels were measured continuously during the baseline and interview periods; data were acquired at a sampling rate of 10 Hz.

As in prior research in nonmedical trauma-exposed samples,[11,15] SC reactivity to recalling the trauma was calculated by subtracting the average SC level in microSiemens (μS) during the last 30 s of the baseline resting period from the maximum SC level (μS) during the trauma interview. Greater positive values indicate more psychophysiological reactivity to recalling the stroke/TIA traumatic event. If participants had SC levels below 1μS during the trauma interview and did not exhibit any psychophysiological response to the trauma interview, then the participant was categorized as a nonresponder and did not contribute SC reactivity data to analyses, as in prior research.[48]

Data Analysis

Descriptive statistics were computed for the sample and compared for participants with and without useable SC data. Additionally, descriptive statistics for SC were computed to characterize psychophysiological responses in the analytic sample. We then conducted unadjusted analyses to examine associations of (1) sociodemographic, (2) medical, and (3) psychosocial factors with SC reactivity. Correlations were used for continuous variables, and *t*-tests and analyses of variance were used for categorical variables. For variables with significant unadjusted associations, we then used multiple linear regression to examine whether associations remained when adjusting for relevant covariates. Covariates for adjusted models included age (given robust associations of age with stroke-induced PTSD) and those significantly associated with SC reactivity in unadjusted analyses. For significant correlates of SC reactivity, a sensitivity analysis was performed testing whether they were also associated with baseline SC.

Analyses were performed with SPSS Version 27.0 (IBM Corp., Armonk, NY), and *P*-value < .05 indicated statistical significance. When appropriate, we also report standardized effect sizes.

Results

Participant Characteristics

Characteristics of participants in the psychophysiology substudy are detailed in Table 1. Participants ranged in age from 19 to 87 years ($M = 60.38$, $SD = 16.49$), and the sample was diverse with respect to race/ethnicity and educational attainment. The mean time between study enrollment and in-hospital psychophysiological data collection was 1.74 days ($SD = 2.34$). Of the 98 individuals who completed the psychophysiology substudy, 89.9% ($n = 88$) had useable SC data, 5.1% had unusable data (ie, recorder malfunction, $n = 5$), and 5.1% ($n = 5$) were considered nonresponders. Participants with and without usable SC data were similar across numerous sociodemographic characteristics, although they differed on educational attainment (Supplemental Table 1). The mean SC level during the last 30 s of the baseline recording period was 2.68μS (range = 0.50-11.24) and the mean maximum SC level during the trauma interview was 3.68μS (range = 0.77-14.94). As expected, the average max SC level during the trauma interview was significantly greater than the average baseline SC level, $t(87) = 7.04$, $P \leq .001$. The mean SC reactivity value was 1.00μS, and there was a wide range in responses (range = −0.22-6.03).

Sociodemographics and SC Reactivity

Unadjusted analyses revealed no significant associations between any of the sociodemographic factors and SC reactivity. As shown in Table 2, female participants had greater SC reactivity than male participants, but this difference was of small effect ($d = 0.24$) and it did not reach the level of

Table 2. Skin Conductance Reactivity According to Sociodemographic and Medical Factors.

Characteristic	Skin conductance reactivity (μS) *M* (*SD*)	*P*	Effect size
Gender		.27	$d = 0.24$
Male	0.84 (1.12)		
Female	1.15 (1.50)		
Race/ethnicity		.21	$\eta^2 = 0.05$
Hispanic	0.91 (1.21)		
Non-Hispanic White	1.45 (1.45)		
Non-Hispanic Black	0.71 (1.01)		
Non-Hispanic other	1.55 (2.55)		
Educational attainment		.14	$\eta^2 = 0.08$
Less than or some HS	0.67 (0.79)		
HS graduate	0.90 (1.02)		
Trade school/some college	0.90 (1.62)		
College graduate	0.96 (1.22)		
Graduate school	1.83 (1.89)		
Index event category		.97	$\eta^2 = 0.001$
Stroke	0.99 (1.29)		
TIA	0.98 (1.62)		
Other	1.10 (1.82)		
Prior stroke history		.53	$d = 0.18$
Yes	1.20 (1.86)		
No	0.96 (1.23)		
In-hospital benzodiazepine administration		.01*	$d = 0.60$
Yes	1.51 (1.52)		
No	0.76 (1.16)		

Abbreviations: *d*, Cohen's d; η^2, eta-squared; HS, high school; M, mean; SD, standard deviation; TIA, transient ischemic attack.

statistical significance ($P = .27$). Younger age was associated with greater SC reactivity, but did not reach statistical significance ($r = -.16$, $P = .15$). There were no significant group differences in SC reactivity across race/ethnicity or educational attainment (Table 2).

Medical Characteristics, In-Hospital Medication, and SC Reactivity

There were no significant associations between stroke severity ($r = .06$, $P = .62$) or the Charlson Comorbidity Index ($r = .11$, $P = .29$) with SC reactivity. Index event category (i.e., stroke, TIA, and other) and prior history of stroke were also not associated with SC reactivity (Table 2). However, a significant association with a medium-to-large effect size ($d = 0.60$) was detected for in-hospital administration of benzodiazepines and SC reactivity, such that participants administered benzodiazepines during hospitalization had significantly greater SC reactivity to the trauma interview than those who were not ($P = .01$; Figure 1A). Receipt of benzodiazepines remained significantly associated with greater SC reactivity when adjusting for age (β=0.24, $P = .045$).

Psychosocial Factors and SC Reactivity

Lifetime cumulative trauma burden and SC reactivity were significantly positively associated in unadjusted analyses ($r = .23$, $P = .04$; Figure 1B). In a regression model adjusting for age and in-hospital benzodiazepine administration, greater cumulative trauma burden remained significantly associated with greater SC reactivity (β=.22, $P = .04$; Table 3). No significant associations with SC reactivity were observed with past month PTSD symptoms due to a prior trauma ($r = -.03$, $P = .80$), peritraumatic threat perceptions ($r = -.09$, $P = .46$), or acute stress symptoms due to stroke/TIA ($r = .03$, $P = .77$).

Sensitivity Analyses

To examine whether associations between significant correlates and SC reactivity were driven by an individual's baseline SC levels rather than the response to the trauma interview, we performed sensitivity analyses testing the association between cumulative trauma burden and in-hospital benzodiazepine administration with average SC levels during the last 30 s of the baseline recording period. We found no significant association between cumulative trauma burden and baseline SC level ($r = -.16$, $P = .13$), and there was no significant difference in baseline SC level for those who did and did not receive benzodiazepines, $t(85) = 0.13$, $P = .90$. Together, these results suggest that associations observed between cumulative trauma burden and benzodiazepine receipt with SC reactivity were specific to psychophysiological reactivity to the stroke-trauma interview.

Discussion

To our knowledge, this is the first study to assess psychophysiological responses in-hospital in the acute aftermath of a medical trauma in stroke/TIA patients. We demonstrated that a low-cost, mobile measurement of SC can be conducted in-hospital and

Table 3. Regression Parameters and 95% CIs for Adjusted Associations of Age, Benzodiazepine Use, and Cumulative Trauma Burden with Skin Conductance Reactivity During the Trauma Interview.

	b (95% CI)	*β*	*P*
Age	−0.00 (−0.02, 0.02)	−0.03	.78
In-hospital administration of benzodiazepines	0.64 (−0.03, 1.31)	0.22	.06
Cumulative lifetime trauma burden	0.11 (0.01, 0.21)	0.22	.04*

Abbreviation: CI, confidence interval.

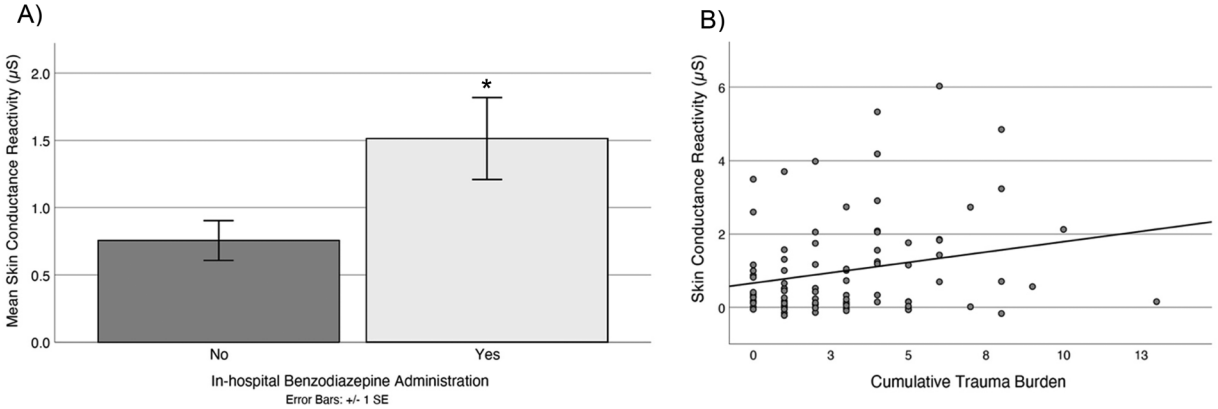

Figure 1. (A) The average skin conductance reactivity while recalling the stroke/TIA event in individuals who were and were not administered benzodiazepines while in-hospital. Error bars indicate ±1 standard error. (B) Scatter plot of cumulative trauma burden and skin conductance reactivity while recalling the stroke/TIA event; *$P = .01$. Abbreviation: TIA, transient ischemic attack.

identify those individuals with the greatest trauma-related sympathetic reactivity in the days following a medical trauma. Further, we found that some (though not all) of the hypothesized risk factors for stroke-induced PTSD were also associated with SC reactivity during a standardized trauma interview, namely in-hospital benzodiazepine administration and greater cumulative trauma burden. Neither benzodiazepine administration nor cumulative trauma burden were related to baseline SC levels, indicating that these variables were specifically related to greater activation in response to recalling the stroke/TIA traumatic event rather than differences in tonic SC levels.

The finding that individuals prescribed benzodiazepines had greater SC reactivity adds to the literature suggesting that benzodiazepine administration in-hospital following a medical trauma may be relevant for risk of subsequent medically induced PTSD symptoms.[26] Furthermore, a recent meta-analysis suggested that benzodiazepine use in individuals recently exposed to trauma was associated with greater likelihood of PTSD development and elevated symptom severity.[49] Despite this evidence, benzodiazepines are widely used in hospitals following medical and nonmedical traumas.[27] Indeed, in our sample, nearly 30% of patients received benzodiazepines in-hospital following their stroke/TIA. We did not have information about the specific reasons for benzodiazepine use or when these medications were administered during hospitalization (e.g., timing of benzodiazepine receipt with respect to the psychophysiology substudy was not known). However, we hypothesize that our medical chart-based indicator of in-hospital benzodiazepine administration may reflect an individual's tendency to respond to novel or uncontrollable situations with fear, and that this tendency could also underlie a greater sympathetic nervous system response to recalling the stroke/TIA traumatic event (as captured with our psychophysiological measure). In the current study, we focused on benzodiazepine administration, as it has been linked to elevated PTSD risk after ACS.[26] Conversely, there is some evidence in the greater nonmedical PTSD literature that additional cardiorelevant medications may be associated with a lower risk of PTSD development, including angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and beta blockers.[50-52] However, information on receipt of these medications in-hospital was not available in the current study. Future longitudinal research is needed to address in more comprehensive ways whether administration of benzodiazepines and these other medications following a stroke/TIA event may relate to SC reactivity and/or impact PTSD symptom onset.

Our finding that greater cumulative trauma burden was associated with greater SC reactivity to recalling the stroke/TIA traumatic event parallels recent research in children demonstrating a positive association between level of trauma exposure and SC reactivity to a trauma interview.[14] Numerous studies have also linked medically induced PTSD risk with exposure to prior stressors and trauma,[29,30,53] especially prior medical trauma.[31] These findings may reflect the theory of stress sensitization, in which individuals may become increasingly sensitized, reacting more strongly to subsequent experiences of trauma and severe stress and potentially have a greater likelihood of developing PTSD following repeated exposure to stressors and traumatic events.[54,55] In contrast to our findings, some studies have found that the link between cumulative trauma burden and medically induced PTSD was present only for those who also developed PTSD symptoms in response to prior trauma.[19,31] In our sample, the range of current PTSD symptoms due to a prior trauma was restricted to lower symptom levels (range = 0-49 out of a possible total of 80). Thus, we may not have had enough variability in PTSD symptom severity, specifically not enough severe symptom presentations, to detect differences. Interestingly, neither peritraumatic threat perceptions nor acute stress symptoms due to stroke/TIA were associated with SC reactivity, even though these measures queried whether individuals felt distressed during and after the stroke/TIA event. However, a number of studies have also demonstrated incongruencies between subjective reports of emotional states and objective measures of psychophysiological arousal, which suggests that self-report of specific emotional states may not always be well-aligned with measures of psychophysiological responses.[56,57] Further, given that acute stress symptoms do not predict subsequent PTSD symptoms linearly,[35] it is of interest to examine the extent to which SC reactivity predicts stroke-induced PTSD symptoms at 1 month and beyond.

We also did not observe significant associations between any of the sociodemographic variables tested and SC reactivity. Illness severity has shown mixed results in its association with PTSD symptom development after medical traumas. For example, a recent study involving patients from our cohort study found a positive association between stroke severity based on NIH Stroke Scale scores and stroke-related PTSD symptom development.[23] In contrast, prior research in individuals evaluated for suspected ACS found that individuals who were later ruled out as having ACS had similar rates of PTSD symptom development as those who experienced a "true" ACS event.[58] In the current study, we did not find that indicators of stroke severity, prior stroke history, or medical comorbidity were related to SC reactivity, but more research is needed to ascertain whether these factors play a role in predicting PTSD symptom development in conjunction with SC reactivity.

There were a number of limitations to the present study. Our sample size was relatively small and may be underpowered for multiple comparisons. Thus, any associations should be viewed as exploratory and in need of confirmation in larger samples. Further, given our examination of correlates, we cannot make causal claims; longitudinal research is needed to better understand these links. In particular, it is of interest to examine whether greater SC reactivity to recalling the stroke/TIA traumatic event predicts PTSD symptom development in stroke/TIA patients, as was previously

demonstrated in a nonmedical trauma population.[15] Despite its limitations, this investigation also has unique strengths. The study employed a multimethod measurement approach, which included self-report, data extraction from patients' medical charts, and objective measurement of psychophysiological responses. Further, the mobile psychophysiological measurement protocol enabled recording in a naturalistic setting and was offered in both English and Spanish, allowing for the inclusion of individuals from a wide range of ages, racial/ethnic groups, and socioeconomic backgrounds, thereby increasing the diversity of our participants and the generalizability of our results.

Conclusion

This study was the first of its kind to collect a measure of psychophysiological reactivity in-hospital in patients who have experienced a medical trauma. In-hospital receipt of benzodiazepines and greater cumulative trauma burden emerged as significant correlates of greater psychophysiological reactivity in the acute aftermath of a stroke/TIA event. The preliminary findings of the present study indicate that more research is needed to understand how this psychophysiological indicator may relate to psychological and cardiovascular health outcomes in this patient population. Future research can be used to determine whether SC reactivity may be a promising brief, noninvasive screening measure that can be used to better identify patients who can benefit early PTSD interventions in the short-term period when individuals are under the care of medical professionals following a serious medical event.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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