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Concerns About Medications Mediate the Association of Posttraumatic Stress Disorder With Adherence to Medication in Stroke Survivors

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Abstract

Objectives—Posttraumatic stress disorder (PTSD) can be a consequence of acute medical events and has been associated with nonadherence to medications. We tested whether increased concerns about medications could explain the association between PTSD and nonadherence to medication in stroke survivors.

Design—We surveyed 535 participants aged 40 years or older who had at least 1 stroke or transient ischemic attack in the previous 5 years.

Methods—We assessed PTSD using the PTSD checklist–specific for stroke, medication adherence with the Morisky Medication Adherence Questionnaire, and beliefs about medications wtih the Beliefs about Medicines Questionnaire. We used logistic regression to test whether concerns about medications mediated the association between stroke-induced PTSD and nonadherence to medication. Covariates for adjusted analyses included age, sex, race, comorbid medical conditions, stroke-related disability, years since last stroke/TIA, and depression.

Results—Symptoms of PTSD were correlated with greater concerns about medications (r= 0.45; P< .001), and both were associated with medication nonadherence. Adjustment for concerns about medications attenuated the relationship between PTSD and nonadherence to medication, from an odds ratio [OR] of 1.04 (95% confidence interval [CI], 1.01–1.06; OR, 1.63 per 1 SD) to an OR of 1.02 (95% CI, 1.00–1.05; OR, 1.32 per 1 SD), and increased concerns about medications remained associated with increased odds of nonadherence to medication (OR, 1.17; 95% CI, 1.10–1.25; OR, 1.72 per 1 SD) in this fully adjusted model. A bootstrap mediation test suggested that the indirect effect was statistically significant and explained 38% of the association of PTSD to medication nonadherence, and the direct effect of PTSD symptoms on medication nonadherence was no longer significant.

Conclusion—Increased concerns about medications explain a significant proportion of the association between PTSD symptoms and nonadherence to medication in stroke survivors.

Though posttraumatic stress disorder (PTSD) was originally understood as a disorder primarily associated with combat, PTSD is increasingly recognized as a common

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psychological consequence of life-threatening medical events such as acute coronary syndrome (ACS), (Edmondson et al., 2012) cancer diagnosis (Andrykowski, Cordova, Studts, & Miller, 1998), and stroke (Kronish, Edmondson, Goldfinger, Fei, & Horowitz, 2012). In a meta-analysis of 24 studies, the prevalence of PTSD due to ACS was estimated at 12% (Edmondson, Richardson, et al., 2012), and research suggests that PTSD due to stroke may be even more common (Kronish, Edmondson, Goldfinger, et al., 2012). In addition to directly causing psychological symptoms, PTSD triggered by medical events may also put patients at increased risk for a worse prognosis from their underlying medical illness. For example, ACS-induced PTSD is associated with a doubling of risk for cardiac event recurrence and mortality up to 3 years after the index event (Edmondson, Richardson, et al., 2012; Edmondson, Rieckmann, et al., 2011; Shemesh et al., 2004; von Känel et al., 2011). It is not known whether stroke-induced PTSD is associated with adverse medical outcomes.

While a number of biological mechanisms, such as increased blood pressure (Muraoka, Carlson, & Chemtob, 1998), endothelial dysfunction (von Känel et al., 2008) and systemic inflammation (von Kanel et al., 2010) have been proposed to explain the association between PTSD and recurrent cardiovascular events in ACS patients, behavioral mechanisms (Newman et al., 2011) such as medication nonadherence are also possible mechanisms (Rahiman et al., 2008; Shemesh, et al., 2004). In survivors of strokes and transient ischemic attacks (TIAs), adherence to risk-reducing medications, including antiplatelet agents, antihypertensive agents, and statins, is especially important for preventing subsequent strokes (Rothwell, Algra, & Amarenco, 2011). However, in the Adherence eValuation After Ischemic Stroke Longitudinal (AVAIL) registry, a large prospective cohort of stroke survivors, 14% of participants self-reported not adhering to medication regimens (Bushnell et al., 2011). To date, most studies have focused on demographic and system-level predictors of nonadherence, many of which may be intractable (Bushnell et al., 2010; Tuhrim et al., 2008). We previously reported that 40% of our sample of predominantly low-income and minority long-term stroke survivors self-reported poor adherence to medication and that 75% reported at least some PTSD symptoms, with 18% of the participants reporting symptoms above the cutoff point for likely PTSD diagnosis. Furthermore, we found that those with the most severe PTSD symptoms were nearly 3 times as likely as those without PTSD symptoms to be nonadherent to medications (Kronish, Edmondson, Goldfinger, et al., 2012).

Social cognitive theories of health behavior such as the health belief model (Rosenstock, 1974) and self-regulation models (Hall & Fong, 2007; Leventhal, Brissette, & Leventhal, 2003; Maes & Gebhardt, 2000) suggest that individuals undertake a cost-benefit analysis when deciding to follow medical treatment; this process involves considering whether the perceived need for treatment outweighs concerns about treatment. Though they did not measure PTSD or other potential influences on concerns about medications, a recent study with 180 stroke survivors found that concerns about medications were among the strongest predictors of stroke survivors' nonadherence to medications both cross-sectionally and prospectively at 1 year poststroke (O'Carroll et al., 2011).

One hypothesis to explain the association between PTSD and nonadherence to medication is that stroke survivors with PTSD have increased concerns about medications, potentially shifting the balance between perceived need and concerns, with the result of decreased adherence. This explanation is plausible, as 2 major categories of PTSD symptoms—hypervigilance and avoidance—may lead those with PTSD as a result of a medical event to perceive their medications as threatening reminders of the event (Shemesh et al., 2001; Shemesh, et al., 2004). While it is possible that other explanations may play a role in the association between PTSD and medication nonadherence, such as altered risk perception in

patients with PTSD (Edmondson, Shaffer, Denton, Shimbo, & Clemow, 2012) or general avoidance of threatening health-related stimuli (Newman, et al., 2011), the hypervigilance and avoidance hypothesis is supported by findings on PTSD and medication adherence in HIV patients (Delahanty, Bogart, & Figler, 2004). Catz et al explained the finding that symptoms of HIV-induced PTSD were associated with skipping highly active antiretroviral therapy by noting that the most frequently cited reason for nonadherence to HIV medications was that "medications remind me that I am HIV positive" (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Chernoff, 2007). Evidence for the hypervigilance and avoidance hypothesis would be a finding that greater concerns about potential threats associated with medications and greater general worry about medications, but not decreased awareness that such medications are medically necessary, mediate the association between PTSD and medication nonadherence. Our aims were to explore the association between beliefs about medications and PTSD in survivors of strokes and TIAs and to determine whether beliefs mediated the association we previously found between PTSD and nonadherence to medication. We hypothesized that greater concerns about medications, but not lower perceptions of the necessity of medications, mediate the association between PTSD symptoms and nonadherence to medication in a large sample of stroke survivors.

Methods

Participants

Participants were recruited between March 2010 and January 2012 as part of the Preventing Recurrence of All Inner City Strokes through Education (PRAISE) clinical trial, which tests the effectiveness of a peer-led educational workshop at improving risk factor control in community-dwelling survivors of strokes and TIAs. Participants were eligible for the trial if they were at least 40 years old and if they self-reported a history of stroke or TIA in the prior 5 years. Participants were excluded if they were not able to provide informed consent, if they did not speak English or Spanish, if they resided in nursing homes or other institutionalized settings, if they were pregnant, or if they were unable to meaningfully participate in the workshop as a result of aphasia or severe cognitive impairment.

Participants were identified through screenings at senior centers, churches, and health fairs; by contacting patients with a history of stroke or TIA who were on hospital registries of an academic medical center, a federally funded neighborhood health center, and the Visiting Nurse Service of New York; and through advertising the study in clinics, local organizations, and newspapers in northern Manhattan and southern Bronx, New York. The data used for the analysis were collected as part of the baseline interview for the trial; no study-related interventions had occurred prior to this baseline interview. All study procedures were designed with the input of a community action board that included individuals from East and Central Harlem. Approval was obtained from the institutional review board of the Mount Sinai School of Medicine, New York, NY. All participants provided written informed consent. More detail concerning the study's methods are given elsewhere (Goldfinger et al., 2012; Kronish, Edmondson, Goldfinger, et al., 2012).

Measures

Symptoms of PTSD and Adherence to Medications—Symptoms of PTSD were assessed with a modified version of the PTSD checklist–specific (PCL), using the stressor "stroke or mini-stroke" (Weathers FW, 1993). The PCL is an extensively validated 17-item scale that corresponds to *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) criteria for PTSD. Participants were asked to rate whether they had specific PTSD symptoms as a result of their stroke or mini-stroke. To make the PCL more homogenous with the rest of the survey and easier to complete for participants with low health literacy,

the instrument was modified from a 5-point ("not at all," "a little bit," "moderately," "quite a bit," or "extremely") to a 4-point ("not at all," "a little bit," "somewhat," or "very much") response scale. In addition, 3 items ("loss of interest or pleasure in doing things", "trouble falling or staying asleep, or sleeping too much," and "Trouble concentrating on things, such as reading the newspaper or watching television") from the Patient Health Questionnaire (PHQ) (Kroenke, Spitzer, & Williams, 2001) were used in place of PCL items as there was substantial content and wording overlap between these items on both instruments.

We submitted the revised scale to a confirmatory factor analysis (CFA) to test the performance of the three altered items. The results of the CFA verified that these 3 PHQ items performed as predicted, loading on first-order PTSD symptom factors, with standardized factor loadings equivalent to PCL items. To allow our scoring to be comparable with that of other studies using the PCL, we recoded PCL scores to reflect the standard 5-point response scale (1 = 1; 2 = 2.33; 3= 3.67; and 4 = 5) so that the range of the total PCL score was the same as that used with the unmodified instrument. A cutoff point of 50 on the PCL has corresponded to a sensitivity of 60% and specificity of 99% in relation to a clinical diagnosis of PTSD in which the triggering event was medical (breast cancer diagnosis). (Andrykowski, et al., 1998). For illustrative purposes, we divided participants into two groups based on PCL score, with ≥ 50 representing a positive screen. Concerns about medications by PTSD group are given in Table 2. The PCL was analyzed as a continuous variable in regression analyses.

Adherence to medications was measured using the 8-item Morisky Medication Adherence Questionnaire (Morisky, Ang, Krousel-Wood, & Ward, 2008). This questionnaire is a self-report measure of adherence that has good internal validity. Each of the 8 items assesses specific medication-taking behaviors such as forgetting to take medications or stopping medication use when one perceives one's medical condition to be under good control. Summary scores on the questionnaire are concordant with objective measures of adherence to medication, including pharmacy refills (Krousel-Wood et al., 2009). Though the scale has been used successfully to assess adherence to a broad range of medications from antiretrovirals (DiIorio et al., 2008) to asthma medications (Joshi et al., 2006), we asked participants to respond to the more general "medicines." To reduce social desirability effects, the questions related to adherence to medication were preceded by the statement, "We want to know how you feel, not how you think doctors or other people you know feel." According to the cutoff points recommended by the developers of the questionnaire, participants who scored less than 6 points were categorized as not adherent to medications and participants who scored 6 to 8 points were categorized as adherent to medications (Morisky, et al., 2008). Internal reliability (Cronbach α) for the scale in this sample is 0.67.

Beliefs About Medications

Concerns About Medications: Concerns about medications were measured using 4 items from a modified version of the concerns about medications scale of the Beliefs about Medicines Questionnaire (BMQ)(Horne, Weinman, & Hankins, 1999). Three items ask participants to rate the degree to which they worry about "having to take your medicines," "long-term effects of your medicines," and "becoming too dependent on your medicines." The fourth item asks how much "medicines disrupt your life." Based on participant feedback during pilot testing, we dropped the fifth item, "my medicines are a mystery to me," and modified the response scale for each item (1, "not at all," to 4, "very much") to make it more similar to the rest of the survey and to simplify the responses for stroke survivors who may have cognitive impairment. The 4 items were summed for a total concerns score. Internal consistency reliability (Cronbach α) for the 4-item scale in this sample was 0.71.

Necessity of Medications: Beliefs about the necessity of medications were assessed using a modified version of the 5-item necessity scale of the BMQ. The 5 items ask participants to rate the degree to which "your health depends on your medications," they would be "ill without your medications," "your health in the future depends on your medications," "your life would be impossible without your medications," and "your medicines protect you from becoming worse." The response scale for each item ranged from 1, "not at all," to 4, "very much," and the 5 items were summed for a total necessity score. Internal consistency reliability (Cronbach α) for the scale in this sample was 0.80.

General Harm and Overuse of Medications: Beliefs that medications are generally harmful or generally overused by physicians were measured with items adapted from the general harm and general overuse scales of the BMQ. Items on the general harm scale ask participants to rate the degree to which medicines are generally harmful (eg, how much do you agree with the following statement: natural remedies are safer than medicines). Items on the general overuse scale ask participants to rate the degree to which physicians overuse medicines (eg, how much do you agree with the following statement: doctors place too much trust in medicines). The response scale for each item ranged from 1, "not at all," to 4, "very much," and the items for each scale were summed for a total score. Internal consistency reliability (Cronbach α) for the 4-item general harm scale in this sample was 0.65 and for the 4-item general overuse scale was 0.64.

Depression symptoms were measured using the 8-item PHQ (PHQ-8). The PHQ-8 has discriminant properties for diagnosing depression similar to those of the 9-item version, (Kroenke, Spitzer, Williams, & Lowe, 2010) and the 9-item version has been validated for use in patients after stroke (Schmid et al., 2011) and in minority populations (Huang, Chung, Kroenke, Delucchi, & Spitzer, 2006). A score of 10 or higher on the PHQ-8 signifies at least mild to moderate depressive symptoms.

Demographic information, including age, sex, race/ethnicity, annual household income, and insurance status, was also collected by patient interview. For cases when data was missing on annual household income (n=40), participants were categorized as having "low income" if they had Medicaid insurance. Three participants were missing information on both income and insurance status and were not included in the adjusted logistic regression models.

Stroke severity was measured using the modified Rankin Scale (Wilson et al., 2002); a score of 3 or higher on this scale signifies at least moderate disability as a result of the stroke. Time since stroke was measured by asking the year of their most recent stroke or TIA (Banks & Marotta, 2007). Number and severity of medical comorbid conditions was measured using the Charlson comorbidity index (Charlson, Pompei, Ales, & MacKenzie, 1987).

Analysis Plan

We tested the hypothesis that concerns about medications significantly mediate the relationship between PTSD symptoms and increased likelihood of nonadherence to medication in 3 steps, based on recommendations by MacKinnon and Dwyer (MacKinnon & Dwyer, 1993) for testing mediation with dichotomous outcomes. First, using linear regression, we estimated the association of PTSD with concerns about medications. Then, using hierarchical logistic regression, we assessed the unadjusted and adjusted associations (95% confidence intervals [CIs]) between PTSD and beliefs about medications and between PTSD and nonadherence to medications. Finally, we tested whether the adjusted relationship between PTSD symptoms and nonadherence to medication was significantly attenuated after adjustment for beliefs about medications. We chose covariates for adjusted analyses based on a review of the literature for important patient-level predictors of poor adherence to

cardiovascular medications (Mann, Woodward, Muntner, Falzon, & Kronish, 2010; Osterberg & Blaschke, 2005). Covariates included age, sex, African American race, time since stroke, severity of stroke disability, number and severity of medical comorbid conditions, and depression symptoms.

We used a new SPSS macro (Hayes, 2012) that calculates total, direct, and indirect effects (total and specific for each mediator), including tests of significance using bootstrap procedures, which do not assume normality of the distribution of the indirect effects and hence provide stronger protection against type 2 error, compared to normal procedures such as the Sobel test. We report results for the bootstrap test, with a resample procedure of 5,000 bootstrap samples (bias corrected and accelerated estimates and 95% CI). Finally, effect ratios were calculated to express the amount of the total effect that is explained by the (total) indirect effects via the mediators. Effect ratios are a preferable (quantitative) way to describe mediated effects, compared to the more common dichotomy of “full” vs. “partial” definitions. For example, an effect ratio of 0.5 would mean that half of the total effects of the independent on the dependent variable is explained by the mediator, assuming no suppressing variables are present in the model (Shrout & Bolger, 2002). For illustrative purposes, we report both the odds ratio associated with a 1 point increase on the PCL and BMQ, and for a 1 standard deviation increase on those measures.

Results

Participants

We surveyed 535 participants for this study. The mean age of participants was 63 years; 59% were women, 80% were black or Latino; 30% never completed high school; and 56% earned less than $15,000 yearly (Table 1). The sample and recruitment strategy has been described in greater detail previously (Goldfinger, et al., 2012; Kronish, Edmondson, Goldfinger, et al., 2012). PTSD symptom scores were elevated (mean [SD] score, 34.42 [13.71]) and positively skewed (range, 17–80). Eighteen percent of participants had symptoms consistent with a diagnosis of PTSD (PCL-S score > 50), and 56% of participants had possible PTSD (PCL-S score, 25–50). Forty-one percent of participants were not adherent to medications according to the Morisky Medication Adherence Questionnaire. Compared with participants without PTSD, nearly twice as many participants with likely PTSD were not adherent (33% vs 65%, $P<.001$).

Relationship Between PTSD Symptoms and Beliefs About Medications

Responses to individual BMQ items are given in Table 2. Concerns about medications were prevalent (mean [SD] score, 7.7 [3.5]); the mean response to questions about concerns was “a little bit.” Symptoms of PTSD were moderately positively correlated with concerns about medications ($r= .45$, $P< .001$).

Beliefs in the necessity of medications were strong (mean [SD] score, 16.7 [3.7]); the mean response to items on the necessity scale was between “somewhat” and “very much.” Symptoms of PTSD were weakly positively correlated with greater belief in the necessity of medications ($r= .11$, $P= .03$). Beliefs in the general harm of medications were moderate (mean [SD] score, 7.56 [2.94]); the mean response to general harm items was “a little bit.” Symptoms of PTSD were positively correlated with greater belief in the harm of medications ($r= .19$, $P< .001$). Beliefs in the general overuse of medications were moderate(mean [SD] score, 8.85 [3.16]); the mean response to items on the general overuse scale was “a little bit.” Symptoms of PTSD were positively correlated with greater belief in the overuse of medications ($r= .22$, $P< .001$).

Logistic regression analysis

Results of logistic regression analyses are given in Table 3. In step 1, two unadjusted logistic regression analyses showed that both PTSD symptoms (odds ratio [OR], 1.05; 95% CI, 1.03–1.06) and concerns about medications (OR, 1.24; 95% CI, 1.18–1.31) were significantly related to increased odds of medication nonadherence. In step 2, after adjusting for demographic, clinical, and depression variables, PTSD symptoms remained significantly related to increased odds of nonadherence to medication (OR, 1.04; 95% CI, 1.01–1.06; ie, OR, 1.63 per 1 SD). However, in step 3, adjustment for concerns about medications attenuated the relationship of PTSD to nonadherence to medication (OR, 1.02; 95% CI, 1.00–1.05; ie, OR, 1.32 per 1 SD). Concerns about medications remained significantly related to increased odds of nonadherence to medication (OR, 1.17; 95% CI, 1.10–1.25; ie, OR, 1.72 per 1 SD).

Bootstrap tests of total, direct, and indirect effects

In the bootstrap test for mediation, after adjustment for all covariates, the total (direct and indirect) effect of PTSD symptoms on odds of nonadherence was b= .035, p=.003, OR= 1.04 per 1 point (OR= 1.61 per SD) increase on the PCL. The direct effect of PTSD symptoms on odds of nonadherence was b= .023, p= .06, OR= 1.02 per 1 point (OR=1.38 per SD) increase on the PCL. The indirect effect of PTSD symptoms on odds of nonadherence through increased BMQ concerns was b= .013 (95% CI= .006–.023), which corresponds to an effect ratio of .38. Thus, 38% of the total effect of PTSD symptoms on odds of nonadherence was explained by the mediated effect through increased BMQ concerns. Further, the direct effect of PTSD symptoms on odds of nonadherence was no longer significant, suggesting mediation.

Sensitivity Analyses

To test whether PTSD's relationship to nonadherence to medication was due to specifically cognitive-affective concerns rather than a more general altered belief about the medical necessity of medications to offset the risk of future adverse medical events, we conducted the same statistical tests as above with the necessity scale of the BMQ in place of the concerns scale. Scores on the necessity scale were unrelated to nonadherence to medication (unadjusted OR, 0.98; 95% CI, 0.93–1.03), and therefore we did not test for mediation. In a post hoc test, we created a variable to represent the discrepancy between participants' perception of the necessity of medications and their concerns about medications and tested it as a mediator of the association of PTSD symptoms to nonadherence. The results were essentially the same as those for the mediation test conducted on BMQ concerns alone.

We conducted another sensitivity analysis to determine whether the mediated effect was due specifically to concerns about medications rather than general negative beliefs about medications, we included all the BMQ scales in the fully adjusted logistic regression model. As in the primary analysis, the association between PTSD and nonadherence to medication remained attenuated (OR, 1.01; 95% CI, 0.98–1.04), and concerns about medications remained significantly associated with nonadherence to medication (OR, 1.15; 95% CI, 1.06–1.25). None of the other BMQ scales were significantly associated with nonadherence to medication (ORs, 0.96–1.07; *P* values, .19–.73).

Finally, since PTSD may be particularly associated with skipping medications rather than merely forgetting medications in some patient populations (Kronish, Edmondson, Li, & Cohen, 2012), we conducted a sensitivity analysis to determine whether the association of PTSD to medication nonadherence was due to participants forgetting their medications or intentionally skipping their medications by conducting analyses identical to the primary mediation analysis except that single Morisky items concerning forgetting or skipping

medications were analyzed as the dependent variable. Unlike Kronish et al. (2012), we found no differential associations by type of nonadherence.

Discussion

Researchers have reported that psychological distress in the form of PTSD symptoms is prevalent after life-threatening medical events (Edmondson, Richardson, et al., 2012), that PTSD due to such events may increase patients' risk for future medical events (Edmondson, Rieckmann, et al., 2011), and that PTSD is related to nonadherence to medication after those events (Kronish, Edmondson, Goldfinger, et al., 2012). However, the mechanisms for the association between PTSD and nonadherence have not been previously investigated. In a large sample of stroke survivors, we found that 38% of the risk for nonadherence to medication associated with PTSD was accounted for by concurrent increased concerns about medications. PTSD was also associated with somewhat increased beliefs in the general harm and overuse of medications in the medical system; however, these beliefs were not associated with nonadherence and did not account for the association between PTSD and nonadherence. Finally, although PTSD symptoms were related to slightly stronger beliefs in the necessity of medications, the perceived necessity of medications did not appear to affect adherence to medication in stroke survivors with PTSD.

In this study, compared with patients without PTSD after stroke, patients with PTSD had increased ambivalence toward medications. Although we did not directly measure the degree to which medications reminded patients of their stroke, this finding is consistent with our hypothesis that medications may serve as particularly potent reminders of trauma in stroke survivors with the hypervigilance and avoidance symptoms of PTSD (Catz, et al., 2000; Chernoff, 2007). However, future research should directly test the extent to which medications serve as reminders of the event before strong conclusions can be drawn. Experimental and observational research has shown that PTSD symptoms are related to increased psychological susceptibility to both conscious and unconscious reminders of mortality and that those reminders of mortality are related to predictable behavioral responses (Abdollahi, Pyszczynski, Maxfield, & Luszczynska, 2011; Edmondson, Chaudoir, et al., 2011; Kesebir, Luszczynska, Pyszczynski, & Benight, 2011; Park, Edmondson, Hale-Smith, & Blank, 2009; Pyszczynski & Kesebir, 2011). Though others have hypothesized that avoiding reminders of the life-threatening medical event might account for the association between PTSD and nonadherence to medication in survivors of ACS (Shemesh, et al., 2001), no prior study has tested any potential mediator of the association.

Limitations

This study should be interpreted with its limitations in mind. First, due to the nature of the parent study, we relied on participants' self-report of stroke for inclusion in the study, and we were limited to self-report measures rather than a clinical diagnosis of PTSD or objective measurement of adherence to medication. Furthermore, adherence to medication and beliefs about medications were measured with reference to "medicines," and we cannot know the extent to which participants responded to questions with reference to their stroke medications or to other types of medications. Similarly, some of the measures used in the study evinced somewhat low internal consistency reliability. Future studies of the association between PTSD triggered by medical events and adherence to medication should incorporate gold standard measures of both PTSD and adherence to medication and should assess more directly whether stroke medications act as traumatic reminders of the stroke. Qualitative and implicit assessment tools such as the Implicit Attitudes Test are promising approaches for elucidating these likely complex associations. (Chambers et al., 2011; Greenwald, McGhee, & Schwartz, 1998).

Also, it is possible that a third variable, such as general neuroticism, could influence both the development of PTSD and increased concerns about medication after stroke. Other simplifications of the model, such as the exclusion of medication type and side effects, polypharmacy, perceived racism, and other barriers to adherence in stroke survivors (Ellis, 2012) may also be a limitation, though their exclusion was in the service of focusing on the specific mechanism by which PTSD was associated with nonadherence. Future research should consider including such variables. Future research should also consider the independent effects of the three PTSD symptom clusters (reexperiencing, avoidance, and hyperarousal) on nonadherence, as some research suggests that the different clusters may carry independent recurrent cardiovascular risk after acute cardiovascular events (Edmondson, Rieckmann, et al., 2011). Finally, because of our study design, geographic location (Harlem and South Bronx, New York), and population of interest, our participants were primarily members of racial and ethnic minority groups and had low socioeconomic status. As such, their beliefs about medications may not be representative of those of other groups, and they may have distinct associations with PTSD and nonadherence to medication.

Conclusions

Nonadherence to medication is a major problem in stroke survivors, given that adherence to medications is the most important component of secondary risk reduction in these patients. This study is the first to demonstrate that concerns about medications account for a significant proportion of the relationship between PTSD and nonadherence to medication in stroke survivors. The results of this study suggest that concerns about medications should be assessed alongside PTSD symptoms in stroke patients in order to better understand potential sources of nonadherence.

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References

Abdollahi A, Pyszczynski T, Maxfield M, Luszczynska A. Posttraumatic stress reactions as a disruption in anxiety-buffer functioning: Dissociation and responses to mortality salience as predictors of severity of posttraumatic symptoms. Psychological Trauma: Theory, Research, Practice, and Policy. 2011; 3(4):329.

Andrykowski MA, Cordova MJ, Studts JL, Miller TW. Posttraumatic stress disorder after treatment for breast cancer: prevalence of diagnosis and use of the PTSD Checklist-Civilian Version (PCL-C) as a screening instrument. Journal of Consulting and Clinical Psychology. 1998; 66(3):586–590. [PubMed: 9642900]

Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke. 2007; 38(3):1091–1096. [PubMed: 17272767]

Bushnell CD, Olson DM, Zhao X, Pan W, Zimmer LO, Goldstein LB, Peterson ED. Secondary preventive medication persistence and adherence 1 year after stroke. Neurology. 2011; 77(12): 1182–1190. [PubMed: 21900638]

Bushnell CD, Zimmer LO, Pan W, Olson DM, Zhao X, Meteleva T, Peterson ED. Persistence With Stroke Prevention Medications 3 Months After Hospitalization Stroke Prevention Medication Use After Discharge. Archives of Neurology. 2010; 67(12):1456–1463. [PubMed: 20697032]

Catz SL, Kelly JA, Bogart LM, Benotsch EG, McAuliffe TL. Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. Health Psychology. 2000; 19(2):124–133. [PubMed: 10762096]

Chambers JA, O'Carroll RE, Hamilton B, Whittaker J, Johnston M, Sudlow C, Dennis M. Adherence to medication in stroke survivors: A qualitative comparison of low and high adherers. British Journal of Health Psychology. 2011; 16(3):592–609. [PubMed: 21199537]

Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of Chronic Disease. 1987; 40(5):373–383.

Chernoff RA. Treating an HIV/AIDS Patient's PTSD and Medication Nonadherence With Cognitive-Behavioral Therapy: A Principle-Based Approach. Cognitive and Behavioral Practice. 2007; 14(1): 107–117.

Delahanty DL, Bogart LM, Figler JL. Posttraumatic stress disorder symptoms, salivary cortisol, medication adherence, and CD4 levels in HIV-positive individuals. AIDS Care. 2004; 16(2):247–260. [PubMed: 14676029]

DiIorio C, McCarty F, Resnicow K, Holstad MMD, Soet J, Yeager K, Lundberg B. Using motivational interviewing to promote adherence to antiretroviral medications: a randomized controlled study. AIDS Care. 2008; 20(3):273–283. [PubMed: 18351473]

Edmondson D, Chaudoir S, Mills M, Park C, Holub J, Bartkowiak J. From shattered assumptions to weakened worldviews: Trauma symptoms signal anxiety buffer disruption. Journal of Loss and Trauma. 2011; 16:358–385. [PubMed: 24077677]

Edmondson D, Richardson S, Falzon L, Davidson KW, Mills MA, Neria Y. Posttraumatic stress disorder prevalence and risk of recurrence in acute coronary syndrome patients: A meta-analytic review. PLoS ONE. 2012; 7(6):e38915. [PubMed: 22745687]

Edmondson D, Rieckmann N, Shaffer JA, Schwartz JE, Burg MM, Davidson KW, Kronish IM. Posttraumatic stress due to an acute coronary syndrome increases risk of 42-month major adverse cardiac events and all-cause mortality. Journal of Psychiatric Research. 2011; 45:1621–1626. [PubMed: 21807378]

Edmondson D, Shaffer JA, Denton Eg, Shimbo D, Clemow L. Posttraumatic stress and myocardial infarction risk perceptions in hospitalized acute coronary syndrome patients. [Original Research]. Frontiers in Psychology. 2012; 310.3389/fpsyg.2012.00144

Ellis C. The association between major depression, health behaviors, and quality of life in adults with stroke. International journal of stroke. 2012 online ahead of print. 10.1111/j. 1747-4949.2011.00708.x

Goldfinger JZ, Kronish IM, Fei K, Graciani A, Rosenfeld P, Lorig K, Horowitz CR. Peer education for secondary stroke prevention in inner-city minorities: Design and methods of the prevent recurrence of all inner-city strokes through education randomized controlled trial. Contemporary Clinical Trials. 2012; 33(5):1065–1073. [PubMed: 22710563]

Greenwald AG, McGhee DE, Schwartz JLK. Measuring individual differences in implicit cognition: the implicit association test. Journal of Personality and Social Psychology. 1998; 74(6):1464–1480. [PubMed: 9654756]

Hall PA, Fong GT. Temporal self-regulation theory: A model for individual health behavior. Health Psychology Review. 2007; 1(1):6–52.

Hayes, AF, Producer. PROCESS: A versatile computational tool for observed variable mediation, moderation, and conditional process modeling [White paper]. 2012. Retrieved from http://www.afhayes.com/public/process2012.pdf

Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. Psychology & Health. 1999; 14(1):1–24.

Huang FY, Chung H, Kroenke K, Delucchi KL, Spitzer RL. Using the Patient Health Questionnaire-9 to measure depression among racially and ethnically diverse primary care patients. J Gen Intern Med. 2006; 21(6):547–552. [PubMed: 16808734]

Joshi AV, Madhavan SS, Ambegaonkar A, Smith M, Scott V, Dedhia H. Association of medication adherence with workplace productivity and health-related quality of life in patients with asthma. Journal of Asthma. 2006; 43(7):521–526. [PubMed: 16939992]

Kesebir P, Luszczynska A, Pyszczynski T, Benight C. Posttraumatic stress disorder involves disrupted anxiety-buffer mechanisms. Journal of Social and Clinical Psychology. 2011; 30(8):819–841.

Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of General Internal Medicine. 2001; 16(9):606–613. [PubMed: 11556941]

Kroenke K, Spitzer RL, Williams JB, Lowe B. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen Hosp Psychiatry. 2010; 32(4):345–359. [PubMed: 20633738]

Kronish IM, Edmondson D, Goldfinger J, Fei K, Horowitz C. Posttraumatic stress disorder and adherence to medications in survivors of strokes and transient ischemic attacks. Stroke. 2012 in press.

Kronish IM, Edmondson D, Li Y, Cohen BE. Post-traumatic stress disorder and medication adherence: Results from the Mind Your Heart study. Journal of Psychiatric Research. 2012; 46(12):1595–1599. [PubMed: 22809686]

Krousel-Wood M, Islam T, Webber LS, Re RN, Morisky DE, Muntner P. New medication adherence scale versus pharmacy fill rates in seniors with hypertension. Am J Manag Care. 2009; 15(1):59–66. [PubMed: 19146365]

Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. The self-regulation of health and illness behaviour. 2003; 1:42–65.

MacKinnon DP, Dwyer JH. Estimating mediated effects in prevention studies. Evaluation Review. 1993; 17(2):144–158.

Maes, S.; Gebhardt, W. Self-regulation and health behavior: The health behavior goal model. In: Boekaerts, Monique; Pintrich, Paul R.; Zeidner, Moshe, editors. Handbook of self-regulation. San Diego, CA, US: Academic Press; 2000. p. 343-368.

Mann DM, Woodward M, Muntner P, Falzon L, Kronish I. Predictors of nonadherence to statins: a systematic review and meta-analysis. Annals of Pharmacotherapy. 2010; 44(9):1410–1421. [PubMed: 20702755]

Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. Journal of Clinical Hypertension. 2008; 10(5):348–354. [PubMed: 18453793]

Muraoka MY, Carlson JG, Chemtob CM. Twenty-four-hour ambulatory blood pressure and heart rate monitoring in combat-related posttraumatic stress disorder. Journal of Traumatic Stress. 1998; 11(3):473–484. [PubMed: 9690188]

Newman JD, Muntner P, Shimbo D, Davidson KW, Shaffer JA, Edmondson D. Posttraumatic stress disorder (PTSD) symptoms predict delay to hospital in patients with acute coronary syndrome. PLoS One. 2011; 6(11):e27640. [PubMed: 22096608]

O'Carroll R, Whittaker J, Hamilton B, Johnston M, Sudlow C, Dennis M. Predictors of adherence to secondary preventive medication in stroke patients. Annals of Behavioral Medicine. 2011; 41(3): 383–390. [PubMed: 21193977]

Osterberg L, Blaschke T. Adherence to medication. New England Journal of Medicine. 2005; 353(5): 487–497. [PubMed: 16079372]

Park CL, Edmondson D, Hale-Smith A, Blank TO. Religiousness/spirituality and health behaviors in younger adult cancer survivors: does faith promote a healthier lifestyle? Journal of Behavioral Medicine. 2009; 32(6):582–591. [PubMed: 19639404]

Pyszczynski T, Kesebir P. Anxiety buffer disruption theory: A terror management account of posttraumatic stress disorder. Anxiety, Stress, & Coping. 2011; 24(1):3–26.

Rahiman A, Saver JL, Porter V, Buxton W, McNair N, Razinia T, Ovbiagele B. In-hospital initiation of secondary prevention is associated with improved vascular outcomes at 3 months. Journal of Stroke and Cerebrovascular Diseases. 2008; 17(1):5–8. [PubMed: 18190814]

Rosenstock IM. The health belief model and preventive health behavior. Health Education & Behavior. 1974; 2(4):354–386.

Rothwell PM, Algra A, Amarenco P. Medical treatment in acute and long-term secondary prevention after transient ischaemic attack and ischaemic stroke. Lancet. 2011; 377(9778):1681–1692. [PubMed: 21571151]

Schmid AA, Kroenke K, Hendrie HC, Bakas T, Sutherland JM, Williams LS. Poststroke depression and treatment effects on functional outcomes. Neurology. 2011; 76(11):1000–1005. [PubMed: 21403112]

Shemesh E, Rudnick A, Kaluski E, Milovanov O, Salah A, Alon D, Cotter G. A prospective study of posttraumatic stress symptoms and nonadherence in survivors of a myocardial infarction (MI). General Hospital Psychiatry. 2001; 23(4):215–222. [PubMed: 11543848]

Shemesh E, Yehuda R, Milo O, Dinur I, Rudnick A, Vered Z, Cotter G. Posttraumatic stress, nonadherence, and adverse outcome in survivors of a myocardial infarction. Psychosomatic Medicine. 2004; 66(4):521–526. [PubMed: 15272097]

Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: new procedures and recommendations. Psychological Methods. 2002; 7(4):422–445. [PubMed: 12530702]

Tuhrim S, Cooperman A, Rojas M, Brust J, Koppel B, Martin K, Chassin M. The association of race and sex with the underuse of stroke prevention measures. Journal of Stroke and Cerebrovascular Diseases. 2008; 17(4):226–234. [PubMed: 18589344]

von Kanel R, Begre S, Abbas CC, Saner H, Gander ML, Schmid JP. Inflammatory biomarkers in patients with posttraumatic stress disorder caused by myocardial infarction and the role of depressive symptoms. Neuroimmunomodulation. 2010; 17(1):39–46. [PubMed: 19816056]

von Känel R, Hari R, Schmid JP, Wiedemar L, Guler E, Barth J, Begré S. Non-fatal cardiovascular outcome in patients with posttraumatic stress symptoms caused by myocardial infarction. Journal of Cardiology. 2011; 58(1):61–68. [PubMed: 21493042]

von Känel R, Hepp U, Traber R, Kraemer B, Mica L, Keel M, Schnyder U. Measures of endothelial dysfunction in plasma of patients with posttraumatic stress disorder. Psychiatry Research. 2008; 158(3):363–373. [PubMed: 18252265]

Weathers, FW.; LT; Herman, DS.; Huska, J.; Keane, T. The PTSD checklist: Reliability, validity, and diagnostic utility. Paper presented at the Annual Meeting of the International Society for Traumatic Stress Studies; San Antonio, TX. 1993.

Wilson JT, Hareendran A, Grant M, Baird T, Schulz UG, Muir KW, Bone I. Improving the assessment of outcomes in stroke: Use of a structured interview to assign grades on the modified Rankin Scale. Stroke. 2002; 33(9):2243–2246. [PubMed: 12215594]

Table 1

Participant Characteristics[a]

Characteristic	Overall (N=535)
Age, y, mean ± SD	63.0 ± 11.3
Women	317 (59)
Race/ethnicity	
Black	210 (40)
Hispanic	212 (40)
White	76 (14)
Other	27 (5)
Income ≤ $15,000/y	300 (56)
Less than high-school education	157 (30)
Preferred language Spanish	127 (24)
Married/live with a partner	192 (36)
Live alone	185 (35)
Employment status	
Full or part time	76 (14)
Unable to work	205 (38)
Retired, in school, or other	252 (47)
No. of prior strokes and TIAs, mean ± SD	1.7 ± 1.2
Time since last stroke or TIA, y, mean ± SD	1.9 ± 1.4
Charlson comorbidity index score, mean ± SD	3.7 ± 2.2
Stroke impact severity (modified Rankin Scale score)	
0–2	287 (54)
3 or 4	248 (46)
Depressed (PHQ-8 score ≥10)	159 (30)
Concerns about medications (mean ± SD BMQ score)	11.2 ± 3.6
Nonadherent to medications (Morisky score, 0–5)	218 (41)

Abbreviations: BMQ, Beliefs about Medicines Questionnaire; PCL-S, PTSD checklist (specific); PHQ-8, 8-item Patient Health Questionnaire; PTSD, posttraumatic stress disorder; TIA, transient ischemic attack.

[a]Data are presented as number (%) unless otherwise specified.

Table 2

Participants Who Responded “Somewhat” or “Very Much” to BMQ, by PTSD Status[a]

	No. (%)		
Belief	**Overall (N=535)**	**PTSD (n= 95)**	**No PTSD (n= 440)**
Concerns			
How much does having to take your medicines worry you?[b]	136 (26)	48 (52)	88 (20)
How much do you worry about the long-term effects of your medicines?[b]	182 (35)	56 (62)	126 (29)
How much do medicines disrupt your life?[b]	89 (17)	40 (45)	49 (11)
How much do you worry about becoming too dependent on your medicines?[b]	152 (29)	50 (54)	102 (23)
Necessity			
How much does your health depend on your medicines?[b]	471 (88)	91 (96)	380 (86)
Would your life be impossible without your medicines?[b]	275 (58)	65 (77)	210 (54)
How ill would you be without your medicines?[b]	340 (74)	71 (85)	269 (72)
How much do you think your health in the future will depend on your medicines?	402 (82)	69 (81)	333 (82)
How much do your medicines protect you from becoming worse?	413 (83)	73 (84)	340 (83)

Abbreviation: BMQ, Beliefs about Medicines Questionnaire.

[a] Sample size varies slightly across items due to missing data.

[b] $P < .05$.

Table 3

Logistic Regression Models Predicting Nonadherence to Medications from PTSD, Demographic and Clinical Covariates, and Medication Concerns[a]

Characteristic	Model 1 (N=535)	Model 2 (N=532)	Model 3 (N=532)
PTSD	1.05 (1.03–1.06)	1.04 (1.01–1.06)	1.02 (1.00–1.05)
Age	…	0.98 (0.96–1.00)	0.98 (0.96–1.00)
Female	…	1.28 (0.86–1.92)	1.26 (0.84–1.90)
Black or African American	…	0.80 (0.55–1.15)	0.85 (0.59–1.24)
Income <$15,000/y	…	1.01 (0.67–1.52)	1.00 (0.66–1.52)
Charlson comorbidity index score	…	1.09 (0.99–1.19)	1.07 (0.98–1.18)
Stroke impact severity (Rankin Scale score)	…	0.97 (0.84–1.13)	0.95 (0.82–1.18)
Years since last stroke/TIA	…	1.17 (1.02–1.33)	1.17 (1.02–1.34)
Depressive symptoms (PHQ-8 score ≥10)	…	1.02 (0.97–1.08)	1.02 (0.97–1.08)
Medication concerns (BMQ score)	…	…	1.17 (1.10–1.25)

Abbreviations: BMQ, Brief Medication Questionnaire; PCL-S, PTSD checklist (specific); PHQ-8, 8-item Patient Health Questionnaire; PTSD, posttraumatic stress disorder; TIA, transient ischemic attack.

[a]Data are presented as odds ratio (95% confidence interval). Ellipses indicate not applicable.