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Anxiety Sensitivity and Medication Nonadherence in Patients with Uncontrolled Hypertension

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Abstract

Objective—Anxiety sensitivity—fear of the negative social, physical, or cognitive consequences of anxiety related sensations — has been linked to cardiovascular disease and adverse cardiovascular health behaviors. Medication nonadherence may account for this association. We examined whether anxiety sensitivity was independently associated with objectively measured medication nonadherence in a multi-ethnic primary care sample.

Methods—Eighty-eight patients with uncontrolled hypertension completed the Anxiety Sensitivity Index and had their adherence to blood pressure (BP) medications measured during the interval between two primary care visits using an electronic pillbox (MedSignals®). Multivariable Poisson regressions were conducted to determine the relative risks of medication nonadherence associated with anxiety sensitivity after adjustment for age, gender, Hispanic/Latino ethnicity, education, total number of prescribed medications, and depressive and posttraumatic stress disorder (PTSD) symptoms.

Results—Nearly twice as many patients with high anxiety sensitivity were nonadherent to BP medications compared to patients with low anxiety sensitivity (65.0% vs. 36.8%; $p=0.03$). Patients with high anxiety sensitivity had higher relative risks of medication nonadherence than their low anxiety sensitivity counterparts (adjusted relative risk [RR]=1.76; 95% CI: 1.03–3.03).

Conclusions—In this first study of the association between anxiety sensitivity and medication adherence, we found that high anxiety sensitivity was strongly associated with BP medication nonadherence, even after adjustment for known confounders. Our results suggest that teaching patients who have uncontrolled hypertension adaptive strategies to manage their anxiety sensitivity may help improve their medication adherence, and thereby lower their cardiovascular risk.

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Keywords

anxiety; cardiovascular disease risk factors; hypertension; medication

Anxiety sensitivity—fear of the negative social, physical, or cognitive consequences of anxiety-related sensations¹⁻³—has been linked to cardiovascular disease^{4,5} and adverse cardiovascular health behaviors.⁵⁻¹¹ Anxiety sensitivity is considered a multi-dimensional and trait-like cognitive vulnerability that exacerbates antecedent levels of anxiety. It is composed of three lower-order and interrelated factors pertaining to fear of anxiety: social concerns (e.g., belief that observable anxiety symptoms will lead to social rejection), physical concerns (e.g., belief that palpitations result in cardiac arrest/heart attack), and cognitive concerns (e.g., belief that concentration difficulties result in mental incapacitation).^{12,13} For example, individuals with high anxiety sensitivity are more likely to make catastrophic interpretations of arousal-related sensations of anxiety and in turn experience increased anxiety, which creates a positive feedback loop and escalating cycle.³ This tendency to fear and catastrophize anxiety-related or arousal-related sensations is thought to lead to avoidance behaviors that limit or remove altogether exposures to anxiety-provoking triggers, situations, and contexts.²

While anxiety sensitivity has been linked to certain cardiovascular health risk behaviors including smoking, drinking alcohol, using illicit drugs, and being less likely to exercise,⁷⁻⁹ to our knowledge, no prior studies have examined the association between anxiety sensitivity and adherence to cardiovascular medications. Medication nonadherence is an established risk factor for cardiovascular disease,¹⁴ and may account for the association between anxiety sensitivity with cardiovascular disease. Anxiety sensitivity may influence medication adherence as it is possible that patients with high anxiety sensitivity experience increased anxiety in the context of perceived medication side-effects or as a response to their hypertension symptoms that mimic anxiety-related sensations; this may lead to avoidance of medications and worse overall medication adherence. Indeed, common side-effects to BP medications and common symptoms of hypertension include dizziness, headaches, and palpitations,^{15,16} which are also common symptoms of anxiety or arousal.¹⁷ We examined whether anxiety sensitivity was independently associated with objectively measured medication nonadherence in a multi-ethnic sample of primary care patients with uncontrolled hypertension. We also explored whether or not specific subscales of anxiety sensitivity predicted medication nonadherence. We were particularly interested in the association of anxiety sensitivity to medication nonadherence independent of depressive symptoms and posttraumatic stress disorder symptoms, two well-established and consistent predictors of medication nonadherence.¹⁸⁻²⁰ We also tested whether anxiety sensitivity was associated with increased self-reported side-effects to BP medications. We hypothesized that individuals with high anxiety sensitivity would be more likely to exhibit poor medication adherence and to report medication side-effects.

Methods

We enrolled a convenience sample of patients with uncontrolled hypertension from a hospital-based primary care clinic in New York City. Patients were eligible if they had elevated blood pressure [BP] on two consecutive clinic visits prior to enrollment (BP 140/90 mm Hg or 130/80 if they had diabetes mellitus or chronic kidney disease) and if they were prescribed at least one BP medication. Patients were ineligible if they were unable to self-manage their BP medications due to dementia, psychosis, active substance abuse, or if they resided in an institutional setting.

Medication adherence was assessed during the interval between two subsequent clinic visits using an electronic pillbox with four compartments (MedSignals; MedSignals Corporation). Each BP medication was stored in a separate compartment, and the pillbox recorded the date and time that each compartment was opened. Adherence to each medication was calculated as the percent of days the correct number of doses were taken as prescribed; adherence to the overall BP medication regimen was calculated as the mean adherence to all monitored medications. Anxiety sensitivity was assessed using the Anxiety Sensitivity Index (ASI) administered in either English or Spanish after completing adherence monitoring.²¹ The Anxiety Sensitivity Index has strong psychometric properties and has been validated in multiple Spanish-speaking samples.²² The internal consistency of this scale was excellent in our sample (Cronbach's $\alpha = 0.91$). Total ASI scores were dichotomized into high (ASI ≥ 36) and low (ASI < 36) anxiety sensitivity categories based on established cut-offs that correspond to clinically significant anxiety levels.²³ In an exploratory analysis, we also calculated total scores for each of the three purported ASI subscales: Physical Concerns, Cognitive Concerns, and Social Concerns.²⁴ Patients' age, gender, ethnicity, and years of education were ascertained by self-report. Depressive symptoms at baseline were measured using the Patient Health Questionnaire (PHQ-8).²⁵ Posttraumatic stress disorder (PTSD) symptoms were measured using the Primary Care PTSD screening questionnaire.²⁶ Number of total prescribed medications was extracted from the electronic medical record. Patients were also asked whether (yes/no) they experienced side-effects from their BP medications. The Institutional Review Board of Columbia University Medical Center approved this study.

Patients were categorized as nonadherent if their adherence to their BP regimen was less than 80%.²⁷ We conducted Chi-square tests, independent samples t-tests, and independent samples Mann Whitney U tests (when variables were not normally distributed) to examine the distribution of demographic and behavioral variables by anxiety sensitivity status. We used logistic regression to determine whether anxiety sensitivity was associated with objectively measured medication nonadherence, independent of age, gender, ethnicity, education, number of prescribed medications, depressive symptoms, and PTSD symptoms. Model 1 estimated the unadjusted association of anxiety sensitivity with medication nonadherence. Model 2 included adjustment for demographics (age, gender, Hispanic/Latino ethnicity, education) and total number of prescribed medications. Model 3 included a final adjustment for depressive symptoms and PTSD symptoms at baseline because prior research has shown that depression and PTSD are associated with medication nonadherence and thus potentially important confounders.^{19,20} Separately, we also examined whether each of the ASI subscales was associated with medication nonadherence in unadjusted models and

whether ASI was associated with medication nonadherence when adding a measure of state anxiety (PROMIS – anxiety)²⁸ to the fully adjusted model. As there was a high nonadherence rate, we used a Modified Poisson regression with a robust error variance²⁹ to determine the adjusted relative risks.

Results

Between October 2011 and November 2013, 113 patients enrolled in the study; 88 had usable pillbox data and complete covariate information. Overall, patients had a mean age of 64.65 ($SD = 8.06$) years, 68 were women (77.3%), 72 were Hispanic/Latino (81.8%), and patients had a mean of 8.52 ($SD = 4.42$) years of education. The mean ASI score was 23.55 ($SD = 14.93$), and 22.7% had high anxiety sensitivity. Patients with high compared to low anxiety sensitivity did not significantly differ from each other on age, gender, ethnicity, years of education, PTSD symptoms, depressive symptoms, or total number of prescribed medications (Table 1). Patients took 10.85 ($SD = 4.12$) prescribed medications on average. Adherence was monitored for a mean of 62.41 days ($SD = 44.53$; range: 359) and 43.2% of patients were nonadherent (<80% of days). Patients with high anxiety sensitivity were also more likely than patients with low anxiety sensitivity to report having side effects from their BP medications (50.0% vs. 23.1%, $p = .01$) (Table 1).

Nearly twice as many patients with high anxiety sensitivity were nonadherent to BP medications compared to patients with low anxiety sensitivity (65.0% vs. 36.8%; $p = 0.03$). Patients with high anxiety sensitivity had higher relative risks of medication nonadherence than their low anxiety sensitivity counterparts in unadjusted models (RR = 1.77; 95% CI: 1.13–2.77), and after adjustment for age, gender, ethnicity, and number of prescribed medications (RR = 1.86; 95% CI: 1.15–2.99), and further adjustment for depressive and PTSD symptoms at baseline (RR = 1.76; 95% CI: 1.03–3.03). Although there was a trend for number of PTSD symptoms ($p = .07$), high anxiety sensitivity was the only factor significantly associated ($p = .04$) with medication nonadherence in our models. Our exploratory analyses indicate that the Cognitive Concerns (RR=1.06; 95%CI: 1.01–1.11) and the Social Concerns (RR=1.08; 95%CI: 1.02–1.15) anxiety sensitivity subscales were particularly predictive of medication nonadherence. Although the Physical Concerns subscale was not statistically associated with medication nonadherence, the relative risk was in the expected direction (RR=1.02; 95%CI: 0.99–1.04).

We conducted a sensitivity analysis wherein we treated anxiety sensitivity as a continuous variable, and found that anxiety sensitivity was linearly associated with risk of medication nonadherence (adjusted RR = 1.02; 95%CI: 1.00–1.04). We also conducted an additional sensitivity analysis where we included state anxiety, as measured by the PROMIS anxiety scale,²⁸ as an additional covariate in our final model. Our results did not change appreciably, although we lost some statistical power by including another covariate in the model. High anxiety sensitivity (RR=1.72, 95%CI: 0.98–3.00) was marginally associated with medication nonadherence, whereas state anxiety (RR=1.00, 95%CI: 0.94–1.07) was not.

Conclusions

In this first study on the association of anxiety sensitivity with medication adherence, we found that high anxiety sensitivity was associated with nearly double the risk of nonadherence to BP medications, even after adjustment for potential confounders. In this sample, the relative risk of medication nonadherence associated with high anxiety sensitivity (RR=1.76) was of the same magnitude as that reported for depression in a meta-analysis of the association between depression and medication nonadherence (RR=1.74).¹⁹ None of the other demographic and behavioral factors were significantly associated with medication nonadherence in this sample. We also found that cognitive concerns and social concerns about anxiety-related sensations were particularly predictive of medication non-adherence. Patients with high anxiety sensitivity were also more likely to report experiencing side-effects from their BP medications.

These results suggest that anxiety sensitivity may be an important yet vastly understudied psychological determinant of BP medication nonadherence in primary care patients with uncontrolled hypertension who are at increased risk for cardiovascular disease. Patients with high anxiety sensitivity might be more likely to misattribute their regular bodily sensations to their hypertension medications and to avoid their BP medications altogether. Alternatively, patients with high anxiety sensitivity might be more hypervigilant of their perceived BP medication side effects (e.g., dizziness) that mimic anxiety symptoms and trigger social and cognitive concerns regarding anxiety or arousal, which in turn leads to worse medication adherence. Indeed, in our sample, patients with high anxiety sensitivity were more likely than patients with low anxiety sensitivity to report having side effects from their BP medications, although our data did not allow us to assess for specific types of side effects. Relatedly, patients with uncontrolled hypertension and with high anxiety sensitivity might also consciously or unconsciously avoid all reminders of their illness, such as their BP medications, which might remind them of their hypertension status and threatening physiology.

While this is the first empirical report to examine the association of anxiety sensitivity with objectively measured medication adherence, our study is not without its limitations. First, this is a cross-sectional study, and thus we are unable to make causal inferences or rule out reverse causality. Future research should use longitudinal designs to examine the long-term effects of anxiety sensitivity in primary care samples, using more contemporary measures of the construct (ASI-3)¹² that can reliably assess the three purported dimensions of anxiety sensitivity, on medication nonadherence and other health behaviors such as smoking and alcohol use, and explore whether treatment of anxiety sensitivity improves medication adherence. Future research should also use larger samples to more comprehensively examine whether anxiety sensitivity and state anxiety are differentially associated with medication nonadherence. Second, this study was drawn from a small convenience sample of patients from a single primary care clinic, and hence its findings may not be generalizable to other populations. Relatedly, given the small sample size, we were not statistically powered to explore whether gender moderates the association of anxiety sensitivity to medication non-adherence, though prior work has shown that depression and anxiety might have differential implications for medication adherence among men and women.³⁰ Third,

we did not conduct comprehensive assessments of psychiatric disorders such as those generated from clinical interviews such as the CAPS for PTSD or the SCID, and thus cannot rule out whether the association of anxiety sensitivity with medication nonadherence is due to confounding from a psychiatric disorder. However, in models that adjusted for depression and PTSD symptoms, and in sensitivity analyses that further adjusted for state anxiety, we continued to see a robust association between anxiety sensitivity and medication nonadherence. This suggests that anxiety sensitivity is a psychological vulnerability that is independent of other psychological markers of medication nonadherence^{19,20} and thus might be particularly relevant for medication adherence in patients at risk of cardiovascular disease.

In conclusion, our results show that patients with high anxiety sensitivity are more likely to exhibit medication nonadherence than their low-anxiety sensitivity counterparts. Our results suggest that teaching patients adaptive strategies to manage their anxiety sensitivity, particularly focused on managing their cognitive and social concerns regarding anxiety- or arousal-related sensations, might help them improve their medication adherence, and thereby lower their cardiovascular risk.

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Highlights

- We examined the association of anxiety sensitivity with medication nonadherence
- Medication nonadherence was measured objectively in patients with hypertension
- High anxiety sensitivity was strongly associated with BP medication nonadherence
- Those with high vs low anxiety sensitivity had a 76% increased risk of nonadherence

Table 1
Sociodemographic Characteristics and Medication Nonadherence by Anxiety Sensitivity Status

	Overall N = 88		Low Anxiety Sensitivity n = 68		High Anxiety Sensitivity n = 20		$\chi^2(df)$ or t(df)	P
	M or No.	SD or %	M or No.	SD or %	M or No.	SD or %		
<i>Demographics</i>								
Age (years)	64.65	8.06	65.28	8.06	62.50	7.86	1.36 (86)	0.18
Female gender	68	77.3%	50	73.5%	18	90.0%	2.39 (1)	0.12
Hispanic/Latino ethnicity	72	81.8%	58	85.3%	14	70.0%	2.43 (1)	0.12
Education (years)	8.52	4.42	8.43	4.42	8.80	4.53	-32 (85)	0.75
<i>Clinical factors</i>								
Number of total medications	10.85	4.12	10.60	4.03	11.70	4.40	-1.05 (86)	0.30
<i>Behavioral factors</i>								
Depressive symptoms	7.05	5.49	6.51	5.27	8.89	6.00	-1.68 (83)	0.10
PTSD symptoms	1.01	1.38	0.90	1.29	1.40	1.60	-1.29 (85)	0.15
<i>Outcome</i>								
Medication nonadherence	38	43.2%	25	36.8%	13	65.0%	5.02 (1)	0.03
Perceived side effects	25	29.8%	15	23.4%	10	50.0%	5.14 (1)	0.02

Note.

PTSD= Posttraumatic stress disorder; Chi-square tests were used for categorical variables. Independent samples t-tests were used for continuous variables, and independent samples Mann Whitney U tests were used for continuous variables that were not normally distributed.

Table 2
 High Anxiety Sensitivity and Relative Risk of Medication Nonadherence in Patients with Uncontrolled Hypertension (N = 88)

	Model 1		Model 2		Model 3	
	RR	95% CI	RR	95% CI	RR	95% CI
<i>Anxiety sensitivity</i>						
Low	Ref		ref		ref	
High	1.77*	1.13 – 2.77	1.86*	1.15 – 2.99	1.76*	1.03 – 3.03
<i>Demographics</i>						
Age			0.98	0.95 – 1.01	0.99	0.96 – 1.02
Female gender			0.84	0.48 – 1.46	0.80	0.46 – 1.40
Hispanic/Latino ethnicity			0.73	0.37 – 1.46	0.82	0.39 – 1.76
Education			1.01	0.95 – 1.07	1.00	0.95 – 1.07
<i>Clinical factors</i>						
Number of total medications			1.00	0.95 – 1.05	0.99	0.93 – 1.05
<i>Behavioral factors</i>						
Depressive symptoms					0.98	0.92 – 1.03
PTSD symptoms					1.21	0.98 – 1.48

Note.

* P < .05. A modified Poisson regression was conducted to calculate the relative risk. PTSD=Posttraumatic stress disorder.