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# Differential sensitivity of the three ASI factors in predicting panic disorder patients' subjective and behavioral response to hyperventilation challenge

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## Abstract

The overall aim of the present investigation was to examine the association between the subscales of the ASI and emotional responding to voluntary hyperventilation challenge in a panic disorder population. Based on findings from [J. Abnorm. Psychol. 110 (2001) 372.], we predicted that the AS-Physical Concerns subscale would best predict the fear response to hyperventilation. We also examined the relative contribution of each of the three ASI subscales in predicting behavioral tolerance to hyperventilation. Participants ( $N = 192$ ) meeting DSM-IV criteria for panic disorder with or without agoraphobia completed the Anxiety Sensitivity Index (ASI) and underwent a voluntary hyperventilation challenge. Consistent with prediction, the AS-Physical subscale significantly predicted subjective fear during the hyperventilation challenge (12% of variance accounted for); whereas only the AS-Social subscale accounted for significant variance (4%) in patients' behavioral tolerance to the hyperventilation challenge.

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## 1. Introduction

Biological challenges such as hyperventilation and inhalation of carbon dioxide enriched air have been widely used in the study of panic disorder. Evidence indicates that compared to normal controls, panic disorder patients display heightened emotional responding to voluntary hyperventilation (Gorman et al., 1994; Holt & Andrews, 1989; Nardi, Valenca, Nascimento, Mezzasalma, & Zin, 2001), inhalation of 5% CO<sub>2</sub> (Gorman et al., 1994; Papp et al., 1997), 7% CO<sub>2</sub> (Gorman et al., 1994; Papp et al., 1997), and 35% CO<sub>2</sub> (Gorman et al., 1990; Griez, Lousberg, van den Hout, & van der Molen, 1987; Perna, Barbini, Cocchi, & Bertani, 1995). Moreover, panic disorder patients show greater anxious responding to hyperventilation challenges compared to individuals suffering from generalized anxiety disorder, or social phobia (Holt & Andrews, 1989; Rapee, Brown, Antony, & Barlow, 1992) and greater sensitivity to 5 and 35% CO<sub>2</sub> than patients with obsessive–compulsive disorder (Griez, de Loof, Pols, Zandbergen, & Lousberg, 1990; Perna, Bertani, Arancio, Ronchi, & Bellodi, 1995), generalized anxiety disorder (Perna, Bussi, Allevi, & Bellodi, 1999; Verburg, Griez, Meijer, & Pols, 1995) or depression (Kent et al., 2001; Perna, Barbini, Cocchi, Bertani, & Gasperini, 1995).

The hypersensitivity to CO<sub>2</sub> challenge observed in panic patients is consistent with both neurobiological (Klein, 1993) and psychological theories of panic disorder. Klein's suffocation alarm theory (Klein, 1993) posits that panic disorder patients have a hypersensitive respiratory control system, causing them to respond with suffocation alarms following an increase of CO<sub>2</sub>. Although panic patients' heightened emotional responding to CO<sub>2</sub> challenge is consistent with Klein's theory, recent tests of the major predictions of the theory have not been favorable. For example, Schmidt, Telch, and Jaimez (1996) found that panic disorder patients respond no differently to an increase or decrease in CO<sub>2</sub>. This finding is consistent with the conclusion drawn by Sinha, Papp, and Gorman (2000) in their excellent review of respiratory challenge studies in panic disorder, namely, "it seems plausible that there is nothing fundamentally abnormal in the respiratory control mechanism of the panic disorder patient" (Sinha et al., 2000, p. 195).

Investigations of potential psychological factors implicated in panic patients' heightened response to respiratory challenge have focused on both psychological trait variables and contextual factors such as instructional set or the presence of safety cues (Rapee, 1995; Schmidt & Telch, 1994; Zvolensky & Eifert, 2001). There is now ample evidence suggesting that individuals who score high on self-report measures tapping sensitivity to bodily cues, e.g., Body Sensation Questionnaire (BSQ; Chambless, Caputo, Bright, & Gallagher, 1984), and the Suffocation Fear Scale (SFS; Rachman & Taylor, 1993) display heightened emotional responding to respiratory challenges (Eke & McNally, 1996; Schmidt & Telch, 1994). However, the Anxiety Sensitivity Index (ASI; Peterson & Reiss, 1987), which taps the fear of anxiety-related symptoms, has shown to be the best

predictor of response to biological challenges in panic disorder as well as non-clinical participants (Donnell & McNally, 1989; Eke & McNally, 1996; Rapee, Brown, Antony, & Barlow, 1992; Telch, Silverman, & Schmidt, 1996). Multiple studies have demonstrated that this association remains significant after controlling for trait anxiety and general mood (Eke et al., 1996; Rapee et al., 1992; Zinbarg, Brown, Barlow, & Rapee, 2001).

Given the multifactorial structure of the ASI, the question arises as to which factor of the ASI is most influential in predicting emotional response to challenge. Rapee & Medoro (1994) found that the ASI total score was even a stronger predictor of anxious responding to hyperventilation when they removed items tapping social evaluative concerns (Items 1, 5, 7, and 13). Similarly, Zinbarg et al. (2001) found that the AS-Physical Concerns subscale was the only one of the three ASI factors that predicted fear response to hyperventilation or inhalation of CO<sub>2</sub>.

To the best of our knowledge, no studies have examined the association between anxiety sensitivity and the behavioral response to hyperventilation. In a recent study from our laboratory, behavioral tolerance to respiratory challenge (as measured by patients' duration of voluntary hyperventilation in seconds when given the instructional set to hyperventilate for as long as they can) predicted agoraphobia status among panic patients, whereas subjective fear in response to hyperventilation did not (Telch, Jacquin, Smits, & Powers, 2002). However, panic disorder patients with and without agoraphobia did not significantly differ on the ASI total score. The question arises whether behavioral tolerance and subjective fear to respiratory arousal are influenced by different AS factors. The overall aim of the present investigation was to examine the association between the subscales of the ASI and emotional responding to voluntary hyperventilation challenge in a large panic disorder sample. Based on findings from Zinbarg et al. (2001), we predicted that the AS-Physical Concerns subscale would best predict the fear response to hyperventilation. We also examined the relative contribution of each of the three ASI subscales in predicting behavioral tolerance to hyperventilation as measured by duration of voluntary hyperventilation.

## 2. Method

### 2.1. Participants

The sample consisted of 192 outpatients (141 women and 51 men) suffering from panic disorder with agoraphobia. All patients were referred to our laboratory from physicians and mental health professionals in the Austin area as part of several panic disorder treatment outcome studies (Telch et al., 1993; Telch, Schmidt, Jaimez, Jacquin, & Harrington, 1995). Further details of the subject recruitment and screening are provided elsewhere (Telch et al., 1993; Telch et al., 1995). All

patients met the following entry criteria: (a) principal Axis I diagnosis of panic disorder with agoraphobia; (b) at least one panic attack during the past 30 days; (c) age 18–65; (d) no recent change in psychotropic medications; and (e) negative for current psychosis, bipolar disorder and substance abuse disorder. Panic disorder diagnoses were derived from the Structured Clinical Interview for DSM-III-R (Spitzer & Williams, 1988). Mean age of the sample was 35.2 years and mean duration of illness was 9.1 years. The ethnic breakdown of the sample was as follows: Caucasian (81%), African-American (8%), Hispanic (6%), Asian (1%), and other 4%. Over half of the subjects were married (56%), 27% were never married, and 18% were divorced or separated.

## 2.2. Procedure

As part of a pretreatment assessment battery, participants completed the Anxiety Sensitivity Index (see below) and underwent a voluntary hyperventilation challenge test. Details of the hyperventilation challenge procedure are presented in Telch et al. (2002). Briefly, participants were instructed to take full vital capacity breaths every 2 s. Participants' rate of breathing was paced using a taped female voice announcing the words "inhale" and "exhale." Prior to starting the rapid breathing procedure, a female experimenter modeled the procedure for the subject and answered any questions. Participants were instructed to perform the rapid breathing procedure for as long as they could. Although the rapid breathing procedure was stopped after 120 s., participants were not informed of this limit. This 120 s. uninformed ceiling allowed us to use hyperventilation duration as a behavioral index of tolerance to the challenge. Immediately after cessation of rapid breathing, participants completed fear ratings (see below).

## 2.3. Measures

### 2.3.1. Anxiety Sensitivity Index

The ASI (Peterson & Reiss, 1987) is a 16-item, paper-and-pencil self-report instrument designed to assess fear of anxiety. Respondents are presented with statements expressing concerns about possible negative consequences of anxiety such as "When I am nervous, I worry that I might be mentally ill." For each statement, respondents rate their magnitude of concern on a Likert-type scale ranging from very little (0) to very much (4). The ASI total score<sup>1</sup> is computed by summing responses across the 16 items. The AS-Physical subscale is computed by summing responses to Items 3, 4, 6, 8–11, and 14. The AS-Mental Incapacitation subscale is computed by summing Items 2, 12, 15, and 16. The AS-Social subscale is computed by summing Items 1, 5, and 13

<sup>1</sup> Although our focus was on the predictive significance of the three subscales of the ASI, analyses of the ASI total score revealed a similar pattern to that seen for the AS-Physical subscale score.

(Zinbarg, Barlow, & Brown). Data on the reliability and validity of the ASI total score (Telch, Shermis, & Lucas, 1989) and its subscales (Zinbarg et al., 1997) have been favorable.

### 2.3.2. Hyperventilation indices

Participants rated their peak fear during the hyperventilation challenge from 1 (none) to 10 (extreme panic). The duration of hyperventilation (in seconds) was recorded and served as an index of behavioral tolerance to the challenge.

## 3. Results

Means and standard deviations for the AS and hyperventilation challenge indices are presented in Table 1. Multiple stepwise regression analyses were performed to determine the relative contribution of the different ASI subscales in predicting responses to the hyperventilation challenge. Separate analyses were performed for each of the two hyperventilation response indices, i.e., subjective fear and behavioral tolerance. Standardized beta coefficients and their respective *P* values are presented in Table 2.

Consistent with prediction, the AS-Physical subscale significantly predicted subjective fear during the hyperventilation challenge (Adjusted  $R^2 = .13$ ,  $P < .01$ ). The AS-Social and AS-Mental subscales accounted for negligible variance (i.e., less than 1%) in subjective fear to the hyperventilation challenge (see Table 2).

In contrast, a different pattern emerged for the prediction of behavioral tolerance to hyperventilation challenge. As seen in Table 2, only the AS-Social subscale accounted for significant variance (4%) in patients' behavioral tolerance ( $\beta = -.21$ ,  $P < .01$ ).

Table 1  
Means and standard deviation of clinical variables

Clinical variable	<i>M</i>	S.D.
<i>ASI</i>		
ASI Tot (0–64)	35.09	12.01
AS-Phys (0–32)	19.69	6.65
AS-Ment (0–16)	6.64	4.18
AS-Soc (0–12)	7.30	2.49
<i>Hyperventilation indices</i>		
Peak fear (0–10)	4.49	2.59
Duration (0–120)	84.25	41.05

ASI Tot: ASI total score; AS-Phys: ASI Physical Concerns subscale; AS-Ment: ASI Mental Incapacitation Concerns subscale; AS-Soc: ASI Social Concerns subscale; Peak fear: self-reported peak fear in response to the hyperventilation challenge; duration: total duration of hyperventilation measured in seconds.

Table 2  
 Betas and explained variance in fear responses and behavioral tolerance to hyperventilation

ASI	Before partialing out variance accounted for by other ASI subscales				After partialing out variance accounted for by other ASI subscales			
	Peak fear		Duration		Peak fear		Duration	
	$\beta$	$R^2$	$\beta$	$R^2$	$\beta$	$R^2$	$\beta$	$R^2$
AS-Phys	.35**	.12	-.13	0	.30**	.07	-.06	0
AS-Ment	.26**	.07	-.15*	.02	.15	.02	-.04	0
AS-Soc	.04	0	-.21**	.04	-.11	.01	-.18*	.03

AS-Phys: ASI Physical Concerns subscale; AS-Ment: ASI Mental Incapacitation Concerns subscale; AS-Soc: ASI Social Concerns subscale.

\*  $P < .05$ , two-tailed.  
 \*\*  $P < .01$  two-tailed.

#### 4. Discussion

The overall aim of the study was to examine the association between the subscales of the ASI and emotional responding to voluntary hyperventilation in a panic disorder population. As predicted, the AS-Physical subscale best predicted peak fear following hyperventilation. Contrary to expectation, behavioral tolerance of hyperventilation was predicted only by the AS-Social subscale.

The current findings replicate and extend those of Zinbarg et al. (2001). Although our findings are consistent with the suggestion that physical concerns may drive fear when exposed to a laboratory challenge that is physical in nature (Zinbarg et al., 2001; Rapee et al., 1992), our findings provide some suggestion that the predictive pattern of the AS subscales depend on the specific modality used in assessing emotional response to challenge. In the case of behavioral tolerance, it was the AS-social embarrassment factor, not the AS-physical factor, that emerged as the only significant predictor. It is also noteworthy that although the AS social embarrassment factor was a significant predictor of behavioral tolerance to hyperventilation, the predictive power as indexed by the proportion of variance accounted for was modest (4%) relative to that observed for the AS-physical factor in predicting subjective fear (12%).

We can only speculate as to how AS-social concerns influence behavioral tolerance to respiratory challenge. Recently, we reported that early termination of voluntary hyperventilation (i.e., low behavioral tolerance) was a good predictor of agoraphobia status among panic disorder patients (Telch et al., 2002). This finding along with previous research demonstrating that level of agoraphobia among panic patients is associated with heightened panic-related social concerns, (Amering et al., 1997; De Jong & Bouman, 1995; Rapee & Murrell, 1988; Telch et al., 1989), suggest the possibility that social concerns operate as a contributing risk factor in both agoraphobia and low tolerance to hyperventilation challenge. One clinical implication of these findings is that panic disorder patients showing

elevation on AS-social concerns might profit from intervention strategies specifically targeting patients' exaggerated threat perception related to the social consequences of anxiety and panic.

Several limitations deserve comment. Absence of a no panic disorder comparison group leaves open the question of whether these ASI subscales predict emotional response to hyperventilation in the absence of panic disorder. Secondly, we cannot rule out the possibility that elevations in the ASI subscales and their association with hyperventilation challenge indices are simply consequences of panic disorder. Prospective studies are needed to determine which ASI subscales, if any, serve to increase risk for the subsequent development of panic attacks, panic disorder, and agoraphobia.

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