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Evoking analogue subtypes of panic attacks in a nonclinical population using carbon dioxide-enriched air[☆]

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Abstract

The increasing recognition that panic attacks are heterogeneous phenomena necessitates better and more objective criteria to define and examine what constitutes a panic attack. The central aim of the present study was to classify subtypes of panic attacks (i.e. prototypic, cognitive, and non-fearful) in a nonclinical sample ($N = 96$) based on the concordance/discordance between subjective and physiological responding to multiple inhalations of 20 and 13% CO₂-enriched air. Results show that a substantial proportion of this nonclinical sample (55.2%) responded to the CO₂ challenge in a manner consistent with clinical and research definitions of different subtypes of panic attacks. The implications of this dimensional approach for discriminating subtypes of panic in the laboratory are discussed as a means to better understand the phenomenology and nature of panic attacks. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Over the past decade, an increasing amount of effort has been devoted to describing the

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nature and phenomenology of panic attacks. Based on the recognition that panic attacks are heterogeneous phenomena with respect to symptom presentation (Whittal, Goetsch, & Eifert, 1996), the development of precise definitions of what constitutes a panic attack is important for research, diagnosis, and treatment purposes (Barlow, Vermilyea, Blanchard, Vermilyea, Di Nardo & Cerny, 1985; Barlow, Brown, & Craske, 1994; Cox, Swinson, Endler, & Norton, 1994). Yet, considerable disagreement exists in how best to classify and define panic attacks and particularly over what qualifies as a panic attack (Beitman, Basha, Flaker, De Rosear, Mukerji & Lamberti, 1987; Klein & Klein, 1989; Kushner & Beitman, 1990; Whittal, Goetsch & Eifert, 1996). This ambiguity has led to concerted efforts to define and qualify different subtypes of panic attacks based on the presence or absence of contextual stimuli associated with panic attacks (i.e. uncued, cued and situationally predisposed panic) and the concordance/discordance between psychological and physiological response domains (Barlow et al., 1994).

With regard to the actual experience of panic, at least three conceptually and topographically distinct subtypes of panic attack have been proposed: prototypic, cognitive, and non-fearful or nonclinical panic¹. Prototypic panic, also described as a Type I 'classic' or 'full-blown' panic attack (Ley, 1991, 1992), is the most stringently defined subtype of panic. According to Barlow et al. (1994), such panic attacks include (a) an intense subjective experience of fear, terror, or discomfort; (b) an objectively measured marked autonomic surge that occurs abruptly (rise time of five minutes or less) and (c) an urge to escape the situation in which the panic occurs. Though this definition of panic entails adequate precision and is useful for research purposes, its precision may come at the expense of scope or generality because it fails to include the full range of experience that may qualify as a panic attack. For example, what about the person who experiences excessive and marked fear or discomfort in the absence of a demonstrable and marked autonomic surge in arousal? To account for such individuals who report and experience panic psychologically but who otherwise experience low levels of autonomic arousal, cognitive theorists (e.g. Clark, 1988) and others (e.g. Ley, 1992) have proposed a cognitive subtype of panic attack: excessive subjective fear or distress in the absence of an objectively measurable and marked autonomic surge (Ley, 1992).

Finally, the non-fearful (Kushner & Beitman, 1990) or nonclinical (Norton, Cairns, Wozney & Malan, 1988) subtype of panic describes a topography of symptoms observed by individuals who experience a marked and abrupt autonomic surge in the absence of heightened subjective distress or fear. Although some have questioned whether persons who experience the autonomic symptoms of panic attacks without distress meet definitional criteria for panic attacks (e.g. Rapee, Ancis & Barlow, 1988), the non-fearful subtype seems to best capture the ubiquitous experience of sub-clinical levels of panic as seen in the general population (Norton, Cox & Malan, 1992) while also stressing the importance of cognitive factors in the psychological experience of panic (McNally, 1990). In view of the debate about the

¹ The terms 'non-fearful' and 'non-clinical' have been independently proposed as descriptors of a subtype of panic attack that is defined, in large part, by marked autonomic arousal and little or non-significant cognitive symptoms of panic (e.g. terror, fear, distress). The extant literature, however, is mixed as to whether both terms are synonymous with respect to the phenomena they describe. To avoid confusion that may arise when using the term 'non-clinical' to describe panic attacks in a non-clinical population, we use the term 'non-fearful' to refer to this particular topography of panic attack.

aforementioned subtypes, research efforts are needed to elucidate the heterogeneous nature, topography, and phenomenology of panic attacks.

One difficulty with attempts to document subtypes of panic attack is that most, if not all, of the relevant research is based largely on clinical anecdotal evidence or retrospective self-report (Eifert, Forsyth, Zvolensky & Lejuez, in press). There are only a handful of laboratory (e.g. Cohen, Barlow & Blanchard, 1985; Lader & Mathews, 1970) and naturalistic (e.g. Hofmann & Barlow, 1996; Hofmann, Bufka & Barlow, in press) published reports where naturally occurring full-blown (i.e. prototypical) panic attacks have been documented using concurrent assessment of subjective and physiological response domains. Documenting different subtypes of panic is notoriously difficult in the absence of some means to reliably evoke panicogenic responses to study the processes involved. Although panicogenic biological challenge procedures (e.g. lactate infusion, carbon dioxide inhalation, hyperventilation) would seem best suited for this purpose, they have been criticized as a means to study panic, in part, because the cause (i.e. the provocation agent) is obvious and therefore makes it an expected event (cf. Barlow et al., 1994). Yet, it is quite possible to evoke topographically different subtypes or symptom presentations of panic attacks using biological challenge procedures (Sanderson & Wetzler, 1990). Such procedures, when combined with concurrent assessment of autonomic and self-report response domains, can be used to assess the nature and phenomenology of panic, the stability of a person's experience of panic across time and the extent to which individual difference factors discriminate between persons based on their particular panic subtype or topography of symptoms. To the best of our knowledge, no research exists that has attempted to classify different subtypes or topographies of panic in response to biological challenge procedures such as inhalations of high concentrations of CO₂-enriched air.

The central aim of the present research, therefore, was to attempt a classification of three subtypes of panic (i.e. prototypic, cognitive, non-fearful) in a nonclinical population based on the concordance/discordance of autonomic and subjective responses to eight repeated 20-s inhalations of either 20 or 13% CO₂-enriched air. Our previous research has consistently shown that both 20 and 13% CO₂-enriched air produce a range of cognitive and autonomic panicogenic effects in nonclinical populations (Forsyth & Eifert, 1998; Forsyth, Eifert & Thompson, 1996; Zvolensky, Lejuez & Eifert, 1998). This challenge method also produces considerable topographic heterogeneity in terms of concordance/discordance of response domains within each dose of CO₂ across participants (Forsyth, Daleiden & Chorpita, in press). Such heterogeneity, though not a specific focus of our previous research, bears directly on (a) the relation between panic provocation procedures and susceptibility to panic in response to biological challenge agents in clinical versus nonclinical populations and (b) the utility of such procedures as analogues to the clinical experience of panic as it occurs in the natural environment. By using two concentrations of CO₂ we wanted to take advantage of a wide range of individual differences in autonomic and subjective responding for purposes of classification.

Other biological challenge research suggests that nonclinical populations typically do not respond to such procedures with panic as assessed via self-report, despite experiencing expected elevations in autonomic arousal (see Rapee, 1995, for a review). Most of this work is based on comparisons of average responding as a function of sample population (e.g. normal versus persons with panic disorder or social phobia) without regard for individual differences in

response to such challenge procedures within a given sample. This, in turn, has led to the somewhat erroneous conclusion that such procedures are panicogenic only in clinical populations, particularly in persons with panic disorder (Rapee, 1995). Thus, an additional purpose of the present study was to address whether a more molecular classification of subjective and autonomic responding to CO₂-enriched air, in a manner consistent with clinical descriptions of panic attack subtypes, would lead to a different conclusion; namely, that a substantial number of nonclinical participants *do* panic but present differently in *how* they panic. We used the prototypic/cognitive/non-fearful classification scheme to examine the extent to which other assessed individual difference factors (e.g. anxiety sensitivity, frequency and severity of DSM-IV panic symptoms) reliably discriminate between our operationally defined panic subtypes and whether liberal and conservative definitions of panic support the validity of the present classification scheme. Finally, in keeping with recent arguments against a simple static classification of subtypes of panic (e.g. Whittal et al., 1996), we examined the consistency of our panic subtypes, or the extent to which participants varied in the topography or type of panic they experienced across multiple trials of CO₂ exposure.

2. Method

2.1. Participants

Ninety-six undergraduate volunteers (48 males and 48 females; $M = 19.8$ yr, $S.D. = 3.13$) served as participants and received course credit. All participants were pre-screened for medical and psychiatric conditions using a semi-structured interview and those reporting past or present histories of any of the following were not allowed to participate: (a) cardiac or respiratory disease, (b) asthma, (c) epilepsy, (d) hypertension, (e) stroke, (f) psychiatric condition or (g) having witnessed someone panic, faint, or have a heart attack. Participants were also excluded if they reported common specific fears or if they had a history of panic attacks.

2.2. Procedure

Equal numbers of males and females were randomly assigned to receive either 20 or 13% CO₂-enriched air. To comply with IRB requirements, and to control for different expectancies regarding the consequences of breathing CO₂-enriched air, we informed all participants of several possible negative consequences of breathing CO₂-enriched air including breathlessness, dizziness, chest pain, and tachycardia. We did not tell participants anything about the onset, timing, frequency of exposures, dose or offset of each inhalation of CO₂.

All participants underwent eight repeated 20-s inhalations of either 20% (20% CO₂, 21% O₂, 59% N₂) or 13% CO₂-enriched air (13% CO₂, 21% O₂, 66% N₂) administered through a continuous positive air pressure Downs C-Pap Mask with nose clip and head strap. Attached to one free port of a manually controlled 3-way stop cock valve (Hans Rudolph) was a 30-l meteorological balloon which was inflated with the CO₂ mixture. Participants breathed the CO₂ gas directly from the balloon reservoir to minimize detection from pressurized CO₂ to

nonpressurized room air. The C-Pap mask was connected to a free 22-mm port of the stop cock valve via 1.8-m of aerosol tubing and the remaining port was left unattached and fed room air. Manual control of the 3-way stop cock valve ensured uninterrupted breathing of the CO₂ gas, ease of switching between CO₂-enriched air and room air during breathing trials, and prevented the gases from being combined. The CO₂ apparatus was in a room adjacent to the subject chamber (cf. Lejuez, Forsyth & Eifert, 1998a; Lejuez, O'Donnell, Wirth, Zvolensky & Eifert, 1998b).

Throughout the procedure, participants sat alone in a comfortable recliner in a dimly lit sound attenuated chamber and were in visual and auditory contact with the experimenter at all times through a two-way mirror and intercom system. A 10-min adaptation-baseline period was followed by eight consecutive 20-s inhalations of CO₂-enriched air. Immediately following each inhalation trial, participants returned to breathing normal room air and recorded their SUDS ratings. Time between each inhalation of CO₂ was allowed to vary randomly (60 to 180-s; see Forsyth et al., 1996; Forsyth & Eifert, 1998). Following the eighth and final CO₂ trial, participants rated the extent and severity of any DSM-IV panic symptoms (DSQ) that they had experienced during the procedure.

2.3. Measures

2.3.1. Physiological measures

A Coulbourn Modular Polygraph, interfaced with Coulbourn's Labline software (high speed videograph), was used for continuous digital monitoring of physiological responses. All physiological channels were calibrated online prior to sampling. Skin conductance was sampled using disposable 8-mm diameter Ag/AgCl electrodes, which were coated with a 0.05-M concentration of NaCl and attached to the skin surface with concentric adhesive collars. Heart rate was sampled using Medi-Trace pre-gelled Ag/AgCl (#GC-11) disposable foam electrodes. Skin conductance levels (SCLs) and responses (SCRs) were directly recorded in microsiemens (mS) in an AC coupling mode with a Coulbourn S71-23 isolated skin conductance coupler which provides a constant 0.5-V across the electrodes. Electrodermal electrode placement followed a standard bipolar palmar configuration on the non-dominant hand. Heart rate was sampled in beats/minute (bpm) using an analogue-to-digital Coulbourn S77-26 tachometer that was fed through an S75-01 bioamplifier. Heart rate was sampled using a standard bilateral electrode configuration (right and left of the sternum just below the clavicle).

2.3.2. Self-report measures

Prior to the experimental procedure, participants completed the following measures: (a) the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky & McNally, 1986), a 16-item questionnaire designed to assess fear of anxiety-related symptoms and (b) the Body Sensations Questionnaire (BSQ; Chambless, Caputo, Bright & Gallagher, 1984), a 17-item measure of fears associated with autonomic arousal (e.g. heart palpitations, dizziness).

During the procedure, participants rated their subjective units of distress (SUDS) following each CO₂ inhalation trial on a 100-mm visual analogue scale anchored from *not at all distressed* to *very much distressed* (Wolpe, 1958).

The Diagnostic Symptoms Questionnaire (DSQ; Rapee, Sanderson, McCauly & Di Nardo,

1992), a 15-item measure of the presence and intensity of 12 somatic and three cognitive DSM-III-R (APA, 1987) panic symptoms, was administered immediately following the procedure. Intensity ratings for each endorsed symptom are made on a 9-point Likert-type scale (0 = *not at all* to 8 = *very strongly felt*). The following composite measures can be derived from the DSQ: total number of physical symptoms and catastrophic thoughts, mean severity of physical sensations and cognitive symptoms and reported fear and panic. Though the DSQ was originally developed based on the DSM-III-R, it is equally relevant to symptoms of panic attacks as outlined in the DSM-IV (APA, 1994).

2.4. Data reduction

2.4.1. Response measures

Electrodermal and cardiac responses were averaged separately in 5-s epochs for each 20-s inhalation trial of CO₂-enriched air. Electrodermal responses (SCRs) were defined as change in skin conductance (i.e., the mean of the last 5-s interval of each trial of CO₂-inhalation minus the mean of the first 5-s interval following CO₂ onset). Heart rate (HR) responses were similarly defined as change in heart rate occurring during each CO₂ trial (i.e. the mean of the last 5-s interval of each trial of CO₂-inhalation minus the mean of the first 5-s interval following CO₂ onset). Subjective distress was defined for each trial as a change in SUDS over pre-experimental baseline SUDS ratings. Electrodermal, cardiac and SUDS responses for each trial were then standardized (i.e. *Z* transformed) to place them on a common metric. Standardized electrodermal and cardiac responses were averaged for each trial to yield a composite index of autonomic responding.

2.4.2. Deriving analogue subtypes of panic attacks

Standardized SUDS ratings and the composite index of autonomic responding were used to derive four conceptually distinct analogue subtypes of panic attacks for each trial. Prototypic panic was defined as marked subjective distress (*Z*-score SUDS > 0) and marked autonomic arousal (Autonomic Composite Index *Z*-score > 0); cognitive panic was defined as marked subjective distress (*Z*-score SUDS > 0), but minimal autonomic arousal (Autonomic Composite Index *Z*-score < 0); non-fearful panic was defined as minimal subjective distress (*Z*-score SUDS < 0) and marked autonomic arousal (Autonomic Composite Index *Z*-score > 0); and non-panic was defined as minimal subjective distress (*Z*-score SUDS < 0) and minimal autonomic arousal (Autonomic Composite Index *Z*-score < 0).

Trial-by-trial categorization of analogue subtypes of panic served as the basis for classifying participants as belonging to one of four groups based on the most frequent subtype of panic that each participant exhibited across trials. Thus, we required that participants exhibited the same subtype of panic during the majority of trials, that is, during 5 or more (63%) of the eight trials. For example, if a participant responded according to the prototypic panic criteria on five or more of the eight trials, then he or she was classified as belonging to the prototypic panic group. This procedure resulted in 81 S's being classified as belonging to either the prototypic panic group ($n = 22$; 23.0%), cognitive panic group ($n = 14$; 14.6%), non-fearful panic group ($n = 17$; 17.7%) or non-panic control group ($n = 28$; 29.1%). Fifteen participants

(15.6%) failed to meet inclusion criteria for any of the four categories and were therefore excluded from subsequent analyses.

3. Results

3.1. Characteristics of derived analogue subtypes of panic attack

Table 1 shows unstandardized means and standard deviations of physiological and self-report measures for the four panic subtype groups. As expected, electrodermal, cardiac and SUDS responses reliably discriminated between groups. Both the prototypic and non-fearful subgroups that were defined, in part, by marked autonomic arousal, differed from the cognitive and non-panic groups across electrodermal and cardiac response domains, whereas SUDS in the prototypic and cognitive groups were significantly elevated relative to the two other groups (Tukey-HSD, $p < 0.05$).

Although an equal number of males and females were represented in the sample, they were not equally distributed between groups. There was an overall difference in the proportion of males and females in each group, $\chi^2(3, N = 81) = 13.59$, $p < 0.004$, with females disproportionately represented in the prototypic panic group (77.3%) while males made up the majority of the non-panic group (75.0%). Likewise, a greater proportion of participants in the prototypic (68.2%) and non-fearful (64.3%) panic groups had received 20% CO₂, whereas the majority of participants in the non-panic group had received 13% CO₂ (71.4%), $\chi^2(3, N = 81) = 9.24$, $p < 0.023$. The distribution of CO₂ dose was equivalent in the cognitive panic group (e.g. 47.1% had received 20% CO₂-enriched air).

To examine consistency of responding, we explored the extent to which participant responding deviated from their panic subtype classification on a trial-by-trial basis. The majority of S's (75%) responded with at least one other panic subtype than the one they had

Table 1

Means and standard deviations of unstandardized electrodermal, cardiac and SUDS responses as a function of analogue panic subtype. Univariate ANOVAS $F(3, 77)$. Means with different superscripts differ, $p < 0.05$ (Tukey-HSD)

| Response domains | Analogue panic subtypes | | | | <i>F</i> | <i>p</i> |
|----------------------------|-----------------------------|----------------------------|------------------------------|----------------------------|----------|----------|
| | prototypic (<i>n</i> = 22) | cognitive (<i>n</i> = 14) | non-fearful (<i>n</i> = 17) | non-panic (<i>n</i> = 28) | | |
| Electrodermal responses | | | | | | |
| <i>M</i> | 3.13 ^a | 0.51 ^b | 2.27 ^a | 0.26 ^b | 13.15 | 0.001 |
| S.D. | 2.95 | 0.61 | 1.77 | 0.83 | | |
| Cardiac responses | | | | | | |
| <i>M</i> | 11.64 ^a | 3.25 ^b | 11.51 ^a | 3.42 ^b | 25.23 | 0.001 |
| S.D. | 4.94 | 4.02 | 4.49 | 3.57 | | |
| Subjective distress (SUDS) | | | | | | |
| <i>M</i> | 49.37 ^a | 53.59 ^a | 14.33 ^b | 10.41 ^b | 34.76 | 0.001 |
| S.D. | 23.34 | 20.47 | 9.09 | 12.61 | | |

been classified with, but 25% of the sample responded with the same panic subtype during each of the eight trials. Although groups did not differ in terms of a tendency toward response stereotypy across trials, $F(3, 77) = 1.94$, ns, participants who were more consistent in how they responded to the CO₂ across trials reported fewer ($r = -0.24$, $p < 0.05$) and less severe ($r = -0.23$, $p < 0.05$) panic symptoms on the DSQ.

3.2. Relation between panic subtypes, anxiety sensitivity and bodily fears

Risk for panic has been related to several psychological variables, among them anxiety sensitivity and misinterpretation of bodily sensations as threatening (see McNally, 1990, for a review). Both the Anxiety Sensitivity Index (ASI) and Bodily Fears Questionnaire (BSQ) are designed to assess such risk factors. We, therefore, examined whether pre-experimental responses on the ASI and BSQ discriminated between panic subtype groups. As can be seen in Table 2, anxiety sensitivity and bodily fears varied reliably as a function of panic subtype [ASI: $F(3, 77) = 4.22$, $p < 0.008$; BSQ: $F(3, 77) = 2.88$, $p < 0.05$]. Scores on the ASI were significantly elevated in the prototypic panic group compared to the non-fearful and non-panic groups, Tukey-HSD, $p < 0.05$. A similar pattern was observed for between group comparisons on the BSQ (see Table 2).

3.3. Uncontrollability in relation to panic subtypes

Uncontrollability has been described as a central psychological risk factor in the experience of panic. One item of the DSQ specifically asks participants to rate (on a 0–8 scale) how much control they felt they had over the sensations produced by the CO₂ during the procedure. Most psychological theories of panic predict that responses to this item should relate strongly to panic (McNally, 1990) and, therefore, also discriminate between subtypes of panic. A between-group comparison of responses to this item revealed a significant effect for group, $F(3, 77) = 6.05$, $p < 0.001$, with the prototypic group reporting a greater sense of uncontrollability ($M = 6.14$) relative to the non-panic group ($M = 3.71$), Tukey-HSD, $p < 0.05$. The cognitive ($M = 5.29$) and non-fearful ($M = 4.92$) panic groups did not differ significantly from one another or the other groups.

3.4. DSM-IV panic symptoms as a function of panic subtype

Table 2 shows means and standard deviations of the frequency and severity of DSM-IV panic symptoms as reported by S's of our derived panic groups and as reported by patients with panic disorder (PD) and panic disorder with agoraphobia (PDA) in response to 5.5% CO₂-enriched air in a previous study. A series of univariate ANOVAs on data from our nonclinical sample revealed significant between-group differences in terms of number of physical symptoms, $F(3, 77) = 5.73$, $p < 0.001$, number of cognitive symptoms, $F(3, 77) = 5.23$, $p < 0.002$, severity of physical symptoms, $F(3, 77) = 10.23$, $p < 0.001$, severity of cognitive symptoms, $F(3, 77) = 3.37$, $p < 0.023$, overall symptom total, $F(3, 77) = 7.36$, $p < 0.001$, overall symptom severity, $F(3, 77) = 8.82$, $p < 0.001$, and on the DSQ item assessing severity of panic or fear, $F(3, 77) = 13.49$, $p < 0.001$ (see Table 2). With some exceptions, the

prototypic and cognitive panic groups reported a greater frequency and severity of DSM-IV panic symptoms compared to both other groups (Tukey-HSD, $p < 0.05$).

As can be seen in Table 3, the most frequently reported symptoms of strong severity (6 or greater on a 0–8 scale) were largely cardiorespiratory; though the actual distribution and percentage of participants endorsing these and other symptoms varied as a function of group. The proportion of participants reporting panic, as assessed by an item of the DSQ, also varied reliably as a function of panic subtype, $\chi^2(3, N = 81) = 14.82, p < 0.002$, with 90.9% of the prototypic panic group and 70.6% of the cognitive panic group reporting panic during the

Table 2

Anxiety sensitivity, bodily fears and DSM-IV panic symptoms in relation to analogue panic subtypes and patients with panic disorder. Univariate ANOVAS $F(3, 77)$. Means with different superscripts differ, $p < 0.05$ (Tukey-HSD). Anxiety sensitivity=ASI total; bodily fears=BSQ total; DSM-IV panic symptoms based on the Diagnostic Symptom Questionnaire. Available comparison data are provided from Rapee et al. (1992) for patients response to 5.5% CO₂-inhalation (PDA=panic disorder with agoraphobia; PD=panic disorder)

| | Analogue panic subtypes | | | | Rapee et al. (1992) | |
|--------------------------------|----------------------------|---------------------------|-----------------------------|---------------------------|---------------------|--------------------|
| | prototypic ($n = 22$) | cognitive ($n = 14$) | non-fearful ($n = 17$) | non-panic ($n = 28$) | PDA ($n = 40$) | PD ($n = 35$) |
| Anxiety sensitivity | | | | | | |
| <i>M</i> | 22.0 ^a | 17.1 | 12.9 ^b | 14.3 ^b | 32.1 | 36.4 |
| S.D. | 10.0 | 10.1 | 7.1 | 7.6 | 11.3 | 10.3 |
| Bodily fears | | | | | | |
| <i>M</i> | 2.1 | 2.1 | 1.7 | 1.8 | | |
| S.D. | 0.58 | 0.69 | 0.43 | 0.49 | | |
| DSM-IV panic symptoms | | | | | | |
| No. cognitive symptoms | | | | | | |
| <i>M</i> | 1.0 ^a | 0.35 ^b | 0.28 ^b | 0.28 ^b | 1.0 | 1.0 |
| S.D. | 1.0 | 0.61 | 0.61 | 0.59 | 1.0 | 0.9 |
| No. physical symptoms | | | | | | |
| <i>M</i> | 6.6 ^a | 5.2 | 5.8 | 4.0 ^b | 5.6 | 5.9 |
| S.D. | 2.1 | 2.4 | 2.5 | 2.0 | 3.2 | 2.7 |
| Severity of cognitive symptoms | | | | | | |
| <i>M</i> | 1.2 ^a | 0.37 | 0.21 | 0.25 ^b | 2.5 | 2.5 |
| S.D. | 2.1 | 0.66 | 0.44 | 0.61 | 2.6 | 2.4 |
| Severity of physical symptoms | | | | | | |
| <i>M</i> | 2.3 ^a | 1.7 | 1.5 ^b | 0.95 ^b | 3.7 | 4.0 |
| S.D. | 1.1 | 0.74 | 0.81 | 0.79 | 2.0 | 1.7 |
| Severity of panic/fear | | | | | | |
| <i>M</i> | 4.4 ^a | 3.1 ^a | 0.86 ^b | 1.1 ^b | 3.6 | 4.3 |
| S.D. | 2.2 | 2.9 | 1.2 | 1.8 | 2.8 | 2.7 |
| Overall symptom total | | | | | | |
| <i>M</i> | 7.6 ^a | 5.6 | 6.1 | 4.3 ^b | 6.6 | 6.9 |
| S.D. | 2.7 | 2.6 | 2.5 | 2.1 | | |
| Overall symptom severity | | | | | | |
| <i>M</i> | 2.9 ^a | 1.8 ^b | 1.6 ^b | 1.1 ^b | | |
| S.D. | 2.1 | 0.90 | 0.85 | 0.88 | | |

procedure. Report of panic did not vary simply as a function of CO₂ dose. It should be noted that the frequency and severity of DSM-IV symptoms in our prototypic and cognitive panic groups were, in many cases, as great or greater than those reported by Rapee et al. (1992) for patients with PDA and PD following 5.5% CO₂-enriched air (see Table 2).

3.5. Liberal and conservative definitions of panic attacks as a function of analogue panic subtype

To examine the actual extent of panic attacks experienced by S's in our sample, we used both a liberal and more conservative definition of panic as described in previous research (e.g. Rapee et al., 1992; Sanderson, Rapee & Barlow, 1988; Sanderson, Rapee & Barlow, 1989). According to the liberal definition, a panic attack was operationalized as the report of four or more DSM-IV panic symptoms on the DSQ, at least one of which was a cognitive symptom, together with a report of fear or panic of an intensity of one or more on the DSQ's 0–8 scale (see Sanderson et al., 1989). The more conservative definition of panic required a panic or fear intensity rating of five or above on the 0–8 scale (i.e. more than moderate fear) in addition to the report of four or more DSM-IV panic symptoms as in the liberal definition of panic (see Rapee et al., 1992).

We found a significant overall between-group difference in the number of S's who met our definitional criteria for panic attacks using both the liberal, [$\chi^2(3, N = 81) = 14.83, p < 0.002$]

Table 3

Rank ordering of percentage of endorsed DSM-IV panic symptoms as a function of analogue panic subtype. Numbers reflect percentage (%) of participants within each group reporting severity of panic symptoms of 6 (strongly felt) or greater on a 0–8 point scale. *R* = rank ordering of the four most frequently reported symptoms

| DSQ panic symptoms | Analogue panic subtypes | | | | | | | | |
|---|--------------------------------|------|-------------------------------|------|---------------------------------|------|-------------------------------|------|-----|
| | prototypic (<i>n</i> = 27) | | cognitive (<i>n</i> = 23) | | non-fearful (<i>n</i> = 18) | | Non-panic (<i>n</i> = 28) | | |
| | <i>R</i> | % | <i>R</i> | % | <i>R</i> | % | <i>R</i> | % | |
| Chest tightness or chest pain | | 18.1 | | 0 | | 0 | | 3 | 3.6 |
| Pounding or racing heart | 2 | 40.9 | 2 | 29.5 | 2 | 7.1 | 2 | 7.2 | |
| Dizziness, lightheadedness, or unsteadiness | 3 | 31.7 | 3 | 11.8 | 2 | 7.1 | 3 | 3.6 | |
| Trembling or shaking | | 18.1 | 4 | 5.9 | 2 | 7.1 | | 0 | |
| Breathlessness or smothering sensation | 1 | 81.8 | 1 | 58.8 | 1 | 42.9 | 1 | 17.9 | |
| Faintness | 4 | 22.6 | | 0 | | 0 | | 0 | |
| Numbness or tingling in face or extremities | 4 | 22.6 | 4 | 5.9 | 2 | 7.1 | | 0 | |
| Choking | | 18.1 | | 0 | | 0 | 3 | 3.6 | |
| Sweating | | 18.1 | | 0 | | 0 | | 0 | |
| Hot flushes or cold chills | | 0 | 4 | 5.9 | 2 | 7.1 | | 0 | |
| Feeling unreal or in a dream | | 9.1 | | 0 | | 0 | | 0 | |
| Nausea or abdominal distress | | 4.5 | | 0 | | 0 | | 0 | |
| Fear of dying | | 9.0 | | 0 | | 0 | | 0 | |
| Fear of going crazy | | 9.0 | | 0 | | 0 | | 0 | |
| Fear of losing control | | 13.6 | 4 | 5.9 | | 0 | 3 | 3.6 | |

and more conservative definition of panic [$\chi^2(3, N = 81) = 18.40, p < 0.001$]. As can be seen in Fig. 1, the liberal definition correctly classified a greater proportion of reported panic in the prototypic and cognitive panic groups relative to the other groups. The more conservative definition, however, resulted in a significant reduction to near zero in the number of persons reporting panic from the non-fearful and non-panic groups. Interestingly, neither the liberal nor conservative definition of panic discriminated between participants solely as a function of the dose of CO₂-enriched air.

4. Discussion

The central aim of the present study was to classify subtypes of panic attacks (i.e. prototypic, cognitive, and non-fearful) based on the concordance/discordance between subjective and physiological responding to multiple high dose inhalations of CO₂-enriched air.

The results of our study provide further evidence that CO₂ challenges are a viable experimental method for producing panic-like responses in the laboratory. For instance, a substantial majority of the present nonclinical sample reported panic-like physical and psychological responses to the CO₂ challenge. In addition, over 90% of S's in the prototypic panic group and over 70% of the cognitive panic group reported panic during the procedure. These two groups also reported a greater sense of symptom uncontrollability and a greater frequency and severity of DSM-IV panic symptoms relative to the non-panic group. It is noteworthy that the frequency and severity of DSM-IV symptoms in our prototypic and cognitive panic groups were, in many cases, as great or greater than those reported by Rapee et al. (1992) for panic disorder patients following inhalation of 5.5% CO₂-enriched air. The

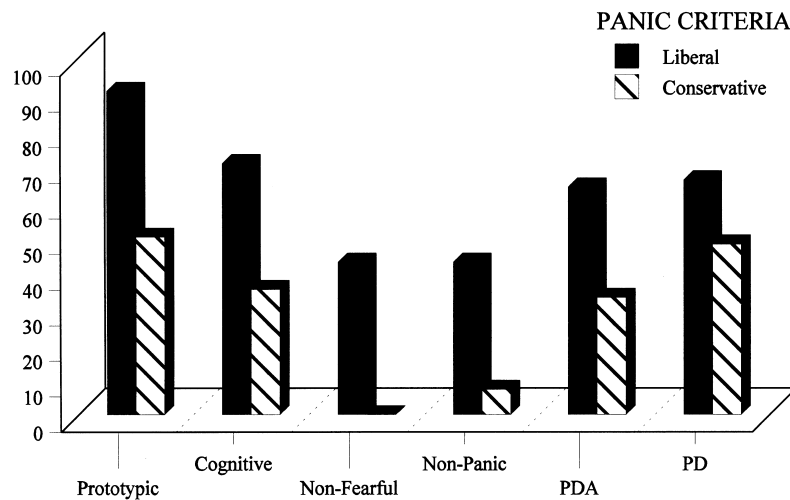


Fig. 1. Proportion of participants in each panic subtype group who reported a panic attack in response to the CO₂ challenge as a function of liberal and conservative criteria for panic. Also presented for comparison purposes are data from Rapee et al.'s (1992) sample of patients' response to 5.5% CO₂-enriched air (PDA = panic disorder with agoraphobia [moderate to severe avoidance]; PD = panic disorder [none or mild avoidance]).

distribution of males and females in our panic subtype groups, particularly a disproportionately higher number of females than males in the prototypic panic group, is also consistent with what is typically observed in studies using clinical populations (Barlow, 1988).

Overall, the results show that a substantial proportion of this nonclinical sample responded to the CO₂ challenge in a manner consistent with clinical and research definitions of different subtypes of panic attacks. The majority of our sample (approximately 75%) displayed a relatively stable pattern of responding within one particular panic subtype, although fewer S's responded with the same subtype on each of the eight trials. Pre-experimental responses on the ASI and BSQ also discriminated between panic subtype groups, that is, anxiety sensitivity and fears of bodily sensations varied reliably as a function of panic subtype and were significantly elevated in the prototypic panic group compared to the non-fearful and non-panic groups. Moreover, liberal and conservative definitions of panic discriminated among panic subtype groups. The conservative definition, in particular, correctly classified a greater proportion of reported panic in the prototypic and cognitive panic groups relative to the other groups. Thus, both definitions of panic support the validity of our particular classification of analogue panic subtypes based on participants' response to CO₂-enriched air.

Although our results support the subtypes used in our study, there are other dimensions that can be used to classify subtypes of panic attack. For instance, panic attacks are often distinguished by whether they are preceded by noticeable environmental or interoceptive cues thereby making the attack unexpected (uncued), situationally bound (cued), or situationally predisposed panic (APA, 1994; Barlow et al., 1994). This cue-based classification system is not incompatible with the subtypes examined in the present study. Rather, it is complementary and can be integrated with the basic scheme used here. For example, it is conceivable that one particular subtype of panic is more likely to be uncued, whereas another type may more likely be cued or situationally predisposed. Thus, one could readily arrange contingencies that are uncued, cued, or predisposing to study how such arrangements influence the severity of panic, the particular subtype of panic shown, and the stability of symptom topography, including patterns of concordance/discordance, across time. Likewise, the classification scheme used herein could be fruitfully integrated with other psychological risk factors such as uncontrollability and unpredictability in relation to perceived or actual threat (e.g. Zvolensky et al., 1998).

Our results suggest that individuals do not respond uniformly to the CO₂ challenge. We also have observed such interindividual differences in clinical populations (Lejuez, Eifert, Zvolensky, & Sheer, 1999). Future biological challenge research with clinical and nonclinical populations therefore should examine and take into account individual differences in response to challenge procedures *within* groups rather than simply collapsing all responding to yield average scores for between group comparisons. Likewise, our subtype classification system did not consider or assess differences in the urge to escape, which is one of the key criteria for prototypic panic (cf. Barlow et al., (1994). There is some evidence to suggest that avoidance is a common response to 20% CO₂ (Lejuez et al., 1998a; Lejuez et al., 1998b). Future research will have to determine, however, whether this feature of panic is present in all types of panic. At this point, we suspect that avoidance is likely to be low in individuals with non-fearful or nonclinical panic.

Despite encouraging results, we realize that conclusions from our findings are limited by the use of a nonclinical population in an analogue research context. However, several additional

lines of research may be addressed with this paradigm. For example, prospective studies could address a number of questions: (a) are persons classified as belonging to the prototypic or cognitive panic groups at increased risk for developing panic disorder; (b) do psychological risk factors (e.g. low levels of predictability and controllability) influence the kind of panic attack one experiences and (c) are there any historical or other individual difference factors that predict a person's panic subtype. In addition, it remains to be seen whether this method of classifying responders to CO₂ could be used as an assessment device for subsequent treatment matching purposes. For example, persons who respond to the CO₂ challenge with a prototypic response type may require a somewhat different treatment regimen than individuals responding with the cognitive or non-fearful subtypes.

In summary, high dose inhalations of CO₂-enriched air is a promising paradigm to evoke and examine panic attack subtypes to study the presence and relative dominance of physiological and cognitive processes involved in the experience of panic. This CO₂ challenge paradigm also may be used as a means to classify subtypes of panic attacks in persons meeting diagnostic criteria for panic disorder, with such information being used to modify or tailor specific treatment targets. Finally, this paradigm could be used to identify persons in the population at risk for the development of panic disorder and quite possibly other anxiety-related disorders where panic attacks are common.

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