Preference between predictable and unpredictable administrations of carbon dioxide-enriched air

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Preference Between Predictable and Unpredictable Administrations of Carbon Dioxide-Enriched Air

Carl Wilbourne Lejuez

Dissertation submitted to the Eberly College of Arts & Sciences at West Virginia University in partial fulfillment of the requirements for the degree of

Doctor of Philosophy in Adult Clinical Psychology

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Morgantown, West Virginia 1999

Keywords: Predictability, Panic Disorder, Anxiety, Choice, Carbon Dioxide, Humans

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ABSTRACT

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Carl Wilbourne Lejuez

Predictability of panic attacks has been identified as an important factor in the development, maintenance, and treatment of panic disorder. Although animal studies typically have found a preference for signaled (predictable) over unsignaled (unpredictable) aversive events, results with human participants have been less clear. Because preference for predictability has a wide range of clinical implications, we examined human preference for predictability in a biological challenge paradigm. Further, we examined the differential effects of predictability as a function of anxiety sensitivity and gender. In general, females showed a significantly greater preference for predictability compared to males, as did high anxious participants compared to their low anxious counterparts. Specifically, high anxious females showed the greatest preference for predictability, high anxious males and low anxious females showed moderate preference for predictability, and low anxious males were indifferent. Although the results suggest the necessity of considering individual difference variables such as gender and anxiety sensitivity, support is provided for the use of prediction testing and other strategies to enhance an individual’s prediction of panic attacks in the treatment of panic disorder.
Acknowledgements/Dedication

Great appreciation goes to Georg H. Eifert for invaluable assistance in the current project, as well as serving as my advisor over the last four years. Although there are several valuable skills that Georg has tried to teach me, I have taken the greatest pain to emulate his ability to prioritize and not sweat the small stuff.

Thanks also goes to Daniel W. McNeil, not only for serving on my committee, but more importantly for modeling upstanding behavior in both professional and personal interactions. Further, he has always been a good sport about my offbeat sense of humor, showing that one can be successful without being uptight. Thanks also to Jerry Richards, also a committee member, who approached this project, as he does most projects, with an interest and critical approach that was inspiring. It has been such a pleasure to work with someone who loves his work as much as Jerry does.

Appreciation goes to the other members of my committee, Kent Parker and Katherine Shear. Special thanks to Michael Zvolensky who has been a springboard for ideas and a valuable intellectual resource, as well as Michelle Heffner who did much of the dirty work including scheduling subjects. Further, I am indebted to John Sorrell for being a great friend and source of strength in tough times, and Derek Hopko who has provided a constant stream of free sodas and junk food, in addition to friendship, that have served to keep me energized throughout the creation of this document.

Finally, I thank my family, and especially my mother, for constant support throughout this long education process. It would be an understatement to say that I could not have done it without her.
The research reported in this dissertation was funded by grants from the West Virginia University Department of Psychology Alumni Fund and the Eberly College of Arts and Sciences.
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Introduction

Predictability of threatening events is considered to be a key variable in the development and maintenance of anxiety (see Foa, Zinbarg, & Rothbaum, 1992; Mineka & Zinbarg, 1996, for reviews). Specifically, unpredictable threatening events are thought to produce greater anxiety-related distress compared to predictable events (cf. Mineka & Kilstrohm, 1978). Although predictability is relevant to anxious responding across many anxiety disorders (Armfield & Mattiske, 1996), perhaps it is most crucial for recurrent uncued and unexpected panic attacks as they occur in Panic Disorder (PD; Barlow, Chorpita, & Turovsky, 1996).

Predictability may be relevant to PD in a number of clinically important ways. First, in regard to symptom presentation, degrees of predictability are used to distinguish between different types of fearful/panic responding (Klein & Klein, 1989). For example, panic attacks are categorized, in part, based upon whether identifiable internal or external events are antecedent and occur in close temporal proximity to an attack (Barlow, 1988). Second, experience with unpredictable events may serve to elevate anxiety-related responding and therefore function as a process variable in the onset and progression of panic pathology (Craske, Glover, & DeCola, 1995). Third, a widely used empirically-validated cognitive-behavioral treatment manual for PD (Mastery of your Anxiety and Panic-II; MAP-II; Barlow & Craske, 1994), contains a module focusing on the predictability of panic attacks. For example, the MAP-II incorporates several exercises that are aimed at helping the patient to identify causes (cues) of unexpected panic attacks. These exercises are intended make the unexpected become more predictable, based on the assumption that this will result in a decrease in anxiety (Rachman, 1990; Rachman & Lopatka, 1986).
Empirical Evidence

Despite the hypothesized association between predictability and PD in humans, the preponderance of empirical evidence that articulates the psychological functions of predictability is based upon research with infrahumans (cf. Minor, Dess, & Overmier, 1991). In a representative study, Seligman (1968) found that operant behavior was disrupted during auditory tone presentations when shock had reliably followed that tone (Predictable Group). When the tone was absent, operant behavior returned to its normal level. In contrast, operant behavior was disrupted at all times for rats exposed to uncorrelated shock and tone presentations (Unpredictable Group). In addition, six of the eight rats in the Unpredictable Group developed stomach ulcers, compared with none of the rats in the Predictable Group (see Estes & Skinner, 1941; Seligman & Meyer 1970; Weiss, 1968; 1970, for similar studies).

To explain the benefits of predictability regarding an aversive stimulus, Seligman formulated the safety-signal hypothesis. This hypothesis suggests that when a stimulus is a reliable predictor of the occurrence of an aversive stimulus, the presence of that stimulus signals danger. Conversely, the absence of the warning stimulus signals safety. Alternatively, the Preparatory Response Hypothesis (Perkins, 1955; Perkins, Levis, & Seyman, 1963), suggests that predictability provides the organism with an opportunity to employ strategies to minimize the resulting pain. Thus, preparatory responses may (a) limit contact with the aversive stimulus via strategies such as postural adjustments or (b) reduce the effects of the stimulus through less direct coping strategies such as distraction. Although the two theories suggest different mechanisms by which predictability affects anxious responding, no conclusive evidence has supported one theory.
over the other, and both may be applicable to varying degrees. It may be that both processes mediate the effects of predictability (Fanselow, 1980).

Although predictability has been studied with human participants in laboratory studies in a similar manner as infrahuman research, there is little consensus regarding its effects (Miller & Grant, 1979). For example, several studies have found humans will choose predictable aversive stimuli over similar aversive stimuli that are unpredictable (Badia, McBane, Suter, & Lewis, 1966; Jones, Bentler, & Petry, 1966; Maltzman & Wolff, 1970), whereas others have found no difference (Furedy & Doob, 1971a; 1971b; 1972). Further, these relatively unreliable findings are apparent across a variety of anxiety-related response domains. For example, research has found self-reported pain and distress are (a) greater to predictable stimuli (Lovibond 1968; Maltzman & Wolff, 1970); (b) greater to unpredictable stimuli (Averill & Rosenn, 1972; Furedy & Chan, 1971; Furedy & Klakey, 1972) and (c) equal for predictable and unpredictable stimuli (Bowers, 1971).

Inconsistent results also have been found in the natural environment. Two studies showed that individuals with predictable panic attacks reported greater distress and more panic symptoms during an attack than did individuals with unpredictable attacks (Margraf, Taylor, Ehlers, Roth, & Agras, 1987; Street, Craske, & Barlow, 1989). Craske et al. (1995) also found that unpredictable panic attacks resulted in greater concern about future panic attacks, but they also found that predictable attacks were related to an increase in avoidance behavior.

Perhaps one reason for the difficulty in determining the effects of predictability in the laboratory is that predictability has infrequently been studied in a manner that is relevant to PD, particularly in laboratory settings. That is, nearly all of the experimental investigations with humans have utilized aversive tactile stimulation as the aversive preparation, a procedure that
produces acute, peripheral pain that differs from the types of bodily sensations characteristic of panic attacks. One way to address this concern is to employ biological challenge procedures that can produce responses that mimic escalating autonomic activity, a defining feature of panic attacks and PD. Carbon dioxide-enriched air (CO₂) is one panic provocation strategy that can produce repeated episodes of abrupt autonomic arousal and the repeated presentation of high concentrations of CO₂ (range: 13.5% - 35% CO₂) is a well-established provocation procedure for PD and related nonclinical populations (see Lejuez, Forsyth, & Eifert, 1998). On a more basic level, CO₂ has been established as an aversive stimulus that individuals will actively work to avoid (Lejuez, O’Donnell, Wirth, Zvolensky, & Eifert, 1998), and it has been shown to produce elevated reports of anxiety (e.g., Beck, Shipperd, & Zebb, 1996; Zvolensky, Eifert, Lejuez, & McNeil, in press; Zvolensky, Lejuez, & Eifert, 1998).

Additionally, the insensitivity of the dependent measures used within laboratory studies of predictability may have led to unclear results. For example, Lejuez (1997) used a behavioral disruption procedure similar to Seligman (1968), and found little difference in the disruption of a simple operant task (i.e., a plunger pull) in the presence of predictable and unpredictable administrations of 20% CO₂. Although other explanations may be used to interpret this lack of findings, the standard conditioned suppression paradigm used with rats may be too simplistic to produce differential results with humans.

Much of the animal work examining predictability has used the conditioned suppression paradigm, but a somewhat smaller body of work has found similar results using a forced-choice paradigm (e.g., Badia, Harsh & Abbott, 1979; Badia, Harsh, Coker, & Abbott, 1976). In this paradigm, an organism is given the choice between experiencing predictable or unpredictable
aversive stimulation, with the primary dependent measure being the distribution of these choices. Such a procedure may be more sensitive than a conditioned suppression procedure because, by design, it forces a choice between the two alternatives.

Using a forced-choice CO₂ paradigm, Lejuez, Zvolensky, Eifert, Sorrell, and Shear (1999) examined choice between predictable and unpredictable administrations of 20% CO₂ in three individuals with PD. Using a single-subject design, each individual was exposed to an average of fourteen days of repeated trials in which a button press determined whether or not CO₂ would be signaled by a tone. The results showed that preference for predictability differed across participants. Specifically, one participant showed a reliable preference for onset predictable administrations, whereas two participants did not.

The results from Lejuez et al. (1999) suggest that not all persons may prefer predictable over unpredictable stimuli. For example, even if predictability has uniform benefits for coping with anxiety-related events, it is not known if individuals will engage in positive coping strategies to maximize the benefits of this variable, as an individual's biological disposition and/or learning history with aversive events may be more suited to adopting a strategy of helplessness in such situations (cf. Seligman, 1968). Thus, in certain situations, individuals may not want to know when an aversive event will begin, especially when direct methods for controlling the event either are not available (e.g., skill deficit) or difficult to utilize. If so, such results would support the incorporation of prediction-based exercises in the psychological treatment of pathological anxiety, but only on an individualized basis (Eifert, Schulte, Zvolensky, Lejuez, & Lau, 1998).
Situational and Individuals Difference Factors

Given that the effects of predictability may vary across individuals, it is important to identify factors that may underlie this difference. One such factor is anxiety sensitivity, defined as the fear of the consequences of anxiety symptoms (McNally, 1994). Persons with PD report particularly high ASI scores relative to normals and persons with other anxiety disorders, and high ASI scores predict the future occurrence of panic attacks in persons without a prior history of panic (Schmidt, Lerew, & Jackson, 1997). Related to predictability, Janis (1958) found that prior to experiencing an aversive and anxiety provoking medical procedure, the provision of information to the patient regarding the procedure was positively correlated with recovery. Janis also suggested that for individuals with low levels of preoperative fear, the benefit of information was reduced. Based on this finding, it could be hypothesized that individuals with high levels of anxiety sensitivity would prefer future aversive bodily events such as a panic attack to be predictable (i.e., information regarding the onset of the attack) as opposed to unpredictable, whereas a similar preference may not occur for individuals with low anxiety sensitivity.

Gender is a second factor that may mediate the effects of predictability. Females are more likely than males to assess risk and actively seek out information regarding unpleasant events (Blanchard, Griebel, & Blanchard, 1995). This hypothesis was supported in a laboratory study by Grusec and Grusec (1971). Participants were told that they would be exposed to either a pleasant (receipt of money) or unpleasant (receipt of electric shock) event and given an envelope that revealed which would occur. The experimenter then left the room and told the participants that he/she would return in 20 min. The dependent measure was the latency from when the experimenter left the room until the participant opened and read the contents of the envelope,
which was significantly shorter for females than males. Increased information seeking in females also has been observed in the natural environment. For example, the higher number of female patients diagnosed with a psychological disorder has been linked to greater information seeking (e.g., more frequent clinic visits) regarding symptoms (Cleary, Burns, & Nycz, 1990; Corney, 1990). Females also have been found to engage in more extensive information seeking behavior regarding physical symptoms (Knight & Elfenbein, 1996) including those indicative of a serious disease such as HIV infection (Wolitski, Bensley, Corby, Fishbein, & Galavotti, 1997).

Although the exact mechanisms underlying a gender difference in information seeking are unclear, Blanchard et al., (1995) have provided evidence that both behavioral and physiological mechanisms regarding stress and threat play an important role. Additionally, a gender difference may at least be partially influenced by differential levels of anxiety sensitivity and general anxiety-related concerns. Specifically, females report a greater number, and more severe, fears than males (Kirkpatrick & Berg, 1982). Further, compared to males, females generally score higher on the ASI (Peterson & Reiss, 1992) and provide higher self-ratings of the intensity of fears related to physical threat (Stewart, Taylor, & Baker, 1997). As such, anxiety sensitivity may play a role in gender-related preference for predictability, however, the degree of influence is unclear and in need of further investigation.

Present Study

Given the hypothesized clinical significance of predictability and the absence of supportive data with humans, the primary purpose of the present study was to determine whether individuals would prefer predictable over unpredictable administrations of CO₂. In the context of a discrete-choice procedure, participants were given the choice between experiencing presentations of CO₂
preceded by a warning signal and otherwise similar presentations that were not preceded by a warning signal. As additional dependent measures comparing predictable and unpredictable CO\textsubscript{2}, physiological responses as well as estimates of self-reported preference, unpleasantness, and anxiety were examined.

The second purpose of the present study was to determine whether preferences are related to anxiety sensitivity and/or gender. Because (a) CO\textsubscript{2} has been shown to produce greater reactivity in individuals scoring high on the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986) than low scorers (Eke & McNally, 1996) and (b) information about aversive events is most useful when anxiety levels are elevated, we expected that participants with high anxiety sensitivity would have greater preference for predictable over unpredictable CO\textsubscript{2} presentations than low ASI participants. Additionally, we expected unpredictable CO\textsubscript{2} to produce high levels of self-reported unpleasantness and anxiety as well as greater physiological arousal than predictable CO\textsubscript{2} in the high anxious participants, than the low anxious participants. Furthermore, the magnitude of these effects, irrespective of predictability, was expected to be greater for the high anxious participants, compared to their low anxious counterparts.

Based on the greater need for information seeking in females compared to males, and the differences in anxiety sensitivity and overall anxiety-related concerns, females were expected to differ from males in the same way that high ASI individuals differed from low ASI individuals. Further, the interaction of Anxiety sensitivity and gender will be examined, with an effort to partial out independent influence of the two variables.
Method

Participants

Participants were 40 undergraduate students (M = 19.1 years; SD = 1.4) at West Virginia University in introductory psychology classes. In total, 623 students completed the ASI screening. In this sample, males recorded a mean ASI score of 17.8 (SD = 7.2) and females recorded a mean ASI score of 20.8 (SD = 8.4). Ten males scoring one standard deviation above the male sample mean (≥ 25) and ten females scoring one standard deviation above the female sample mean (≥ 29) comprised the high ASI group, whereas ten males scoring one standard deviation below the male sample mean (≤ 11) and ten females scoring one standard deviation below the female sample mean (≤ 12) comprised the low ASI group. This gender stratification procedure was used to control for the confounding of gender and anxiety sensitivity level, as females score higher on the ASI compared to males (Peterson & Reiss, 1992). The mean ASI scores across the four groups were 8.7 (SD = 2.4) for low ASI males, 9.5 (SD = 1.9) for low ASI females, 30.8 (SD = 4.6) for high ASI males, and 38.8 (SD = 7.9) for high ASI females. Concerning ASI score across gender, high ASI males and females differed significantly (F(1, 19) = 7.73, p = .012). The distribution of these scores in relation to their striated mean, however, was equivalent across the two groups. Specifically, for both males and females, 5 were one SD above, 3 were 2 SD above, 2 were 3 SD above their respective means. Low ASI males and females did not differ. Further, collapsing across low and high ASI categories, ASI scores for males and females did not differ.

Potential participants were first screened for past/present anxiety-related psychological concerns using the anxiety disorders section of the Structured Clinical Interview for DSM-IV (SCID-IV; First, Spitzer, Gibbon, & Williams, 1996). All interviews were completed by a SCID-
IV certified rater. Participants meeting criteria for a past or present anxiety disorder were excluded. Second, participants completed a brief medical screening interview previously employed in our laboratory (e.g., Forsyth & Eifert, 1998), and excluded from the study if they reported past or present angina, asthma, cardiovascular problems, epilepsy, hypertension, or a history of such problems in their first-order families. In total, three participants were excluded for a personal history of asthma. Participants were asked to refrain from strenuous physical exercise and the consumption of caffeine 12 hours prior to experiment, as such activities may elevate somatic activity and thereby impede accurate physiological assessment. All participants received course work extra credit for their participation in the experiment.

**Materials and Apparatus**

Sessions were conducted in a 2-m X 6-m experimental room in the Department of Psychology at West Virginia University. Participants sat at a desk supporting a Laser 48633SX computer, a Laser SVGA color monitor, a mouse, and a keyboard. The experimenters sat in an adjacent room containing an apparatus for providing participants with either room air or a mixture of 20% carbon dioxide-enriched air (20% CO$_2$, 21% O$_2$, 59% N$_2$). CO$_2$ was stored in a 101-cm cylinder and fed through a 5-cm X 5-cm hole via aerosol tubing from the experimenter room to a positive-pressure downs C-pap mask worn by the participant. An automated apparatus, described in Lejuez, Forsyth, and Eifert (1998), was used for CO$_2$ delivery. A one-way mirror allowed the experimenters to observe all session events.

**Physiological assessment.** A Coulbourn Modular Polygraph was used to digitally record physiological data on-line at a sample rate of 10 samples/sec across all channels using Coulbourn’s Lablinc polygraph software (High Speed Videograph). All physiological channels
were calibrated on-line prior to sampling. Physiological responses were sampled using disposable 8 mm diameter Ag/AgCl electrodes which were coated with a .05 molar concentration of NaCL and attached to the skin surface with concentric adhesive collars. Skin conductance levels (SCLs) were directly recorded in microsiemens (mS) in an AC coupling mode with a Coulbourn S71−23 isolated skin conductance coupler that provided a constant 0.5 volts across the electrodes. Electrode placement followed a standard bipolar palmar configuration on the participant's non-dominant hand. To assess for differential breathing processes during the experiment, we assessed expired levels of CO$_2$ (PCO$_2$) using an Ohmeda 5200 (BOC Health Care) PCO$_2$ monitor that received input from a connection to the expiration hole of the mask worn by the participant. PCO$_2$ levels were examined in the 30-s period immediately following termination of CO$_2$ delivery, as research in our laboratory has shown this period captures the peak effects of CO$_2$ on physiological, motor, and cognitive behavior.

**Self-report measures.** Three self-report measures were used in the current study. First a visual analog scale was used to measures preference between the predictable and unpredictable trials. For this comparison, the letters “T” and “N” were placed on opposite ends of a 100-mm horizontal line; participants were asked to draw a vertical line at some point across the horizontal line indicating predictability preference. To determine preference, the distance of the vertical line drawn from the center of the 100-mm horizontal line was measured, with a maximum score of +50 mm for predictable CO$_2$ and –50 mm for unpredictable CO$_2$. Additionally, self-report of anxiety and unpleasantness were collected via questions provided on the computer monitor. First, participants rated the unpleasantness of the previous CO$_2$ presentation (“how unpleasant was breathing the carbon dioxide just now?”) on a likert scale ranging from 0 (not unpleasant) to 10
(extremely unpleasant). Second, participants rated their current anxiety level (“what is your current anxiety level”) on a likert scale from 0 (no anxiety) to 10 (extreme anxiety). Participants responded to the questions by typing in a number on the attached keyboard.

Screening. The ASI was used as a screening measure for participation. The ASI is a 16-item self-report questionnaire that assesses fear of anxiety-related symptoms based on the belief that such sensations have negative consequences (e.g., physical illness). Respondents rate the degree to which they agree or disagree with each item on a 5-point Likert-type scale with anchors of 0 (very little) and 4 (very much). The ASI total score is derived by summing all responses, with total scores ranging from 0 to 64. The ASI has sound psychometric properties (Peterson & Reiss, 1992) and has been shown to predict anxious and panic responding in the laboratory and natural environment (Schmidt, Lerew, & Jackson, 1997).

Procedure

Upon arrival, participants completed the consent form. After completing the consent form, participants were seated in the participant room and the c-pap mask was placed over their mouth and nose. Participants were then asked to remove any jewelry (e.g., a watch). After the experimenter left the room, participants sat quietly for a 5-min adaptation period in which baseline physiological responses were measured. The remainder of the experiment consisted of a 50-min experimental session, separated into 1-min trials, consisting of 2 phases.

Phase 1. The aim of Phase 1 was to provide participants with forced exposure to predictable and unpredictable CO₂ presentations. Forced exposure was used in Phase 1 to increase the likelihood that choices in Phase 2 would more likely be based upon actual exposure to the
experimental contingencies. Prior to the start of Phase 1, the experimenter entered the participant room and provided the following written instructions:

During this experiment, you will breathe regular room air through a mask. Occasionally, the concentration of carbon dioxide through the breathing mask will be increased. For many individuals, CO\textsubscript{2} produces a variety of temporary effects including mild chest pain, racing heart, shortness of breath, faintness, dizziness, sweaty palms, increased breathing and blurred vision. This part of the experiment is separated into several experimental periods. At the start of each period, either the letter “T” or “N” will appear on the computer screen. When you see this letter, type it into the attached keyboard. When the letter T is typed, a tone will come from the computer if carbon dioxide is scheduled to be presented in that period. Furthermore, the sound of the tone will change 5 seconds before the CO\textsubscript{2} occurs. If CO\textsubscript{2} is not scheduled to occur in that period, no tone will be presented. In contrast, if the letter “N” is pressed, a tone will not be provided even if CO\textsubscript{2} is scheduled in the upcoming period. Thus, when CO\textsubscript{2} is presented, it always will be proceeded by a tone when “T” is typed and never proceeded by a tone when “N” is typed. There is no time limit for typing a letter once it appears on the screen, but long delays will increase the duration of your participation. Following each presentation of CO\textsubscript{2}, several questions will be presented on the computer screen. Please answer these questions using the attached keyboard.

Phase 1 lasted 30 min, which included 24 1-min trials and 6 1-min rest periods (each following a CO\textsubscript{2} presentation). Within these 24 trials, 6 included a CO\textsubscript{2} presentation and 18 did not. Trials without CO\textsubscript{2} were used to enhance the overall unpredictability of when CO\textsubscript{2} presentations would occur. The duration of each CO\textsubscript{2} presentation was 20 s.

In Phase 1, each trial began with the appearance of either the letter “T” or “N” on the computer screen. This letter appeared in the center of the screen in 12 point font. The letter “T” signified that the CO\textsubscript{2} would be signaled by a tone from the computer, thus making the presentation predictable. In contrast, the letter “N” signified that the CO\textsubscript{2} would not be signaled
by a tone from the computer, thus making the presentation unpredictable. The trial began once the letter on the screen was typed on the keyboard by the participant. The order of the first and subsequent presentations of “T” or “N” were determined by the computer in a semi-random fashion for each participant, with the constraint that the same letter could never appear three times in a row.

During a trial including a predictable CO$_2$ administration, a 200 Hz tone was sounded at the start of the trial (i.e., first tone). Five s before the presentation commenced, the tone changed to 320 Hz and continued until the termination of the CO$_2$ presentation (i.e., second tone). Thus, the initial tone signaled that CO$_2$ would occur within that trial and the change in tone signaled exactly when the CO$_2$ would occur. During a trial including an unpredictable CO$_2$ administration, no warning tones were provided.

At the conclusion of each CO$_2$ presentation and the following rest period, yet prior to the start of the next trial, self-reported unpleasantness and anxiety were assessed. At the conclusion of Phase 1, participants completed the visual analog scale to assess self-reported preference for the predictable/unpredictable CO$_2$ administrations. Following completion of the self-report measures at the conclusion of Phase 1, participants were given a 5 min. break.

Phase 2. The aim of Phase 2 was to evaluate predictability preference for CO$_2$ presentations. After the 5-min. break, the experimenter initiated Phase 2 by providing the following written instructions:

In the remainder of the experiment, the letters “T” and “N” will appear together on the computer screen and you may pick the one you prefer. Once you see this pair of letters, type the preferred letter on the provided keyboard. Otherwise, the remainder of the experiment is identical to what you have just completed.
The Phase 2 procedure was identical to Phase 1 with two exceptions. First, to limit the participants overall exposure to CO₂, fewer trials were used in Phase 2. Specifically, Phase 2 lasted 20 min, which included 16 1-min trials and 4 1-min rest periods (each following a CO₂ presentation). Within these 16 trials, 4 included a CO₂ presentation and 12 did not. Second, the participant could choose whether a CO₂ presentation would be predictable or unpredictable. To provide this choice, the letters “T” and “N” appeared together on the screen at the start of each trial. Each time the two letters appeared on the computer screen, the participant would type the preferred letter. Once the preferred letter was typed, the trial would begin and proceed as in Phase 1.

Unlike Phase 1, visual analog preference was not collected at the conclusion of Phase 2 to prevent the potentially confounding effect of an unequal number of predictable and unpredictable CO₂ presentations.

Results

Choice Responding

The primary dependent measure was choice between predictable CO₂ (“T”) and unpredictable CO₂ (“N”) in Phase 2. To provide this choice score, the number of choices of the predictable CO₂ alternative were summed such that scores could range from 18 for extreme choice of the predictable alternative to 0 for extreme choice of the unpredictable CO₂ alternative.

Choice ratings were evaluated with a 2 x (ASI: high, low) 2 x (Gender: male, female) ANOVA. There was no interaction of ASI and gender regarding choice alternatives. As shown in the left panel of Figure 1, a main effect was evident for anxiety sensitivity, with high ASI participants ($M = 13.15$, $SE = .84$) choosing predictable CO₂ administrations more often than
their low ASI counterparts ($M = 9.8, SE = 0.97$ [$F(1, 39) = 8.27, p = .007$]). In a related way (right panel of Figure 1), a main effect was evident for gender, with females ($M = 13.35, SE = 0.9$) choosing predictable CO$_2$ more than males ($M = 9.6, SE = 0.88$ [$F(1, 39) = 10.4, p = .003$]).

![Figure 1](image-url)  

**Figure 1.** Number of choices of the predictable alternative across ASI and gender.

Given that the high ASI females ($X = 38.8$) had higher ASI scores than the high ASI males ($X = 30.8$), it could be suggested that the gender effect actually may have been due to higher female ASI scores. To address this issue, a one-way Analysis of Covariance (ANCOVA)
was conducted with gender as a between subjects factor and ASI score as a covariate. After controlling for the effects of differing preexperimental ASI scores, females again were shown to choose predictable CO\(_2\) more frequently than males (\(F(1, 39) = 7.6, p = .009\)). This result suggests that gender affected preference, at least somewhat independent of ASI score.

Although the reported main effects suggest within factor differences in choice scores, these results do not establish if the choice scores for the participants as a whole, or any particular group of participants (e.g., high ASI females) differed from a score of 9 (i.e., indifference). A choice score of 9 was used to signify indifference because it comprised an equal number of choices for the predictable and unpredictable alternative. To provide a general assessment of choice regarding predictable and unpredictable aversive events, we employed a one-sample t-test to compare mean choice scores across all participants to a choice score of 9. This analysis indicated that choice of predictable CO\(_2\) (\(M = 11.48, SE = 0.69\)) was greater than the indifference value of 9 (\(t (39) = 3.59, p = .001\)).

To more closely examine this effect across groups, a one-tailed one-sample t-test was used to determine if the mean choice score for each group was different than the indifference value in the direction of predictability. As shown in Figure 2, choice scores for High ASI females (\(t(9) = 6.95, p <.001\)), High ASI males (\(t(9) = 1.9, p = .046\)), and Low ASI females (\(t(9) = 1.91, p = .044\)) all were greater than 9. In contrast, choice scores for low ASI males did not differ from 9. To further investigate the groups preferring predictability, a one-tailed independent sample t-test found that choice scores for High ASI females were greater than that for both High ASI males (\(t(18) = 2.3, p = .017\)) and Low ASI females (\(t(18) = 1.83, p = .042\)). Choice scores for High ASI males and Low ASI females did not differ.
Figure 2. Number of choices of the predictable alternative across low ASI males, low ASI females, high ASI males, and high ASI females.
Visual Analog Scale

Phase 1 preference responding on the visual analog scale was examined with a 2 x (ASI: high, low) 2 x (Gender: male, female) ANOVA. There was no interaction for anxiety sensitivity and gender. Similar to choice, the left panel of Figure 3 showed that preference for the predictable alternative was higher for high ASI participants ($M = 16.73$, $SE = 5.86$) compared to low ASI participants ($M = -1.26$, $SE = 4.09$; $F(1, 39) = 6.19$, $p = .018$). Although the right panel of Figure 3 showed that the preference for the predictable CO$_2$ alternative was higher for females ($M = 11.3$, $SE = 5.78$) than for males ($M = 4.17$, $SE = 4.98$), this difference was not statistically significant.
Figure 3. VAS score comparing preference between predictable and unpredictable trials across ASI and gender.

As with choice responding, we assessed for general patterns of responding across all participants with a one-sample t-test. Preference for the predictable CO\textsubscript{2} alternative ($M = 7.75$, $SE = 3.75$) was rated as greater than 0 (i.e., the indifference value; $t (39) = 2.03, p < .05$). This result, however, may have been primarily due to high ASI females. As shown in Figure 4, although the preference scores for the high ASI females, high ASI males, and low ASI females were greater than 0, this difference from 0 only was statistically significant for high ASI females.
(t(9) = 2.86, p = .009). Although the mean preference score for low males was in the direction of unpredictability, this score was not significantly different than 0. (t(9) = 2.86, p = .009).

Figure 4. VAS score comparing preference between predictable and unpredictable trials across low ASI males, low ASI females, high ASI males, and high ASI females.

In general, preference of predictable CO\textsubscript{2} was similar to the distribution of choice. Suggesting synchrony across overt-motor and self-report responses, a moderate to high
correlation ($r = .6, p < .01$) was found between preference scores as indexed by the visual analog scale at the conclusion of Phase 1 and the distribution of choices in Phase 2.

**Self-Reported Unpleasantness**

Self-reported unpleasantness was examined with a 2 x (ASI: high, low) 2 x (Gender: male, female) 2 x (Predictability type: predictable CO$_2$, unpredictable CO$_2$) x 10 (trials) ANOVA with repeated measures on trials. No interactions were evident. There was a main effect for anxiety sensitivity, with self-reported unpleasantness being rated higher by high ASI participants ($M = 5.43, SE = 0.46$) than low ASI participants ($M = 3.0, SE = 0.46$ [F(1, 39) = 12.53, p = .001]). In a similar way, unpleasantness was rated higher by females ($M = 5.03, SE = 0.52$) than males ($M = 3.4, SE = 0.58$ [F(1, 39) = 5.63, p = .023]).

**Self-Reported Anxiety**

Self-reported anxiety was examined with a 2 x (ASI: high, low) 2 x (Gender: male, female) 2 x (Predictability type: predictable CO$_2$, unpredictable CO$_2$) x 10 (trials) ANOVA, with repeated measures on trials. There were no interactions. There was a main effect for anxiety sensitivity, with greater self-reported anxiety being reported by high ASI participants ($M = 5.08, SE = 0.43$) relative to low ASI participants ($M = 2.28, SE = 0.54$ [F(1, 39) = 16.83, p < .001]). Self-reported anxiety was rated higher by females ($M = 4.13, SE = 0.57$) than males ($M = 3.23, SE = 0.58$), but this difference was not statistically significant.

**Expired CO$_2$ levels (PCO$_2$)**

To examine differences in CO$_2$ consumed between groups individuals, PCO$_2$ was evaluated during the 30-s period immediately following each CO$_2$ presentation using a 2 x (ASI: high, low) 2 x (Gender: male, female) 2 x (Predictability type: predictable CO$_2$, unpredictable CO$_2$) ANOVA with repeated measures on trials.
CO₂) x 10 (trials) ANOVA, with repeated measures on trials. There were no interactions. A main effect of ASI was found, with PCO₂ levels for low ASI participants (M = 52.6, SE = 2.37) being higher than for their high ASI participants (M = 45.2, SE = 2.13 (F(1, 39) = 5.3, p = .03). No difference in PCO₂ levels across groups was evidenced in the absence of CO₂ presentations.

**Skin Conductance Levels**

Although preexperimental skin conductance levels were assessed, these levels were considerably higher than during the CO₂ free periods in the actual sessions, which may have been a result of preexperimental anticipatory anxiety. Thus, the average of the first five seconds of all trials in which a CO₂ delivery was not scheduled to occur (i.e., CO₂ free trials) was used as a baseline-like comparison period. Regarding skin conductance levels during (a) during CO₂ free trials or (b) CO₂ trials including the actual CO₂ presentations or the 30-s rest period immediately following the CO₂ presentation, there were no interactions or main effects of ASI, gender, and predictability type (predictable or unpredictable CO₂).

Despite the absence of differential effects, we observed several general effects of CO₂. First, skin conductance levels increased from an average level of 0.71 (SE = 0.06) during CO₂ free trials to 1.39 (SE = 0.26) during the first warning tone (t(39) = 2.88, p = .008) and 1.23 (SE = 0.21) during the second warning tone (t(39) = 2.67, p = .013) prior to predictable CO₂ administrations. Skin conductance levels also increased from CO₂ free trials to 1.18 during the 20-s CO₂ durations, collapsed across predictable and unpredictable administrations (t(39) = 3.99, p = .001).
Discussion

When given the choice between predictable and unpredictable administrations of 20% CO₂, participants opted for predictability. Further examination, however, shows that this effect was strongest for females compared to males as well as high anxiety sensitive participants compared to their low anxious counterparts. As indexed by choice responding, high anxious females showed the greatest for predictability, high anxious males and low anxious females showed moderate preference for predictability, and low anxious males were indifferent. Similar results were found using the VAS to index preference between trials in which CO₂ was predictable and unpredictable.

Regarding self-report and physiological responses, predictable CO₂ presentations compared to unpredictable CO₂ presentations were (a) rated as equally unpleasant and anxiety provoking and (b) resulted in similar changes in skin conductance levels. These results do not indicate an effect of predictability, but self-report and physiological measures often have been shown to be somewhat insensitive in studies showing preference for information regarding aversive medical procedures (see Ludwick-Rosenthal & Neufeld, 1988 for a review).

Although differential effects of predictable and unpredictable CO₂ were not reported, CO₂ did have a more pronounced effect on females compared to males (unpleasantness) and on high ASI individuals compared to low ASI individuals (unpleasantness and anxiety).

General Effects

The present results provide preliminary experimental support for the use of prediction testing and other strategies to enhance an individual’s ability to identify cues for panic attacks in the treatment of PD. Nevertheless, the factors underlying the benefits of predictability remain
somewhat unclear. Although both the safety-signal (Seligman, 1968) and the preparatory response hypothesis (Perkins, 1955) imply preference for predictable CO$_2$, several aspects of the results are not consistent with the latter hypothesis. First, PCO$_2$ levels suggest that participants did not breathe less during predictable CO$_2$ presentations than during unpredictable presentations. Although other types of coping strategies (e.g., distraction) may have been employed, the differences between predictable and unpredictable CO$_2$ can not be ascribed to breath holding, an obvious preparatory-response for predictable CO$_2$ presentations.

Second, when participants rated the unpleasant and anxiety-provoking qualities of the CO$_2$, immediately after each presentation, no difference was found between predictable and unpredictable CO$_2$. In contrast, differences were found when participants indicated their preference between the predictable and unpredictable trials at the conclusion of Phase 1. Thus, a focus on the actual aversive stimulus found no difference between predictable and unpredictable CO$_2$ presentations, whereas a focus on the entire context (i.e., considering both trials in which CO$_2$ was present and absent), did reveal preference for predictability. Although fundamental differences between the scale used to rate unpleasantness and anxiety compared to the VAS scale used to compare preference might account for the observed differences, the benefits of predictability may extend beyond simply just preparing for the presentation of the aversive stimulus.

In addition to the above points, the potential difficulty of controlling panic-related symptoms, even when the onset is predicted, suggest that the safety-signal hypothesis may be more relevant than the preparatory-response hypothesis to the benefits of predictability in the natural environment. Specifically, applying the safety-signal hypothesis to PD takes the focus
away from actual panic attacks and instead focuses on the absence of panic related stimuli and the safety that can be ascribed to the absence of those stimuli. Thus, the safety-signal hypothesis may be most relevant when an individual is not experiencing a panic attack. Consequently, individuals with PD might be taught to identify stimuli associated with panic attacks to more clearly identify periods of safety and thereby reduce worry regarding future attacks.

**Anxiety Sensitivity and Gender Effects**

Although the present results provide general support for preference of predictability, the ASI and gender effects provide more detailed insight into the potential processes underlying this preference. As a possible explanation of the ASI effect, individuals in the high ASI group reported the CO₂ (collapsed across predictable and unpredictable administrations) to be more unpleasant and anxiety provoking than individuals in the low ASI group (cf. Eke & McNally, 1996). Consequently, the increased effects of CO₂ for the high ASI individuals may have been related to the preference for predictable CO₂, whereas the limited effects of the CO₂ for the low ASI individuals may have been related to the greater level of indifference regarding predictability. Thus, a higher concentration and/or longer duration of CO₂ might produce greater preference for predictability for low ASI individuals in general and specifically for low ASI males whose ratings of unpleasantness and anxiety were considerably lower than that for the other groups.

Higher ASI scores in the natural environment and a greater number of reported anxiety-related concerns fears for females compared to males may serve as a potential explanation of the gender effect (Kirkpatrick & Berg, 1982; Stewart, Taylor, & Baker, 1997). Because females in this study had higher ASI scores than males, one could suspect that the gender effect was due to differences in anxiety sensitivity. A covariate analysis, however, found that a strong gender effect
also was evidenced after controlling for ASI score, suggesting that gender effects are at least at some level orthogonal from ASI effects.

As an alternative hypothesis, it has been suggested that females engage in information seeking regarding future unpleasant events more than males (Blanchard et al. 1995). Supporting this hypothesis, females frequently chose predictability despite the fact that the predictable CO\textsubscript{2} remained both aversive and anxiety provoking. Thus, these results suggest that information regarding both danger and safety may have benefits to the individual, independent of the reported aversiveness of the unpleasant stimulus.

Potential limitations

One concern regarding the present results is that predictability might have been beneficial because participants were taking a deep breath during the warning signal and then holding their breath during the following CO\textsubscript{2} presentation; a strategy that cannot be employed in response to unpredictable administrations. To address this issue, the present study monitored PCO\textsubscript{2} levels during CO\textsubscript{2} presentations. As PCO\textsubscript{2} levels showed similar CO\textsubscript{2} levels during predictable and unpredictable administrations, the benefits of predictability can not be tied to a decrease in CO\textsubscript{2} inspired during predictable administrations. There is evidence, however, that PCO\textsubscript{2} levels were lower for high ASI individuals compared to low ASI across both predictable and unpredictable administrations. This result suggests that despite breathing in less gas (i.e., passive avoidance), high ASI individuals engaged in more extreme choice of and preference for predictable CO\textsubscript{2}, and reported greater anxiety and unpleasantness of CO\textsubscript{2} in general. Interestingly, such preparatory responses had little positive effect, suggesting that aversiveness is not necessarily correlated with absolute PCO\textsubscript{2} levels.
Despite the validity check provided by the PCO₂ monitor, potential limitations remain when using a preset duration, and not PCO₂ levels, to determine the duration of each CO₂ presentation. Although PCO₂ levels across predictable and unpredictable administrations did not differ in the current study, the potential for such differences in future studies is of concern.

Further, little is known regarding the factors determining the effects of CO₂ across different individuals. That is, are factors such as gender, weight, or physical fitness important in determining the effects of CO₂, and should they be used to determine an individualized duration presentation as opposed to a uniform duration across all participants? For example, the fact that females reported the CO₂ as more unpleasant than the males may reflect real differences in the actual effects of CO₂ across gender, or instead a greater propensity in females to report psychological and physical symptoms than males (Cleary, Burns, & Nycz, 1990; Corney, 1990; Knight & Elfenbein, 1996; Wolitski, Bensley, Corby, Fishbein, & Galavotti, 1997). Although such questions are valid and deserve empirical investigation, the skin conductance effects in the present study suggest that the CO₂ methodology at least was effective in producing an anxious state in most participants.

Conclusions

A large body of animal research has suggested the benefits of predictability of aversive events (Badia, Harsh, & Abbott; Seligman, 1968; Weiss, 1968, 1970). Despite the absence of clear results with humans, the concept of predictability has been integrated into the etiology and treatment of clinical anxiety, including PD. Regarding this integration, our results support the continued attention focused on the role of predictability for anxiety-related responding in PD and
related nonclinical populations, while highlighting the importance of attending to individual
difference variables such as anxiety sensitivity and gender.

The present results show preference for predictability, but questions as to why this
preference exists are more difficult to answer. Our results appear to favor the safety-signal
hypothesis, but it remains possible that both safety signals and the opportunity to prepare for an
aversive event may mediate preference for predictability (Fanselow, 1980). As the purpose of the
present experiment was not to provide a direct test of either, the exact mechanisms underlying
preference for predictability of panic attacks needs to be examined in future research.
References


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April 15, 1999

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PUBLICATIONS

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**BOOK CHAPTERS AND OTHER PUBLICATIONS**


**CONFERENCE PRESENTATIONS**

**1999**


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Lejuez, C. W., Eifert, G. H. (1997, May). Conditioned suppression as a function of signaled and unsignaled inhalations of 20% carbon dioxide-enriched air. In J. C. Crosbie (Chair), Human operant studies of punishment and conditioned suppression. Symposium conducted at the 23rd annual meeting of the Association for Behavior Analysis, Chicago, Ill.


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