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Cardiovascular activity in blood-injection-injury phobia during exposure: Evidence for diphasic response patterns?

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ABSTRACT

Exposure to feared stimuli in blood-injection-injury (BII)-phobia is thought to elicit a diphasic response pattern, with an initial fight-flight-like cardiovascular activation followed by a marked deactivation and possible fainting (vasovagal syncope). However, studies have remained equivocal on the importance of such patterns. We therefore sought to determine the prevalence and clinical relevance of diphasic responses using criteria that require a true diphasic response to exceed cardiovascular activation of an emotional episode of a negative valence and to exceed deactivation of an emotionally neutral episode. Sixty BII-phobia participants and 20 healthy controls were exposed to surgery, anger and neutral films while measuring heart rate, blood pressure, respiratory pattern, and end-tidal partial pressure of carbon dioxide (as indicator of hyperventilation). Diphasic response patterns were observed in up to 20% of BII-phobia participants and 26.6% of healthy controls for individual cardiovascular parameters. BII-phobia participants with diphasic patterns across multiple parameters showed more fear of injections and blood draws, reported the strongest physical symptoms during the surgery film, and showed the strongest tendency to hyperventilate. Thus, although only a minority of individuals with BII phobia shows diphasic responses, their occurrence indicates significant distress. Respiratory training may add to the treatment of BII phobia patients that show diphasic response patterns.

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Blood-injection-injury (BII) phobia is among the most prevalent specific phobias, with an estimated lifetime prevalence of 2–5% (Bienvenu & Eaton, 1998). Among the anxiety disorders, it is unique in that it is often accompanied by vasovagal fainting (Engel, 1978). The particular physiological phenomena underlying such dysregulation and its possible functional significance have been subject to much speculation in the past (Alboni, Alboni, & Bertorelle, 2008; Graham, Kabler, & Lunsford, 1961; Marks, 1988). One prevalent view characterizes the autonomic regulation as a diphasic response pattern (Graham et al., 1961). That is upon exposure, individuals first experience a fight-flight response with heart rate (HR) and blood pressure (BP) increases that are typical for phobic reactions. However, this is followed by a conservation-withdrawal phase that is accompanied by a steep decline in heart rate and blood pressure. Such response patterns have been shown in some studies (e.g., Öst, Sterner & Lindahl, 1984; Steptoe & Wardle, 1988; Vögele, Coles, Wardle, & Steptoe, 2003), although it has recently been argued that the actual empirical basis is not convincing enough to claim that such a regulatory pattern is representative for the population of individuals with BII-phobia (Ritz, Meuret, & Ayala, 2010). A number of laboratory studies have not observed such patterns in BII-phobia samples on average (Lumley & Melamed, 1992; Sarlo, Buodo, Munafò, Stegagno, & Palomba, 2008; Sarlo, Palomba, Angrilli, & Stegagno, 2002), whereas others have observed instances of diphasic responses in varying numbers of patients (Gerlach et al., 2006; Öst et al., 1984; Ritz, Wilhelm, Gerlach, Kullowatz, & Roth, 2005), or in some but not all autonomic parameters (Vögele et al., 2003). Other factors beyond dysfunctional diphasic autonomic response patterns have been proposed as relevant to BII-phobia, such as parasympathetic excitation associated with disgust (Page, 1994), specific cognitive and affective experiences (Cisler, Olatunji, & Lohr, 2009; de Jong & Merckelbach, 1998; Page, 1994; Sledge, 1978; Tolin, Lohr, Sawchuk, & Lee, 1997), or central nervous system pathways, but none have succeeded so far in providing an integrated model of the vasovagal dysregulation in BII-phobia. Evidence for diphasic response patterns in other populations prone to vasovagal fainting, such as blood donors, has also been questioned recently (Holly, Gilchrist, & Ditto, 2012).

One problem with determining a diphasic response pattern unique to BII-phobic fear is the lack of firm criteria for such a pattern (Ritz et al., 2010). Studies have not systematically included control conditions to identify diphasic response trajectories, such







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as neutral or other emotional stimulation. Extended exposure to a stimulus could be accompanied by a benign initial activation (associated with a brief increase in arousal experience at the beginning of the presentation) and subsequent deactivation (subsequent habituation) that would simulate a diphasic response pattern. Some of the response patterns reported in the literature could reflect such benign regulatory adjustments (Page, 2003; Vögele et al., 2003). If a diphasic pattern should be indicative of clinically relevant dysregulation in individuals with BII-phobia, it would be expected that within a given individual the initial phase was associated with exaggerated autonomic activation that went beyond that achieved by other non-phobic negative stimuli, whereas the second phase would be accompanied by a deactivation below normal levels achieved by extended exposure to a benign neutral stimulus (for a detailed discussion of these methodological issues, see, Ritz et al., 2010).

Furthermore, in examining evidence for physiological dysregulation in BII-phobia, we recently found that affected individuals tended to take deeper breaths in response to exposure, sometimes resulting in critical drops in CO₂ levels (Ritz et al., 2005; Ritz, Wilhelm, Meuret, Gerlach, & Roth 2009). Hyperventilation is known to cause strong reductions in cerebral blood flow and has often been observed in studies of vasavagal syncope induced by tilttable testing (e.g., Lagi, Cencetti, Corsoni, Georgiadis, & Bacalli, 2001; Norcliffe-Kaufmann, Kaufmann, & Hainsworth, 2008; Novak et al., 1998). However, it is not known whether hyperventilation typically accompanies diphasic responses or whether this phenomenon is independent of this type of cardiovascular perturbation. Different types of physiological dysregulation may require different intervention techniques and empirical guidance would be needed to decide whether muscle tension techniques, breathing retraining, or both types of interventions were recommendable.

In the present study, we sought to examine potential differences between individuals with BII-phobia in response trajectories across different types of emotion provocation, including exposure to a fear-evoking BII stimulus. To this end we utilized data from a film viewing study (Ayala, Meuret, & Ritz, 2010), in which individuals with BII-phobia and healthy controls had viewed neutral, anger, and surgery films among other film material, while physiological parameters were measured continuously. We applied an in-depth analysis of cardiovascular response patterns across a BII-relevant film and two reference films of a neutral and negative (anger) quality. We expected that using these reference stimuli as more stringent criteria would only yield a limited number of BII phobics with autonomic dysregulation consistent with a diphasic response pattern. However, we expected diphasic regulatory pattern, if they were demonstrated, to be clinically relevant, with these individuals characterized by a greater experience of distress, an exaggerated respiratory reactivity, and more severe illness.

If successful in identifying a distinct subgroup of BII-phobia individuals, our selection criteria would be helpful for future basic research and for more individualized tailoring of behavioral intervention for affected patients. The standard behavioral intervention technique recommended for BII-phobia and other conditions accompanied by vasovagal fainting has been applied tension (Ditto, France, Lavoie, Roussos, & Adler, 2003; Holly, Torbit, & Ditto, 2012; Kozak & Montgomery, 1981; Öst, Sterner, & Fellenius, 1989), with the rationale that it would counteract the excessive drops in HR and BP in the second phase of the diphasic response trajectory. The justification for this treatment rests on the demonstration of the representativeness of the diphasic response pattern, or alternatively a monophasic response pattern with substantial drops in HR and BP (Ayala, Meuret, & Ritz, 2009; Ritz et al., 2010). Thus, an additional aim of the present analysis was to explore the prevalence of monophasic response patterns across cardiovascular parameters, such as pure HR and BP activations or deactivations beyond reference levels. Whereas an earlier analysis of these data had focused on a detailed exploration of respiratory patterns in BII phobia participants and healthy controls across a range of emotional films (Ayala et al., 2010), the present analysis sought to determine the prevalence of diphasic and monophasic cardiovascular response patterns and their potential association with illness-related variables, emotion and symptom experience, and physiology.

Method

Participants

Eighty participants between the ages of 18 and 50 were enrolled for a laboratory session of film viewing. Participants were recruited through flyers on university campus and community advertisements. BII-phobia recruitment targeted individuals that were "intensely fearful of seeing blood, injuries, or needles", whereas recruitment of healthy controls targeted "healthy men and women to participate in a laboratory study investigating physiological responses to daily life experiences". Of the total of 80 participants recruited, 60 were diagnosed with BII phobia and 20 were genderand age-matched healthy controls. Mean age was 27.7 years (SD = 9.0), 82.5% were female. Sixty-five percent of participants identified themselves as White, 13.3% as Asian or Pacific Islander, and 15% as African American. Seven percent endorsed Hispanic ethnicity. All BII phobia participants met DSM-IV criteria for specific phobia – BII type, Forty-seven percent of the BII phobia participants also met criteria for a comorbid disorder, including other specific phobia subtypes, panic disorder, obsessive-compulsive disorder, generalized anxiety disorder, mild major depressive disorder, binge eating disorder, and body dysmorphic disorder. Structured clinical interviews for DSM-IV criteria (SCID-I, First, Spitzer, Gibbon, & Williams, 1994) confirmed diagnoses, or absence of thereof, with high inter-rater reliability for BII phobia ($\kappa = 1.00$) and comorbid diagnoses ($\kappa = 0.80-1.00$). The interviews were conducted by trained doctoral students in clinical psychology. Forty-five percent of patients reported a history of fainting that including loss of consciousness in situations related to blood, injury, or needles. Five participants were on a stable dose of antidepressant medication. Exclusion criteria were a history of stroke, cardiac disease, family history of cardiac disease before the age of 55, seizures, and lung disease, as well as current diabetes, hypertension, hypercholesterolemia, and pregnancy. Current smokers were also excluded because of the known influences of tobacco smoking on the autonomic system. Psychological exclusion criteria were a history of Bipolar I, current alcohol/substance abuse or dependence, or psychosis. For healthy controls, exclusion criteria were current or past history of specific phobia – BII type and any current symptoms of psychiatric disorder. To help insure adequate differentiation between the BII-phobia and control samples, individuals with mild to moderate BII-related anxiety but not fulfilling all DSM-IV criteria for specific phobia – BII type were excluded, whereas participants with no more than very mild anxiety that is typical when getting an injection were included. An additional 122 participants (98 for BII phobia, 24 for healthy control) were phone screened and subsequently excluded from participation for the following reasons: history of cardiac disease [2], family history of cardiac disease before the age of 55 [3], seizures [3], asthma [1], diabetes [2], hypertension [4], hypercholesterolemia [3], pregnant [1], smoker [15], Bipolar I [1], current substance abuse [4], not meeting criteria for BII or healthy controls during phone screen [29], not meeting criteria for BII or healthy controls during the SCID interview [3], eligible, but never scheduled session [29], and, eligible, but failed to come to session [22].

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