Clinical characteristics of latent classes of CO2 hypersensitivity in adolescents and young adults

Lance M. Rappaport*, Christina Sheerin, Jeanne E. Savage, John M. Hettema, Roxann Roberson-Nay

Virginia Institute for Psychiatric and Behavioral Genetics, Department of Psychiatry, Virginia Commonwealth University, 800 E Leigh Street, Suite 101, Richmond, VA, USA

ARTICLE INFO

Article history:
Received 1 October 2016
Received in revised form 22 February 2017
Accepted 28 March 2017
Available online 30 March 2017

Keywords:
Adolescence
Young adulthood
Carbon dioxide
Anxiety
Panic

ABSTRACT

Although breathing CO2–enriched air reliably increases anxiety, there is debate concerning the nature and specificity of CO2 hypersensitivity to panic risk and panic disorder versus anxiety disorders and related traits broadly, particularly among adolescents and emerging adults. The present study sought to clarify the association of CO2 hypersensitivity with internalizing conditions and symptoms among adolescents and young adults. Participants (N = 628) self-reported anxiety levels every 2 min while breathing air enriched to 7.5% CO2 for 8 min. Growth mixture models were used to examine the structure of anxiety trajectories during the task and the association of each trajectory with dimensional and diagnostic assessments of internalizing disorders. Three distinct trajectories emerged: overall low (low), overall high (high), and acutely increased anxiety (acute). Compared to the low class, the acute class reported elevated neuroticism, anxiety sensitivity, and stress whereas the high class reported elevated anxiety symptoms, depression symptoms, neuroticism, anxiety sensitivity, and increased likelihood of an anxiety disorder diagnosis. Moreover, the acute and high classes reported experiencing a panic-like event at a higher rate than the low class while participants in the high class terminated the task prematurely at a higher rate. The present study clarifies the nature of response to CO2 challenge. Three distinct response profiles emerged, which clarifies the manifestation of CO2 hypersensitivity in anxiety disorders with strong, though not unique, associations with panic-relevant traits.

© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

Anxiety disorders have long been associated with increased sensitivity to physiological distress and subsequent cognitive, affective reactions. Biological challenges, such as the inhalation of air enriched to elevated concentrations of carbon dioxide (CO2; i.e., the CO2 challenge task), and subsequent elevations in heart rate due to hypercapnia and respiratory acidosis, are reliable, standardized methods to assess subsequent cognitive, affective (e.g., anxiety), and physiological responses (Griez & Schruers, 2003; Zvolensky & Eifert, 2001). The CO2 challenge task has been a particularly relevant biological challenge task due to its resemblance to physiological components of a panic attack (Papp, Klein, & Gorman, 1993). Participant responses to the CO2 challenge task show considerable heterogeneity with stronger reactivity evident in panic disorder (PD) or panic attacks as compared to nonclinical control participants (Coryell, 1997; Goodwin, Hamilton, Milne, & Pine, 2002; Griez, de Loof, Pols, Zandbergen, & Lousberg, 1990; Kent et al., 2001; Papp et al., 1993; Perna, Barbini, Cocchi, Bertani, & Gasperini, 1995; Rassovsky & Kushner, 2003).

However, the specificity of CO2 hypersensitivity to panic and related conditions is unclear (Zvolensky & Eifert, 2001) given that individuals with other anxiety disorders show hypersensitivity (i.e., elevated reactivity) to the CO2 challenge, including social anxiety disorder (Gorman et al., 1990; Schmidt & Richey, 2008), specific phobia (Caldirola, Perna, Arancio, Bertani, & Bellodi, 1997; Gorman et al., 1990; Schmidt, Timpano, & Buckner, 2008), generalized anxiety disorder (GAD; Verburg, Griez, Meijer, & Pols, 1995), and PTSD (Muhtz, Yassouridis, Daneshi, Braun, & Kellner, 2011). Moreover, even among community samples, dispositional anxiotypic
traits (e.g., anxiety sensitivity and trait anxiety) are associated with elevated CO$_2$ hypersensitivity (McNally, 2002; Telch, Harrington, Smits, & Powers, 2011; Vickers, Jafarpour, Mofidi, Rafat, & Woznica, 2012; Zinbarg, Brown, Barlow, & Rapee, 2001; Zvolensky & Eifert, 2001).

The broad association of CO$_2$ hypersensitivity with anxiety disorders as compared to the hypothesized association with panic represents a distinction in conceptualization of anxiety disorders (e.g., Papp et al., 1993) and in the Research Domain Criteria framework proposed by the National Institute of Mental Health (NIMH; Insel et al., 2010) between two related, yet distinct, constructs of responses to acute threat (fear) and potential harm (anxiety). In this framework, CO$_2$ hypersensitivity among individuals with broad anxiety disorders and related traits may reflect an underlying, chronically elevated anxiety, which appears elevated in response to a range of psychological and physiological stressors (e.g., Roberson-Nay, Beadlo, Gorlin, Latendresse, & Teachman, 2015). However, another group of individuals may show lower initial anxiety and an acute reaction to the unique conditions of the CO$_2$ challenge. In the parlance of the RDoC framework, the former would characterize responses to potential harm whereas the latter would characterize responses to acute threat. The unique conditions of the CO$_2$ challenge task may permit identifying and distinguishing between these two types of responses. Moreover, the characterization of these responses may be most informative during a critical period in the development of the anxiety response.

Extant research into the clinical correlates of CO$_2$ hypersensitivity has primarily focused on adult samples (e.g., Vickers et al., 2012), resulting in a further gap in knowledge as to the manifestation and diagnostic specificity of CO$_2$ hypersensitivity among children, adolescents, and young adults. This gap is critical given changes in the nature of anxiety over the course of child development (McLaughlin & King, 2015; Pine & Fox, 2015). Increased prevalence of PD in late adolescence and early adulthood, as compared to childhood, may suggest the emerging expression of panicotypic responses among older adolescents. As such, older adolescent participants may show greater reactivity to a CO$_2$ challenge task (i.e., elevated CO$_2$ hypersensitivity). Additionally, an adolescent and young adult sample may provide a particularly informative timing to understand the manifestation and clinical correlates of CO$_2$ hypersensitivity.

Operationalization of CO$_2$ hypersensitivity varies across studies by assessment of distress through self-report (e.g., of anxiety/distress or panic symptoms) or psychophysiological assessment (e.g., respiratory rate), concentration of CO$_2$ (ranging from 4% to 65%), and duration of exposure to CO$_2$-enriched air (ranging from 5 s to 20 min; Zvolensky & Eifert, 2001). However, certain parameters seem to provide the strongest assessment of response to the task. For example, lower CO$_2$ concentrations produce a gradual and sustained arousal, which permits a more fine-grained measure of respiratory physiology and sensitivity than higher concentrations administered briefly (Battaglia, Ogliari, D'Amato, & kinkead, 2014; Sanderson, Rapee, & Barlow, 1989). Similarly, among the variety of indices for response to the task, self-reported anxiety appears to have the most support as a useful marker for anxiety disorders and related traits (Coryell, Fyer, Pine, Martinez, & Arndt, 2001; Roberson-Nay et al., 2015; Vickers et al., 2012).

However, the analysis of self-reported anxiety varies between peak anxiety (Wetherell et al., 2006), rate of anxiety increase during the task (Kaye et al., 2004), and the presence of a panic-like event (Kaye, Young, Mathias, Watson, & Lightman, 2006), which have all supported the association of CO$_2$ hypersensitivity with anxiety disorders (Vickers et al., 2012). Moreover, the manifestation of anxiety and fear processes may be obscured by existing assessments of CO$_2$ hypersensitivity. For example, peak anxiety fails to differentiate between chronic elevations in anxiety and acute response to the task. Rate of anxiety increase during the task may index acute response but conflates the chronically elevated and consistently low groups. Additionally, whereas the experience of a panic-like event indexes a face valid construct, this assessment is limited to the manifestation of panic-like symptoms to the exclusion of other manifestations of distress.

Instead, considerable inter-individual heterogeneity in the trajectory of anxiety may be indicative of underlying classes of participants who share a common trajectory during the task. This notion was recently suggested by Roberson-Nay and colleagues who, with a sample of 376 individuals, suggest that the latent classes of participants may describe a class with consistently high anxiety (i.e., high) and a class who show an acute increase in anxiety during the task (i.e., acute) as compared against a third, consistently low anxiety class (i.e., low) (Roberson-Nay et al., 2015). These class descriptions are consistent with the theory suggested by the RDoC framework, though Roberson-Nay et al. (2015) support the external validity of these classes based on the association of the high and acute classes with higher scores on the anxiety sensitivity inventory, the stress subscale of the Depression, Anxiety, and Stress scales (DASS), and the agoraphobic subscale of the Fear Questionnaire. To clarify the manifestation of fear and anxiety in CO$_2$ hypersensitivity, further work is needed to replicate the structure of latent classes and to clarify their association with both fear- and anxiety-related traits (e.g., anxiety sensitivity) and anxiety disorders.

I.1. The present study

CO$_2$ hypersensitivity appears to be strongly associated with a range of anxiety-related outcomes, although the nuances of CO$_2$ hypersensitivity as a marker of panic syndromes, anxiety disorders, or broader psychological traits (e.g., anxiety sensitivity) warrant continued investigation and clarification, particularly within adolescence. The present study sought to examine the latent class structure of self-reported anxiety response during the CO$_2$ challenge task in an adolescent and young adult population. Latent growth mixture models were used to allow for the analysis of varied response trajectories to capture inter-individual heterogeneity in patterns of response to the task with the aim of identifying classes of responding that may align with different systems involved in varying responses. We sought to expand upon prior work from our group using this method (Roberson-Nay et al., 2015) by examining the latent class structure in a larger epidemiological sample of adolescents and young adults and to examine the validity of the latent class structure with internalizing disorders and panic syndromes as well as a wider range of diagnostic and dimensional measures of clinical correlates to inform upon the clinical implications of the varied responses to the task.

We hypothesized that three distinct trajectories of self-reported anxiety (low, acute, and high) would be found in this sample, in line with previous findings (Roberson-Nay et al., 2015). Given the developmental timing of panic risk during late adolescence and early adulthood (Kessler et al., 2005), we hypothesized that older age would be associated with greater anxiety response during the task. We further hypothesized that membership in the high class would be associated with multiple anxiety conditions, as well as high levels of related dimensional correlates, while the acute class would be associated with increased dimensional correlates and panic-related disorders (e.g., panic attacks), though not other clinical diagnoses.

Finally, we compared the latent growth mixture model to existing assessments of CO$_2$ hypersensitivity based on self-report, which has shown the largest and most consistent role as a risk
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات