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INTRODUCTION

Stress Sensitivity and Stress Sensitization in Psychopathology: An Introduction to the Special Section

Kate L. Harkness
Queen's University

Elizabeth P. Hayden
University of Western Ontario

Nestor L. Lopez-Duran
University of Michigan

The goal of this special section is to examine the mechanisms of enhanced sensitivity and sensitization to stress as they influence the etiology and pathophysiology of psychopathology. The concept of enhanced sensitivity to stress as a key endophenotype for major depressive disorder, anxiety disorders, and schizophrenia has its origins in animal models, which have shown that early environment and gene expression interact to predict individual differences in stress reactivity (see Meaney, 2001 for a review). The application of this concept to the development of psychopathology has been extensive, with cognitive-affective, psychoneuroendocrinological, and neurogenetic models of stress sensitivity emerging in the past decade (e.g., Lopez-Duran, Kovacs, & George, 2009; Pezawas et al., 2005; Vrieze & Claes, 2009). The related construct of stress *sensitization* has its origins in the early animal models of electrophysiological kindling, as well as stimulant sensitization (Goddard, McIntyre, & Leech, 1969; Robinson & Becker, 1986). Application to psychopathology was initiated by Robert Post's (1992) seminal finding that there is a greater role for major life stress in triggering first episodes of affective disorder than recurrences, and that increasingly more minor levels of stress are required to precipitate episodes of affective illness over time (Monroe & Harkness, 2005). The *kindling hypothesis* of major affective psychopathology has since been refined and expanded through detailed meta-analysis and theoretical review (Breese, Overstreet, & Knapp, 2005; Monroe & Harkness, 2005; Post & Weiss, 1998; Stroud, Davila, & Moyer, 2008), and is now viewed as "the major integrative conceptual system available to guide thinking and research on [affective pathology] and its recurrence over time" (Monroe & Harkness, 2005, p. 418).

The broad consensus the field has reached concerning the importance of stress sensitivity and stress sensitization in the etiology and maintenance of psychopathology is reflected in the fact that individual differences in response to threat and loss is the first domain in the Research Domain Criteria (RDoC) Matrix developed by the National Institutes of Mental Health (NIMH) as a strategy to guide research on mechanisms of psychopathology (Insel et al., 2010). This strategy encourages a cross-disciplinary, multimethod approach to understanding stress processes in psychopathology at multiple levels of analysis (Cuthbert & Kozak, 2013).

The 12 articles in this special section focus on some of the most crucial and unanswered questions regarding the underlying mechanisms and functional consequences of stress sensitivity and stress sensitization in psychopathology. They do so by addressing a very wide variety of psychopathologies, from disorders long known to involve heightened stress sensitivity and sensitization, such as major depressive disorder (Farb, Irving, Anderson, & Segal, 2015), bipolar disorder (Muhtadie & Johnson, 2015; Weiss et al., 2015), anxiety disorders (Morris & Rottenberg, 2015; Farmer & Kashdan, 2015), and psychosis (Hernaus et al., 2015), to disorders for which an emphasis on stress mechanisms is more novel, such as tobacco addiction (Bradford, Curtin, & Piper, 2015). The heterogeneity of clinical manifestations of stress sensitivity and sensitization strongly underscores the transdiagnostic nature of these etiological and pathological mechanisms, and opens the door to new, fine-grained tests of their potential overlapping and differential operations across psychopathologies.

Furthermore, the articles address the constructs of stress sensitivity and stress sensitization using state-of-the-art, and often novel, methodologies. Stressful life events are assessed with rigorous contextual interview and rating systems that permit examination of the contribution of stress unconfounded by psychopathology or other diathetic biases (Weiss et al., 2015). Ecological momentary assessments that permit the fine-grained examination of minor, daily stressors that may drive the sensitization process over time are also featured (Hernaus et al., 2015; Ruscio, Gentes, Jones, Hallion, & Coleman, 2015), as are well-validated laboratory stress paradigms that permit a controlled examination of neuroendocrinological and physiological responses to stress (Bradford et al., 2015; Hinnant, Erath, & El-Sheikh, 2015; Morris & Rottenberg, 2015; Muhtadie & Johnson, 2015; Laurent, Gilliam, Wright, & Fisher, 2015). Most novel in this area is the article by Hernaus and colleagues (2015) that integrates positron emission tomogra-

Kate L. Harkness, Department of Psychology, Queen's University; Elizabeth P. Hayden, Department of Psychology, University of Western Ontario; Nestor L. Lopez-Duran, Department of Psychology, University of Michigan.

Correspondence concerning this article should be addressed to Kate L. Harkness, Department of Psychology, Queen's University, 62 Arch Street, Kingston, Ontario, Canada K7L 3N6. E-mail: harkness@queensu.ca

phy (PET) and intensive daily life event sampling to examine stress-induced [18]fallypride displacement in the ventromedial prefrontal cortex as a dopaminergic mechanism of reactivity to stressful life events in psychosis.

This special section also focuses on an important terminological distinction between two related but distinct stress mechanisms that are often conflated. Individuals who are *sensitive* to stress possess this characteristic as a putative trait that develops through genetically mediated transactional relations between temperamental characteristics and the early contextual environment (e.g., Meaney, 2001). As such, we should be able to see heightened stress sensitivity even prior to the development of psychopathology. This construct is highlighted in several of the articles. For example, Hankin, Badanes, Smolen, and Young (2015) find temporal stability of limbic-hypothalamic-pituitary-adrenal (LHPA) axis reactivity to stress in children even before the development of psychopathology. This stability is correlated with genetic polymorphisms in key serotonergic and glucocorticoid genes that regulate the stress response. Similarly, in a longitudinal study of children spanning over 6 years, Laurent et al. (2015) report that temporal stability over early childhood in elevated morning cortisol levels predicted a hyperreactive cortisol response to stress and anxiety symptoms in late childhood. The results of both of these studies converge to suggest that genetically mediated stability in LHPA reactivity may underlie at least in part the endophenotype of heightened stress sensitivity.

In contrast, individuals who are *sensitized* to stress become so over time through repeated exposure to external, as well as endogenous, stressors. As such, increasingly minor stressors maintain the disorder than were required to trigger its initial onset (e.g., Monroe & Harkness, 2005). Using sophisticated contextual interview assessment of life events, Weiss et al. (2015) found evidence for prospective stress sensitization in bipolar disorder, such that individuals with more prior episodes of bipolar illness reported a higher frequency of minor negative and positive life events prior to recurrent episodes of depression and hypomania, respectively. Further support for the mechanistic role of stress sensitization is reported by Ruscio et al. (2015) who found that stress-induced rumination mediated the relation of stress to symptoms of anxiety and depression, and this mediating effect of rumination was stronger for those with a prior history of generalized anxiety and/or major depressive psychopathology.

Enhanced stress sensitivity and sensitization have been included in conceptual models of psychopathology. Yet, the specific mechanisms by which these stress processes impact the onset and course of psychiatric disorders are not fully understood. These articles focus on several mechanistic accounts of stress sensitivity and sensitization, including hyper-reactivity of the LHPA axis (Hankin et al., 2015; Laurent et al., 2015), negative attentional bias and rumination (Farb et al., 2015; Ruscio et al., 2015), as well as striatal dopamine release (Hernaus et al., 2015) and dopamine-mediated reward learning (Bradford et al., 2015; Morris & Rottenberg, 2015). The theoretical article by Farb et al. (2015) provides a particularly sophisticated model of stress sensitization as a pathophysiological mechanism of recurrence in major depression that integrates several of the constructs examined in this section. Specifically, it proposes that sensitization over time in the depressed individual is mediated by the dual cognitive processes of dysphoric attention and dysphoric elaboration/rumination. As such, increasingly minor life events activate a neural circuit involving increased activity in the amygdala, anterior insula, and anterior cingulate cortex and decreased activity in the dorsolateral prefrontal cortex. All of these articles open the door to more cross-disciplinary and multimethod work that seeks to integrate these diverse mechanisms into a unified theoretical account.

Finally, heightened sensitivity and sensitization to stress are at their essence developmental phenomena that emerge over time through transactional relations with genetic, contextual, and other biopsychosocial factors. Several of the articles highlight the dynamic relation of stress to psychopathology through the use of longitudinal designs spanning many months or years (Hankin et al., 2015; Laurent et al., 2015) or through designs that zoom in to examine moment-to-moment stability and change in reactivity (Hernaus et al., 2015; Ruscio et al., 2015). Others examine specific moderators of the impact of stress sensitivity. For example, in a sample of adolescents with externalizing symptoms, Hinnant et al. (2015) found that a physiological marker of reduced stress sensitivity (low resting respiratory sinus arrhythmia) was associated with increased delinquency and drug use, but only in the context of harsh parenting, and primarily for boys. The concept of reduced stress sensitivity was also explored by Liu (2015). Drawing on diverse literatures, this theoretical article articulates the hypothesis that exposure to moderate levels of stress may inoculate, or "steel," the individual against future threats, whereas exposure to both low and high levels of stress may heighten reactivity to future threats. This article raises the intriguing question of what are the optimal environments that foster stress resilience, and challenges the assumption that stress and negative outcomes show a simple, linear relationship.

The motivation to publish this special section was driven by our perception of strong interest in the topic. Consistent with this perception, the response to our section call was overwhelming, with more than 75 abstracts submitted spanning a large variety of clinical populations, ages, methodologies, and research questions. The 12 included here met the very high standards for publication in the *Journal of Abnormal Psychology* and represent the state of the field. These articles address only a small subset of questions concerning the roles of stress sensitivity and sensitization in psychopathology; nevertheless, it is our hope that presenting these as a section will stimulate further research building on this work, research that will ultimately speak further to theory and prevention of the onset and maintenance of stress-related psychopathology.

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