



Anticipatory sensitization to repeated stressors: The role of initial cortisol reactivity and meditation/emotion skills training



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Summary Anticipation may play a role in shaping biological reactions to repeated stressors—a common feature of modern life. We aimed to demonstrate that: (a) individuals who display a larger cortisol response to an initial stressor exhibit progressive anticipatory sensitization, showing progressively higher cortisol levels before subsequent exposures, and (b) attention/emotional skills training can reduce the magnitude of this effect on progressive anticipatory sensitization. Female school teachers ($N=76$) were randomly assigned to attention/emotion skills and meditation training or to a control group. Participants completed 3 separate Trier Social Stress Tests (TSST): at baseline (Session 1), post-training (Session 2), and five months post (Session 3). Each TSST session included preparing and delivering a speech and performing an arithmetic task in front of critical evaluators. In each session participants' salivary cortisol levels were determined before and after the stressor. Control participants with larger cortisol reactivity to the first stressor showed increasing anticipatory (pre-stressor) cortisol levels with each successive stressor exposure (TSST session)—suggesting progressive anticipatory sensitization. Yet this association was absent in the training group. Supplementary analyses indicated that these findings occurred in the absence of group differences in

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cortisol reactivity. Findings suggest that the stress response can undergo progressive anticipatory sensitization, which may be modulated by attention/emotion-related processes. An important implication of the construct of progressive anticipatory sensitization is a possible self-perpetuating effect of stress reactions, providing a candidate mechanism for the translation of short-to-long-term stress reactions.

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1. Introduction

There has been growing interest in biological responses to *repeated* exposure to stressful circumstances, in part because life experience often involves sets of related stressful events rather than a single event in isolation. Habituation can occur after repeated exposure to similar stressors, resulting in a reduced response to subsequent events (Antelman, 1988; Kirschbaum et al., 1995; Schommer et al., 2003). However, in certain contexts many individuals do not show habituation. In fact, individuals can instead become *sensitized* to the stressor. In such cases, stress responses increase, rather than decrease, with each subsequent exposure (Antelman, 1988). Sensitization of relevant biological systems may serve an important mediating role underlying the effects of chronic and repeated stressor exposure on mental and physical health (Antelman, 1988; Post and Weiss, 1998; Cohen et al., 2007). Therefore, greater understanding of the processes that influence sensitization is critical for linking transient stress responses to habitual stress patterns.

Stressful situations can activate the hypothalamic–pituitary–adrenal (HPA) axis, resulting in an increase in cortisol secretion, which is thought to affect physical and emotional health (McEwen, 2004; Miller et al., 2007; Taylor and Stanton, 2007). Empirical evidence from animal as well as human studies indicates that cortisol levels can increase not only in response to a stressor (Dickerson and Kemeny, 2004), but also in anticipation of a stressful event (Ottenweller et al., 1989; Smyth et al., 1998; Rohleder et al., 2007; Engert et al., 2013). Threats in an animal's life are often predictable, allowing the animal to anticipate (i.e., to foresee and deal with in advance) many stressors (Sapolsky et al., 2000). From an evolutionary perspective, being able to correctly anticipate potential threats is adaptive, since it allows an individual to start making behavioral, cognitive, and physiological adjustments that are necessary to deal with the threat, even before the threat occurs, possibly avoiding it altogether (Schulkin et al., 1994; Denson et al., 2009; Waugh et al., 2010; Schulkin, 2011). Anticipation is particularly important for humans, with their greater capacity for abstract thought and symbolic representation. However, these greater cognitive abilities may also have negative consequences: *Chronic overestimation* of the probability of impending negative events may have negative long-term effects on health (Schulkin, 2011).

Surprisingly little is known about the factors that control the magnitude of biological responses in anticipation of upcoming events. Animal studies suggest that the intensity of an initial stressor predicts an animal's anticipatory cortisol reaction to subsequent similar stressors (Pitman et al., 1990). It is not known whether there is a direct relation between stressor intensity and subsequent anticipatory

cortisol levels, or whether this association is actually due to the larger psychobiological responses that follow more intense initial stressors. The magnitude of initial cortisol reactivity (which shows large inter-individual differences) may be a better predictor of anticipatory cortisol levels prior to subsequent stressors than the objective intensity of the initial stressor.

Consistent with Bell and colleagues' (Bell et al., 1995) definition of time-dependent sensitization as "progressive response amplification to repeated, intermittent stimuli over time" (p. 84; also see (Antelman et al., 1980; Strakowski and Sax, 1998)), we hypothesized that individuals who mount a larger cortisol response to an initial stressor would show a steeper increase in their anticipatory cortisol levels with each additional exposure to a similar stressor (i.e., *progressive anticipatory sensitization*). Conversely, individuals who mount a small cortisol response to an initial stressor might either show a small increase—or even a decrease—in their anticipatory cortisol levels with each additional exposure to a similar stressor. The novel approach adopted in this study is to apply the concept of progressive sensitization to the area of anticipatory cortisol levels and HPA axis functioning. This approach may further our understanding of the biological and health implications of responses to repeated stress exposure.

Given the link between repeated stressors and susceptibility to different types of health problems as well as disease progression (Antelman, 1988; Post and Weiss, 1998; Segerstrom and Miller, 2004; Chandola et al., 2006; Cohen et al., 2007) it would also be important to understand what processes might influence the degree of sensitization in order to identify possible points of intervention. We propose that two specific processes would be central to the ability to reduce anticipatory stress responses. First, we conjecture that a reduction in the persistent focus on possible future occurrences and a shift in attention toward one's experience in the present moment would reduce anticipation. Second, we propose that an increase in the capacity to understand and regulate one's emotions would likely reduce the negative affective component of anticipation.

If anticipation is an important mechanism in the sensitization process, then intervention strategies could target these processes with the aim of shifting attention toward present moment experience and increasing the ability to understand and regulate emotion. One key component of such an intervention could be meditation since the thrust of many meditation techniques is the development of the ability to direct one's attention toward the experience in the moment (Wallace and Shapiro, 2006). A large number of studies indicate that meditative practice, including mindfulness practices, enhances attentional processes (Tang et al., 2007; MacLean et al., 2010; Prakash et al., 2010; Menezes

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