



# Post-stress rumination predicts HPA axis responses to repeated acute stress



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Received 2 May 2014; received in revised form 21 July 2014; accepted 22 July 2014

## KEYWORDS

Acute stress;  
Habituation;  
Rumination;  
Hypothalamic-pituitary-adrenal axis;  
Cortisol;  
Perseverative cognition

**Summary** Failure of the hypothalamus-pituitary-adrenal (HPA) axis to habituate to repeated stress exposure is related with adverse health outcomes, but our knowledge of predictors of non-habituation is limited. Rumination, defined as repetitive and unwanted past-centered negative thinking, is related with exaggerated HPA axis stress responses and poor health outcomes. The aim of this study was to test whether post-stress rumination was related with non-habituation of cortisol to repeated stress exposure. Twenty-seven participants ( $n = 13$  females) were exposed to the Trier Social Stress Test (TSST) twice on consecutive afternoons. Post-stress rumination was measured after the first TSST, and HPA axis responses were assessed by measuring salivary cortisol 1 min before, and 1, 10, 20, 60, and 120 min after both TSSTs. Stress exposure induced HPA axis activation on both days, and this activation showed habituation indicated by lower responses to the second TSST ( $F = 3.7$ ,  $p = 0.015$ ). Post-stress rumination after the first TSST was associated with greater cortisol reactivity after the initial stress test ( $r = 0.45$ ,  $p < 0.05$ ) and with increased cortisol responses to the second TSST ( $r = 0.51$ ,  $p < 0.01$ ), indicating non-habituation, independently of age, sex, depressive symptoms, perceived life stress, and trait rumination. In summary, results showed that rumination after stress predicted non-habituation of HPA axis responses. This finding implicates rumination as one possible mechanism mediating maladaptive stress response patterns, and it might also offer a pathway through which rumination might lead to negative health outcomes.

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## 1. Introduction

Psychosocial stress has been shown to be predictive of negative health outcomes over time (Cohen et al., 2007). In addition to being exposed to long-term, chronic stress, or to single traumatic experiences, individuals are exposed to daily occurrences of potentially stressful experiences. Acute stress causes biological responses, such as hypothalamic-pituitary adrenal (HPA) axis and sympathetic nervous system (SNS) activation (Gouin et al., 2012). While most investigations of stress responses involve exposing participants to novel, one-time stressors, people in everyday life experience similar or identical stressors many times over. This makes it important to examine responses to repeated stressors. In particular, the extent to which individuals are able to habituate (i.e., show decreased physiological activation) in response to repeated stressors may have implications for long term health (e.g., McEwen and Lasley, 2003). Therefore, understanding determinants of habituation vs. non-habituation is necessary to understand inter-individual differences in the health effects of everyday stress. One factor that might explain non-habituation of stress responses is rumination. Rumination, defined here as negative and unwanted past-centered repetitive thoughts, may be particularly likely to exacerbate the physiological stress response because it could interfere with healthy post-stress emotional and cognitive processing of a situation (Takano and Tanno, 2009; Teasdale, 1999) and thereby inhibit habituation across repeated stressors. Although rumination has been studied in relation to initial cortisol responses to stress, no studies have examined rumination and cortisol responses to repeated stress.

Acute psychosocial stress stimulates the two major stress response systems, the SNS and the HPA axis, resulting in increases of stress hormones epinephrine and norepinephrine as well as cortisol. When an acute stressor is repeated, the majority of individuals show habituation of the HPA axis (Epel et al., 2000; Kirschbaum et al., 1995; Kudielka et al., 2006; Schommer et al., 2003; Wüst et al., 2005). Of note, habituation is not seen in the SNS and other stress responsive systems (Schommer et al., 2003; von Kanel et al., 2006).

HPA axis habituation is thought to generally be adaptive (McEwen, 2003, 2004; McEwen and Lasley, 2003). The allostatic load model puts forth the idea that activation of stress systems that is either sustained or not balanced or counter-acted by another system can put wear and tear on dependent systems. This has been shown to lead to negative health consequences (McEwen and Lasley, 2003). For example, an allostatic load index has been shown to be predictive of long-term health (Juster et al., 2010).

In line with this theory, inter-individual differences in habituation have been found to be related cross-sectionally with reduced psychosocial and biomedical health. Kirschbaum et al. (1995) found lower self-esteem and higher depressed mood in a subgroup of male participants who did not show HPA axis habituation to repeated laboratory stress (Kirschbaum et al., 1995). Furthermore, self-report measures of vital exhaustion have also been related to reduced habituation to stress over time (Kudielka et al., 2006). Additionally, women with greater central fat

showed sensitization, rather than habituation, of the cortisol response to repeated acute stress (Epel et al., 2000). Finally, while genetic factors were not found to be related with cortisol response patterns to repeated stress (Wüst et al., 2005), individuals in an active episode of major depression displayed non-habituation, while healthy controls habituated (Morris and Rao, 2014).

One factor that could potentially explain why some individuals do not habituate might be rumination. Rumination is a well-studied psychological construct that is predictive of future depression occurrence (Nolen-Hoeksema, 2000; Robinson and Alloy, 2003), and has been correlated with altered stress responses (Brosschot et al., 2006). Broadly defined, rumination consists of 'past-centered negative, unwanted and persistent thoughts', and has components of emotional upset, anger, and depression (Nolen-Hoeksema et al., 2008; Segerstrom et al., 2000). Rumination is distinct from worry, as it is past-oriented while worry is considered to be future-centric. Rumination can be viewed as a 'response-style'; that is, when presented with a stressful experience, people may tend to ruminate about it, as opposed to engaging in another coping style such as distracting themselves from the stressor (Nolen-Hoeksema et al., 1993). Generally, rumination is considered to be a maladaptive response to stress, and it has been related to many negative psychological outcomes. For example, rumination has been shown to be a precursor of future depression (Nolen-Hoeksema, 2000; Robinson and Alloy, 2003). It has often been shown that women ruminate more than men, a finding that may help to explain sex discrepancies in depression rates (Strauss et al., 1997). According to the perseverative cognition theory, rumination can have prolonged physiological consequences, such as post-stress heart rate elevations (Brosschot et al., 2006). Recent work has shown that higher levels of rumination are related to non-adaptation of heart rate responses to repeated stress (Johnson et al., 2012). A recent review paper indicated that both trait and state-based rumination measures are related to heightened cortisol responses to a variety of different stressors (Zoccola and Dickerson, 2012). Trait-rumination measures have been found to be correlated with both increases in cortisol stress responses in some studies (Zoccola et al., 2010) and decreases in others (Zoccola et al., 2008). Other work has failed to find any relationship between trait rumination and acute stress responses (Young and Nolen-Hoeksema, 2001), suggesting a complex relationship between trait-based rumination and acute stress responses that may be very dependent on how trait rumination is conceptualized and measured.

Post-stress state rumination measures have been generally related to increased cortisol responses to acute stress (Zoccola et al., 2008, 2010), and as shown by a meta-analysis of more than 60 acute stress studies, cortisol responses were significantly higher in context that were related with repetitive thoughts and brooding (Denson et al., 2009). However, it should be noted that some factors, such as physical activity levels, have been shown to moderate this relationship (Puterman et al., 2011). It has also been shown that experimentally inducing rumination increases cortisol responses (Byrd-Craven et al., 2011; Zoccola et al., 2014). The relationship between rumination and cortisol adaptation to repeated stress is so far unknown.

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