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Resilience to the effects of social stress: Evidence from clinical and preclinical studies on the role of coping strategies

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ABSTRACT

The most common form of stress encountered by people stems from one's social environment and is perceived as more intense than other types of stressors. One feature that may be related to differential resilience or vulnerability to stress is the type of strategy used to cope with the stressor, either active or passive coping. This review focuses on models of social stress in which individual differences in coping strategies produce resilience or vulnerability to the effects of stress. Neurobiological mechanisms underlying these individual differences are discussed. Overall, the literature suggests that there are multiple neural mechanisms that underlie individual differences in stress-induced resilience and vulnerability. How these mechanisms interact with one another to produce a resilient or vulnerable phenotype is not understood and such mechanisms have been poorly studied in females and in early developmental periods. Finally, we propose that resilience may be stress context specific and resilience phenotypes may need to be fine-tuned to suit a shifting environment.

1. Introduction

The most common form of stress encountered by people stems from one's social environment and is perceived as more intense than other types of stressors (Almeida, 2005). Socially stressful events such as bullying, loss of a loved one, and psychological abuse are well documented to contribute to psychopathology (Kendler et al., 1999; Kessler, 1997; Bjorkqvist, 2001). In fact, stress exposure is an independent risk factor for psychiatric disorders such as depression, anxiety and posttraumatic stress disorder (PTSD) (Kendler et al., 1999; Kessler, 1997; Javidi and Yadollahie, 2012). However the pathogenic potential of a stressor does not solely depend on the severity of the stress exposure as evidenced by the great individual variability in the consequences of exposure to stressful events. Indeed, a recent study indicates that among older US veterans who have been exposed to a high number of lifetime traumas, about 70% are resilient in later life (Pietrzak and Cook, 2013). One feature that may be related to differential susceptibility to stress is the type of strategy used to cope with the stressor, either active or passive coping (Veenema et al., 2003). Active coping is defined as a behavioral response people engage in that uses one's own resources to minimize the physical, psychological or social harm of a situation (Folkman and Lazarus, 1980) and is related to resiliency to stress (Southwick et al., 2005). In humans, developing social support and friendships (Kral et al., 2014; Yi et al., 2005) as well as having secure relationships reduces suicidality in veterans of Operation Enduring Freedom and Operation Iraqi Freedom (Youssef et al., 2013), and is essential to establishing resilience. Furthermore, characteristics of active coping that reduce stress and symptoms of mental illness include the following: creating a sense of coherence in their lives (Matsushita et al., 2014) or in the community (Hall et al., 2014), exercising self-control (Moses, 2014), developing a strong sense of identity including professional identity for workplace resilience (Hunter and Warren, 2014), maintaining a realistic perception of threat (Karstoft et al., 2013), possessing optimism (McGarry et al., 2013; Boyson et al., 2014), having a sense of purpose (Pietrzak and Cook, 2013), and the use of problem-focused coping (Yi et al., 2005). However not all coping strategies are adaptive; passive coping is characterized by feelings of helplessness, relying on others for stress resolution and is associated with vulnerability to psychopathology (Zeidner and Norman, 1995; Folkman and Lazarus, 1980; Billings and Moos, 1984). Consistent with this view, vulnerable individuals use

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passive coping strategies such as avoidance and blaming others (Yi et al., 2005). Therefore, the impact of a stressor on an individual's psychological well-being depends to a considerable extent on the strategy used to cope with the stressful life event.

2. Focus of this review

Resilience can be defined as positive adaptation, or the ability to maintain or regain mental health, despite experiencing adversity and challenges (Herrman et al., 2011; Karatsoreos and McEwen, 2013). In order to understand the biological basis of how some individuals are resilient to social stress and how others are vulnerable, we will focus on studies in which variations in the impact of stress are observed. That is, the focus is on studies in which subgroups of individuals defined as vulnerable or resilient emerge following exposure to the same stressor and not on studies that examine mechanisms that modify the impact of social stress homogenously in all subjects. This is because not all mechanisms that uniformly reduce the impact of stress necessarily underlie resilience. They may underlie resilience or they may not, but focusing on studies in which subpopulations emerge will allow the determination of those specific mechanisms demonstrated to underlie resilience and/or vulnerability. Further, because of the robust impact that stress has on mental health, we have a particular focus on those studies in which measures related to psychopathology are assessed. Furthermore, in clinical literature, varying coping strategies have been associated with differences in susceptibility to stress-related pathology. As such, we also focus on the role that various coping strategies may play in vulnerability to psychosocial stress exposure. Finally, there are a substantial number of studies examining epigenetic mechanisms underlying resilience to social stress but these are covered elsewhere in this issue and excellent recent reviews have been published (Wu et al., 2013; Griffiths and Hunter., 2014; Nestler, 2014). Therefore, the impetus for this review is to highlight how mechanisms linked to either a passive or active coping strategy in the face of chronic psychosocial stress may underlie the pathogenesis of stress vulnerability and resiliency.

3. The resident-intruder paradigm of social stress

The resident-intruder paradigm is an ethologically relevant animal model of social stress (Miczek, 1979) that has proven useful for identifying mechanisms mediating resilience or vulnerability to stress-related consequences (Wood et al., 2010, 2013a; Koolhaas et al., 2007; Krishnan et al., 2007; Berube et al., 2013). This model is commonly employed using rodents (rats, mice, hamsters) or tree shrews and involves subjecting a male “intruder” to aggressive threats from a larger, unfamiliar male “resident” by placing it in the resident's home cage for a period consisting of anywhere from 5 to 60 min (Krishnan et al., 2007; Bhatnagar and Vining, 2003; Wood et al., 2010; Miczek, 1979; Sgoifo et al., 1996; Buwalda et al., 1999). The acute response to social defeat (minutes to hours) results in robust sympathetic activation eliciting 30 times the number of arrhythmias as compared to other non-social experimental stressors such as foot shock or restraint (Sgoifo et al., 1999). Social stress also produces vagal withdrawal, increased blood pressure, elevated plasma catecholamines, hyperthermia, and increased activation of the hypothalamic–pituitary–adrenal (HPA) axis (Wood et al., 2010; Sgoifo et al., 1999; Tornatzky and Miczek, 1994, 1993; Bhatnagar et al., 2006). These acute physiologic stress responses are comparable to those reported in response to an experimental model of psychosocial stress in humans. For example, the Trier Social Stress Test is designed to exploit the reactivity of the stress response to socially challenging situations in humans and produces robust activation of the HPA axis and the sympathetic nervous system (Hellhammer and Schubert, 2012; Kirschbaum et al., 1993). In both humans and animals, these acute responses are adaptive in helping the individual cope with the stressor. However, if these stress responses are unabated in the face of chronic stress as may occur under conditions of inefficient stress coping, this can lead to pathological changes promoting psychiatric disorders such as depression, generalized anxiety and post-traumatic stress disorder.

4. Coping influences individual differences in reactivity to, and consequences of, social stress in the resident-intruder and visible burrow models

It is generally considered that two coping response patterns are distinguishable in response to social stress (Koolhaas et al., 1999). One is considered the active (or proactive) response and is characterized by territorial aggression and control, as was originally described by Walter Cannon (Cannon, 1915). The second category of stress coping response is defined as passive (or reactive) and is characterized by immobility and low levels of aggression (Engel and Schmale, 1972). These two coping strategies have distinct and opposing sets of behavioral characteristics (reviewed in Koolhaas et al. (1999)). Coping styles have now been identified in a range of species from fish to rodents and pigs to humans and non-human primates (reviewed in Koolhaas et al. (1999)) and are considered to be trait characteristics that are stable over time and across situations (Koolhaas et al., 2007). In addition to the distinct behavioral characteristics displayed by the active and passive coping strategies, these strategies are also characterized by differences in physiological and neuroendocrine endpoints (reviewed in Koolhaas et al. (1999)). Freezing, a characteristic behavior of passive coping, is accompanied by low plasma norepinephrine and high plasma corticosterone levels. Furthermore, passive coping is associated with high HPA axis reactivity (Korte et al., 1992). In contrast, active coping is distinguished by low HPA axis reactivity and high sympathetic reactivity to stressful situations (Fokkema et al., 1995). Based on these diverse physiological responses to stress in actively versus passively coping individuals, under conditions of chronic stress when the coping response is not adequate to mitigate the impact of stress on the body, negative stress-induced physiological and psychological consequences may ensue. The majority of the studies discussed below are in the context of exposure to psychosocial stress in rodents under conditions in which death is not imminent. It is important to note that whether a specific coping strategy is adaptive (i.e. resulting in decreased impact of stress on the body) is dependent on the environment and type of stress. For example, the studies discussed below indicate that passive coping (i.e. submissive, immobile responses) is maladaptive under conditions of repeated exposure to brief social stress. However, under conditions where a weaker organism is confronted with a life-threatening situation involving a predator, passive immobility rather than fighting and struggling will likely increase the chance of survival. Therefore passive immobility may be considered adaptive under conditions where there is no possibility of escaping or winning the fight (Bracha et al., 2004). Therefore the concept of a particular coping strategy leading to healthy adaption must be a fluid concept; a specific coping strategy may be considered adaptive in one context and maladaptive in another.

Two experimental animal models have been particularly important in understanding the impact of coping strategies on the physiological and behavioral consequences of social stress, the resident-intruder paradigm originally developed by Miczek (1979) and the visible burrow system (VBS) developed by Blanchard, Blanchard, Sakai and colleagues (Blanchard et al., 2011; Tamashiro et al., 2005). Other models of social stress have been developed,