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Social stress contagion in rats: Behavioural, autonomic and neuroendocrine correlates

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ABSTRACT

The negative emotional consequences associated with life stress exposure in an individual can affect the emotional state of social partners. In this study, we describe an experimental rat model of social stress contagion and its effects on social behaviour and cardiac autonomic and neuroendocrine functions. Adult male Wistar rats were pair-housed and one animal (designated as "demonstrator" (DEM)) was submitted to either social defeat stress (STR) by an aggressive male Wild-type rat in a separate room or just exposed to an unfamiliar empty cage (control condition, CTR), once a day for 4 consecutive days. We evaluated the influence of cohabitation with a STR DEM on behavioural, cardiac autonomic and neuroendocrine outcomes in the cagemate (defined "observer" (OBS)). After repeated social stress, STR DEM rats showed clear signs of social avoidance when tested in a new social context compared to CTR DEM rats. Interestingly, also their cagemate STR OBSs showed higher levels of social avoidance compared to CTR OBSs. Moreover, STR OBS rats exhibited a higher heart rate and a larger shift of cardiac autonomic balance toward sympathetic prevalence (as indexed by heart rate variability analysis) immediately after the first reunification with their STR DEMs, compared to the control condition. This heightened cardiac autonomic responsiveness habituated over time. Finally, STR OBSs showed elevated plasma corticosterone levels at the end of the experimental protocol compared to CTR OBSs. These findings demonstrate that cohabitation with a DEM rat, which has experienced repeated social defeat stress, substantially disrupts social behaviour and induces short-lasting cardiac autonomic activation and hypothalamic-pituitary-adrenal axis hyperactivity in the OBS rat, thus suggesting emotional state-matching between the OBS and the DEM rats. We conclude that this rodent model may be further exploited for investigating the neurobiological bases of negative affective sharing between social partners under chronic social stress conditions.

1. Introduction

Stress is increasingly present in everyday life in our fast-paced society and strongly influences our mental and physical well-being. It is well established that exposure to chronic stressful life events can favour the onset and progression of both psychological (e.g., depression, anxiety) and physical (e.g., cardiovascular) disorders in vulnerable individuals (Bjorkqvist, 2001; Rozanski et al., 2005; Slavich, 2016; Strike and Steptoe, 2004). In this context, the question arises as to what extent the adverse emotional consequences associated with stress exposure in family or friends have the potential to negatively impact our life, independently from whether or not we are directly exposed to stressful life events. Indeed, humans are highly sensitive to the emotional state of their social partners and may unconsciously adopt it through social interactions. In social neuroscience, the transmission of affect from one person to another is defined as affect contagion and has been suggested to function, in part, to facilitate social connection and coordination (Butler, 2011; Hatfield et al., 1994). The subjective state resulting from affective contagion is referred to as affective (or emotional) empathy (Bernhardt and Singer, 2012; Christov-Moore et al., 2014; de Waal, 2008). For example, the contagion of depressive symptoms is relatively well documented, as depression in family or friends might cumulatively increase the likelihood that a person will exhibit depressive behaviours (Bastiampillai et al., 2013; Joiner, 1994).

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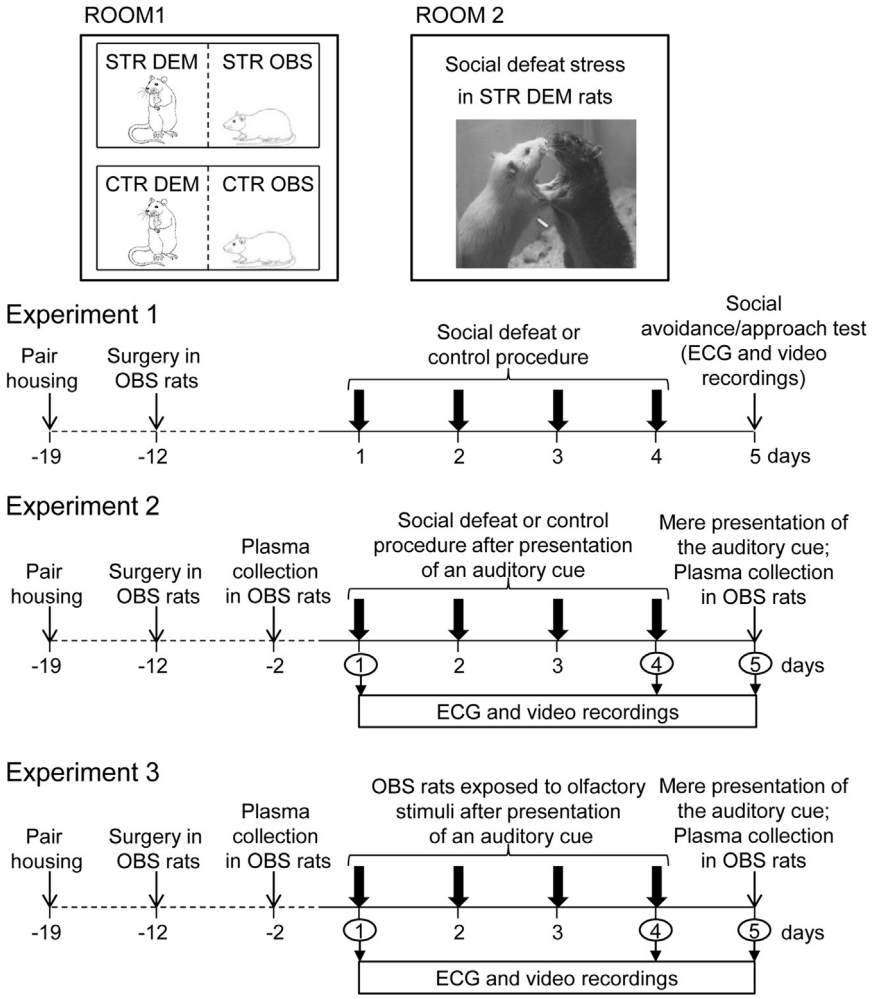

Fig. 1. Top panel: representative housing conditions in room 1 for observer (OBS) and demonstrator (DEM) rats of the stress (STR) and control (CTR) groups, with social defeat episodes that took place in room 2. Bottom panel: timeline of the three experiments (detailed procedures are described in the text).

Moreover, observing or interacting with an individual experiencing acute stress can activate the physiological stress response in the observer, as evidenced by increases in sympathetic nervous system activity and activation of the hypothalamic-pituitary-adrenal axis (Buchanan et al., 2012; Engert et al., 2014; Soto and Levenson, 2009).

Since the seminal study by Church (Church, 1959), many studies, performed mostly in the contextual fear conditioning paradigm, have demonstrated that also rodents can be attuned to the affective state of a social partner (reviewed in Meyza et al., 2016; Panksepp and Lahvis, 2011). For example, after a painful (e.g., acetic acid) or stressful (e.g., foot shock) stimulus is delivered to a rodent (the demonstrator) in the presence of an observer rodent, the observer may mimic the demonstrator's behavior as if it was directly experiencing pain or stress (Bredy and Barad, 2009; Langford et al., 2006). The social transfer of fear between rats can also occur through social interaction in the absence of direct observation. For example, during a social interaction with a recently fear-conditioned partner, naïve cagemate observers showed increased freezing behaviour and neuronal activation in the amygdala and prefrontal cortex (Knapska et al., 2006; Mikosz et al., 2015). Importantly, emotional contagion in rodents appears to be dependent on familiarity (Gonzalez-Liencres et al., 2014; Jeon et al., 2010), similarly to humans (Engert et al., 2014; Martin et al., 2015). So far only a few rodent studies have investigated the effects of chronic stress in demonstrators on behavioural and physiological parameters in observers (e.g.: Gilmore et al., 2008; Boyko et al., 2015; Carrillo et al., 2015). For example, demonstrator mice were submitted to daily restraint stress for 15 days in close proximity to, but not in view of cagemate observers (Gilmore et al., 2008). When demonstrator mice returned to the cage, their observer partners showed higher increases in heart rate and core body temperature compared to observers of non-stressed animals, although this response habituated over time (Gilmore et al., 2008). In another study, naïve rats were each housed with two rats that showed depressive-like behaviours after 5 weeks of chronic unpredictable stress (Boyko et al., 2015). Interestingly, naïve rats exhibited depressive-like behaviours (i.e., anhedonia and passive coping strategy during a forced swim test) after 5 weeks of cohabitation in the same cage with depressed rats (Boyko et al., 2015). These findings suggest that in rodents, similarly to humans, behavioural and physiological responses of an individual may be influenced by the affective state of its social partners.

Given that the most relevant stress factors associated with human psychopathology are thought to originate from an adverse social environment (Bjorkqvist, 2001; Rozanski et al., 2005; Slavich, 2016; Strike and Steptoe, 2004), in this study we attempted to set up an experimental rat model of social stress contagion by using a stress paradigm (social defeat) with high translational and naturalistic relevance for the human condition (Sgoifo et al., 2014; Carnevali et al., 2017). In particular, we tested the hypothesis that cohabitation with a demonstrator rat, which has been repeatedly submitted to social defeat stress in a separate room, would elicit behavioural, cardiac autonomic and neuroendocrine changes in the social partner.