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Heart rate response to post-learning stress predicts memory consolidation

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ABSTRACT

Stressful experiences are often well remembered, an effect that has been explained by beta-adrenergic influences on memory consolidation. Here, we studied the impact of stress induced heart rate (HR) responses on memory consolidation in a post-learning stress paradigm. 206 male and female participants saw 52 happy and angry faces immediately before being exposed to the Cold Pressor Test or a non-stressful control procedure. Memory for the faces and their respective expression was tested twice, after 30 min and on the next day. High HR responders (in comparison to low HR responders as well as to the non-stressful control group) showed enhanced recognition memory one day after learning. Our results show that beta-adrenergic activation elicited shortly after learning enhances memory consolidation and that the stress induced HR response is a predictor for this effect.

1. Introduction

Stressful situations often create long lasting memories. Abundant evidence indicates that the high memorability of stressful and arousing events results from an enhancement of consolidation processes (Roozendaal, 2002; Roozendaal & McGaugh, 2011). During stress, activation of the sympathetic nervous system will lead to a state of arousal through beta-adrenergic stimulation of peripheral (i.e. the heart) and central (i.e. the amygdala) target tissues (Chrousos, 1998; Chrousos & Gold, 1992; Johnson, Kamilaris, Chrousos, & Gold, 1992). Depending on the type and severity of the stressor (Dickerson & Kemeny, 2004; McRae et al., 2006), activation of the HPA axis will result in a release of cortisol, a steroid hormone that readily passes the blood–brain-barrier (Mason, Pariante, Jamel, & Thomas, 2010; Murphy, Cosgrove, McIlquham, & Pattee, 1967; Pardridge & Mietus, 1979). Animal experiments could demonstrate that stress effects on consolidation are driven by beta-adrenergic mechanisms and corticosteroid hormones (McGaugh, 2000; Roozendaal, McEwen, & Chattarji, 2009). Specifically, stress leads to beta-adrenoreceptor activation within the basolateral amygdala, and it has been shown that such amygdala activation strengthens memory consolidation via its widespread network of efferent projections to other brain regions (McGaugh, 2004; Roozendaal & McGaugh, 2011).

In line with the animal model, considerable evidence suggests an involvement of the adrenergic/noradrenergic system in human memory regulation (Chamberlain, Muller, Blackwell, Robbins, & Sahakian, 2006; Lonergan, Olivera-Figueroa, Pitman, & Brunet, 2012; van Stegeren, 2008). A well replicated finding is that administration of the nonspecific beta-blocker propanolol before learning leads to impaired emotional memory (Cahill, Prins, Weber, & McGaugh, 1994; Maheu, Joober, Beaulieu, & Lupien, 2004; O'Carroll, Drysdale, Cahill, Shajahan, and Ebmeier, 1999a; Strange & Dolan, 2004; van Stegeren, Everaerd, Cahill, McGaugh, & Gooren, 1998). Conversely, enhancing noradrenergic turnover potentiates emotional memories (O'Carroll, Drysdale, Cahill, Shajahan, and Ebmeier, 1999b). However, these results remain somehow equivocal with respect to the postulated actions on consolidation since the observed effects could theoretically also be explained by influences on encoding. To overcome this problem, a paradigm has been introduced in which adrenergic manipulations are administered post-learning as this allows for a clear attribution to consolidation. Applied after learning, exogenous triggering of beta-adrenergic transmission via administration of adrenaline or yohimbine also led to enhanced memory performance (Cahill & Alkire, 2003; Southwick et al., 2002).

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However, albeit the evidence for beta-adrenergic modulation of memory consolidation from studies administering exogenous adrenergic agents, studies seeking to establish a relationship between *endogenous* markers of post-learning beta-adrenergic activation and memory consolidation have been less conclusive. These studies have typically measured concentrations of salivary alpha-amylase (sAA), an enzyme thought to reflect sympathetic activation via an adrenergic mechanism (Dantzer & Kalin, 2009; Nater et al., 2005; Strahler, Mueller, Rosenloecher, Kirschbaum, & Rohleder, 2010). An association between memory consolidation and sAA was first reported by Smeets, Otgaar, Candel, and Wolf (2008). The authors applied the Cold Pressor Test (CPT) immediately after learning of emotional and neutral words. sAA and cortisol concentrations rose significantly after the stress intervention and were both positively correlated to cued recall performance assessed 24 h later. In contrast, other studies (Bryant, McGrath, & Felmingham, 2013; Felmingham, Tran, Fong, & Bryant, 2012) measuring sAA after post-learning administration of CPT could not find an effect of sAA levels on delayed free recall of neutral and emotional pictures. Similarly, two studies applying the Trier Social Stress Test after learning of emotional words (Smeets et al., 2009) or pictures (Preuss & Wolf, 2009) failed to detect any influence of stress induced sAA rise and delayed free recall performance. Nevertheless, endogenously elicited post-learning arousal per se does enhance memory consolidation as has been frequently demonstrated in the above mentioned as well as other studies that unfortunately did not provide any physiological indicator of beta-adrenergic activation (Anderson, Wais, & Gabrieli, 2006; Beckner, Tucker, Delville, & Mohr, 2006; Cahill, Gorski, & Le, 2003; Liu, Graham, & Zorawski, 2007; Nielson & Powless, 2007).

Collecting sAA is a comparatively young approach to the assessment of beta-adrenergic activation and until now there is no consensus on the appropriateness of its use (Bosch, Veerman, de Geus, & Proctor, 2011). Conversely, there is a long standing tradition in using cardiovascular parameters to quantify beta-adrenergic activation and its impact on multiple aspects of cognition. Most surprisingly, the predictive value of cardiovascular indicators went widely unnoticed in research of stress effects on consolidation. Within this context, the stress induced heart rate (HR) response seems to be an especially promising indicator. Pharmacological agents that have been successfully employed to modify memory show commensurate alterations in HR (Cahill & Alkire, 2003; O'Carroll et al., 1999a) and also change the HR response to stress (Houben, Thien, Wijnands, & Van't Laar, 1982; Victor, Leimbach, Seals, Wallin, & Mark, 1987). Furthermore, both tonic and phasic HR responses during encoding have repeatedly been shown to be involved in emotional memory enhancement (Abercrombie, Chambers, Greischar, & Monticelli, 2008; Buchanan, Tranel, & Adolphs, 2006; Jennings & Hall, 1980).

Thus, in the current study we attempted to assess the impact of the stress induced heart rate response on memory consolidation in a paradigm of post-learning stress. Using a substantial sample and the CPT as predominantly adrenergic stressor (Pascualy et al., 2000; Ward et al., 1983) we hypothesized that the magnitude of the stress induced heart rate response would predict memory performance on the next day. 206 male and female participants saw a set of 52 happy and angry faces immediately before being exposed to the CPT or a control procedure (warm water). Memory for the faces and their respective expression was tested twice, after 30 min and on the next day. To prevent loss of statistical power when assessing the influence of the heart rate response within the stress group, we doubled its size with respect to controls thereby enabling us to compare equally sized groups of high HR responders, low HR responders and controls.

2. Materials and methods

2.1. Sample

206 healthy right-handed men ($N = 100$) and women ($N = 106$) (mean age: 23 years, SD: 2.9 years) participated in the experiment. They were randomly assigned to either the stress group (CPT, $N = 135$, 70 female) or a control condition (warm water bath, $N = 71$, 36 female). Sex was balanced in the whole sample and across experimental conditions. Subjects were mostly students from the University of Trier, recruited via Email Digest and placard. Participation was limited to right handed, healthy Caucasians with normal weight (Body Mass Index between 19 and 25) and age between 18 and 35 years. Applicants were not included if they showed any evidence of acute or chronic diseases of the circulatory system (deviations from sine rhythm, glaucoma, Raynaud's disease, history of fainting, resting blood pressure above 140/90 mmHg), history of psychiatric disease or family history of arterial hypertension, and cerebral or aortic aneurisms. Blood pressure was measured and normal sine rhythm confirmed during a ten minute resting period. Furthermore, the following exclusion criteria were applied: smoking of more than five cigarettes per day, drug intake or current use of medication, increased objective or subjective sensitivity to cold.

A personal screening interview determined if all criteria for inclusion in the study were met. All participants were informed about their right to stop the experiment at any time and gave written informed consent. They were compensated with 30.00 € after completion of the whole experiment.

2.2. Procedure

2.2.1. General procedure

The study was conducted over two subsequent days. On the first day, the study protocol started with a ten minute resting period during which baseline measurements for heart rate and blood pressure were taken. Hereafter, the acquisition phase began in which participants were presented with the to-be-remembered stimuli. Immediately following acquisition, the CPT or a control procedure with warm water was carried out. A five minute resting period followed during which heart rate and blood pressure were measured. To prevent any stress effects on memory retrieval, a simple reaction time task was performed before the first memory test took place. The task lasted about 15 min. Thus, about 20 min following the stress procedure and 30 min after acquisition the first recognition memory test was conducted. The memory test concluded the experimental session for that day.

On the next day, participants returned to the lab for a second memory testing. After completion of the task they were compensated with 30.00 € and dismissed. All experimental sessions were carried out between 13:30 and 18:00 to control for diurnal variations in individual cortisol levels. All procedures were approved by the ethical committee of the state's medical association (Landesärztekammer Rheinland-Pfalz).

2.2.2. Acquisition

During acquisition participants saw a set of 52 male faces, half of them with an angry and the other half with a happy expression. Additionally, three faces were shown before and after the actual stimulus set to control for primacy and recency effects. These were not included in any memory tests. Each face was presented on screen for 3 s during which participants were instructed to watch it attentively. After presentation of each face they were asked to