



Positive modulation of a neutral declarative memory by a threatening social event



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ABSTRACT

Memories can be altered by negative or arousing experiences due to the activation of the stress-responsive sympatho-adrenal-medullary axis (SYM). Here, we used a neutral declarative memory that was acquired during multi-trial training to determine the effect of a threatening event on memory without emotional valence. To this end, participants received a new threatening social protocol before learning pairs of meaningless syllables and were tested either 15 min, 2 days or 8 days after acquisition. We first demonstrated that this threatening social situation activates not only the SYM axis (Experiment 1) and the hypothalamus–pituitary–adrenal axis (HPA; Experiment 2), but also, it improves the acquisition or early consolidation of the syllable pairs (Experiment 3). This improvement is not a transient effect; it can be observed after the memory is consolidated. Furthermore, this modulation increases the persistence of memory (Experiment 4). Thus, it is possible to affect memories with specific events that contain unrelated content and a different valence.

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1. Introduction

Negative or arousing experiences can alter cognitive processes, such as memory (Diamond, Campbell, Park, Halonen, & Zoladz, 2007). Exposure to a situation that is perceived as threatening or excessively demanding (i.e., a stressor) induces the release of hormones and other cellular mediators, which can promote adaptation and the onset of coping responses, thereby orchestrating an emotional response to the stressor (Joëls & Baram, 2009). The effect on memory processes is in part due to the activation of the stress-responsive sympatho-adrenal-medullary (SYM) and hypothalamus–pituitary–adrenal (HPA) axes (Allen, Kennedy, Cryan, Dinan, & Clarke, 2014).

Although negative emotional states may be elicited by a variety of circumstances, those that threaten a social goal and affect the

ability to overcome that threat produce a stress reaction (Lazarus, 1966). A social-evaluative threat occurs when an important aspect of self-identity is or could be negatively judged by others and the outcome of the situation is uncontrollable (Dickerson & Kemeny, 2004). In the laboratory, the Trier Social Stress Test (TSST) is a protocol that can be particularly useful for inducing this type of response in humans (Kirschbaum, Pirke, & Hellhammer, 1993).

It is commonly accepted that stress facilitates memories with emotional content but that it either impairs or has no effect on neutral information (Nater et al., 2007; Smeets, Giesbrecht, Jelicic, & Merckelbach, 2007; Smeets, Otgaar, Candel, & Wolf, 2008; Wolf, 2009); however, other reports have shown that stress may in fact improve neutral memory (Schwabe, Bohringer, Chatterjee, & Schachinger, 2008).

We designed a multi-trial memory task that consisted of learning a list of five pairs of meaningless syllables (each pair was formed by a cue syllable that was associated with a response syllable (Forcato et al., 2007)). In contrast with our paradigm, other tasks have employed a single training trial using an episodic or semantic memory with mixed content (emotional vs. neutral), which, in turn, is modified by the stressful situation (Dongaonkar,

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Hupbach, Gomez, & Nadel, 2013). Here, the clear advantage was the use of a pure neutral declarative memory that was acquired during multi-trial training. During this training, it is possible to determine the inclusion criteria for the subjects' level of learning. Then, under this experimental condition, it was possible to analyze the effect of a threatening event on memory without emotional valence.

Based on the TSST, we designed a new threatening social protocol. In this original version, subjects interacted with a virtual auditory panel (VAP). This new protocol included a VAP that was generated by only one researcher, thereby reducing the costs and optimizing the organization of the experiment schedule. We first evaluated whether the VAP induced the activation of the SYM axis (Experiment 1) by administering the protocol following the acquisition of a neutral declarative memory. Then, we compared the effects of the VAP with those of the TSST protocol using the same physiological measures plus cortisol, thereby demonstrating a similar activation not only of the SYM axis but also of the HPA axis (Experiment 2). We next analyzed the VAP's effects on memory, by testing 15 min (short-term, Experiment 3), 2 days or 8 days after acquisition (long-term and forgetting, Experiment 4).

In doing so, we found that a threatening social situation that activates the SYM and HPA axes can modulate the acquisition and/or early consolidation of a non-related neutral declarative task. This modulation is not a transient effect; its consequences were observed after the memory was consolidated, and it modified the persistence of memory. Another important contribution is the possibility of studying the effects of a stressor on a pure neutral memory (with a controlled level of learning). This allows for a new line of studies in which researchers can develop their understanding of the relationship between this memory type and the physiological changes that are induced by stress.

2. Methods

One hundred and seventy-six undergraduate and graduate students from Buenos Aires University (Argentina) participated in the current study. Prior to the experiments, participants provided a written informed consent that was approved by the Ethics Committee of the Review Board of the National Society of Clinical Research (Sociedad Argentina de Investigación Clínica). The following students were excluded from the experiments: students with cardiovascular and endocrine diseases; students having physical illnesses or being on any kind of medication; female students with no normal menstrual cycles (28–30 days), taking contraceptive pills, or within the 1st–14th day of the menstrual cycle. Current or lifetime psychopathology and/or substance abuse were assessed by a clinical psychologist.

2.1. Virtual-Auditory Panel (VAP) protocol

We designed a threatening protocol to evaluate a negative emotional response in the participants before they learned a neutral memory task. The VAP protocol consisted of three phases (Fig. 1). **Phase 1** was an undemanding attentional task, in which 16 landscape images were shown on the screen for 5 s each. The images appeared randomly and were presented in two blocks. Participants were asked to rate the images in a scale using the keyboard (from 1 to 5) according to their likes. This undemanding task lasted 5 min and was used as the skin conductance baseline level. In **Phase 2**, participants had to prepare a speech to advertise themselves as the best candidate for a professional position; this phase lasted 5 min. Finally, in **Phase 3**, the experimenter explained to the participants that a hospital committee was following the presentation online. Participants had to talk to a webcam which was located on

the back wall; participants were provided with headphones and a microphone to deliver their speech. As in the TSST protocol (Kirschbaum et al., 1993), after the presentation, participants had to perform an arithmetic task. The experimenter used a pitch modifier provided with three different voices (virtual panel) that simulate a hospital committee. This virtual panel allowed a reliable environment using pre-recorded ambient sound (consisting of different office sounds such as engines, papers, keys, and chairs). Thus, the experimenter could interact with the participants in a way similar to the TSST.

Besides, we designed a non-threatening protocol, similar to the VAP but without the main stress components (such as social threat and uncontrollability) (Dickerson & Kemeny, 2004). We called it fake VAP (VAPf). The first two phases of this protocol were identical to the previous protocol. In contrast, in **Phase 3**, participants had to write down the speech and resolve the arithmetic task. In order for both protocols to last the same time, we included other tasks such as different multiplications, additions or symbol translations.

The virtual panel software and the pre-recorded ambient sound were programmed in Cycling'74. Max/msp 5.0. All the sound devices (microphones and headphones) were plugged in a 5-channel stereo mixer (SKP Pro audio VZ 5 series) connected to the experimenter's computer, located in the contiguous room. All the wires were hidden from the subjects' view.

2.1.1. Measurements

Before **Phase 1**, we obtained the baseline measurements for the State Trait Anxiety Inventory (STAI), blood pressure, and heart rate. Blood pressure and heart rate were taken at four different time points: t0 (before **Phase 1**), t1 (after **Phase 2**), t2 (after the speech presentation) and t3 (after the arithmetic task) (Fig. 1). Skin conductance level (SCL) was recorded during the entire experiment; we defined the SCL baseline level as the continuous measure during **Phase 1** (Fig. 1). At the end of **Phase 3**, blood pressure, heart rate and the STAI were measured for the last time. The STAI was measured 10 min after the end of the arithmetic task.

2.1.1.1. Subjective rating. Cognitive stress and anxiety were measured using the STAI (Spielberger, Gorsuch, & Lushene, 1970) before and after the administration of the procedures (before Phase 1 and 10 min after Phase 3 respectively).

2.1.1.2. Blood pressure (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)) and Heart Rate (HR). Blood pressures were assessed using an Omron HEM 7220 Premium digital Tensiometer (<http://omronhealthcare.com/products/7-series-upper-arm-blood-pressure-monitor-bp760/>). Cardiovascular measurements were taken before Phase 1 (t0), after Phase 1 (t1), at the end of the speech (t2), and at the end of the arithmetical task (t3) (Fig. 1).

2.1.1.3. Electrodermal activity. Electrodermal activity was measured along the entire experiment, using an input device with a sine-shaped excitation voltage (± 0.5 V) of 50 Hz, derived from the main frequency used in Psychlab Precision Contact Instruments (<http://www.psychlab.com/>). The input device was connected to two Ag/AgCl electrodes of 20 mm \times 16 mm. The electrodes were located in the intermediate phalanges of the index and middle fingers of the non-dominant hand. Data were analyzed with Matlab (Mathworks Inc. Sherborn, MA, USA) and Ledalab (Benedek & Kaernbach, 2010).

2.1.1.4. Neuroendocrine response to HPA axis activity. Free salivary cortisol was measured in all groups before Phase 1 and 10 min after Phase 3. Samples were collected using Salivette sampling

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