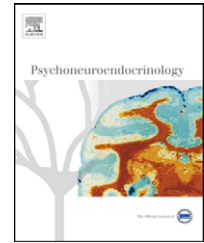




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Neuroendocrine and psychometric evaluation of a placebo version of the ‘Trier Social Stress Test’

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Summary The “Trier Social Stress Test” (TSST) is one of the most prominent laboratory stress paradigms. It is often used to investigate the effects of stress on cognitive or affective parameters. Such studies need a non-stress control condition. However, control conditions currently employed are often rather ill defined and do not parallel important modulating variables, e.g., physical or cognitive load of the TSST. We here introduce a placebo version of the TSST, which contains a free speech and a simple mental arithmetic task without uncontrollability and social-evaluative threat. In two studies, this control condition was evaluated using salivary markers of stress reactivity (cortisol and alpha-amylase) and a questionnaire for anticipatory cognitive stress appraisal (PASA). In experiment 1 participants who were treated with the placebo condition showed no cortisol response and a small, but significant salivary alpha-amylase (sAA) response. Both responses were significantly smaller than those of TSST-treated participants. The placebo-treated participants also rated the treatment situation as less stressful. In experiment 2 a crossover study with the use of an intercom to instruct the participants and ensure their compliance was conducted. Again there was a strong cortisol response to the TSST, which differed significantly from the cortisol levels observed during the placebo condition. Importantly the cortisol response was not influenced by treatment order (TSST or placebo first). However, in this study we found similar reactions between TSST- and placebo-treated participants with regard to sAA-response. We suggest that the introduced placebo protocol for the TSST is a promising tool for future psychobiological research. The exact procedure for a given experiment should be tailored to the specific needs of the empirical question studied.

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1. Introduction

Studies on psychological stress effects have used different types of stress tasks, like emotion induction procedures, public speaking tasks, cognitive tasks, noise exposure and tasks which combine public speech and cognitive tasks (Biondi and Picardi, 1999). Already Cannon (1935) empha-

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sized the importance of psychological and emotional stimuli in activating the “fight-or-flight-response”. Mason (1968a,b) referred to Cannon’s concept of stress and assumed that psychological variables such as novelty, unpredictability, anticipation of negative outcome and ego-involvement are factors that most commonly define a stressful situation. Nearly 40 years later Dickerson and Kemeny (2004) delivered a quantitative summary of the empirical evidences for Mason’s assumptions by meta-analytically reviewing more than a hundred laboratory stress studies. They found *uncontrollability* and *threat to the social self and the self-esteem* to be especially effective for inducing a significant cortisol response and being implemented into several psychosocial laboratory stressors. The combination of an evaluated public speech and a cognitive task integrates these factors and reliably stimulates the hypothalamus–pituitary–adrenal (HPA) axis in the laboratory (Linden et al., 1998; Biondi and Picardi, 1999; Dickerson and Kemeny, 2004; Kudielka and Kirschbaum, 2005)

One prominent laboratory stress procedure is the “Trier Social Stress Test” (TSST), published by Kirschbaum et al. (1993). This active performance task consists of a public speech and a mental arithmetic task (see description below). The participants’ self-esteem is threatened by a committee that pretends to evaluate the participants’ performance without any signs of social support. Thus the participant does not know whether his/her behaviour is accurate, which leads to feelings of uncontrollability. This procedure was designed to be in accordance with Mason’s assumptions (1968a,b) and is quite effective in activating the HPA and the sympathetic nervous system (SNS; e.g. Kirschbaum et al., 1999; Schommer et al., 2003; Kern et al., 2008).

Studies using the TSST can be divided into two experimental approaches. One strategy is to use the TSST to investigate the neuroendocrine stress response (e.g. cortisol response) and to compare the stress responsivity between certain groups of interest, e.g. women versus men (Kirschbaum et al., 1999; Kudielka and Kirschbaum, 2005), young versus old (Kudielka et al., 2004a), ‘normal’ versus diseased (Stones et al., 1999; Buske-Kirschbaum et al., 2002; Gaab et al., 2002; De Vente et al., 2003; Rohleder et al., 2003; Ahrens et al., 2008) or whites versus blacks (Chong et al., 2008). In these studies the cortisol stress response is the dependent variable of interest and the stress response is assessed by comparing poststress cortisol levels with a pre-stress baseline measure.

Another approach is to use the TSST to induce stress and to test the effects of stress and its biological responses on cognitive or affective outcome measures (e.g. Kuhlmann et al., 2005; Schoofs et al., 2008) or on physiological measures (e.g. Nater et al., 2006; Rohleder et al., 2006a). In these studies the TSST is used for the creation of the independent variable (stress versus no stress). In the latter design the stress condition has to be contrasted with a non-stress control condition. Although the TSST has been widely used, there is a lack of a standardized control condition or a “placebo version”. When researchers make use of an appropriate control condition the internal validity and the statistical conclusion validity increases, due to the exclusion of confounding variables (Cook and Campbell, 1979; Krauth, 2000). Thus an appropriate control condition helps to eliminate alternative explanations for

a detected causal relationship between an independent and a dependent variable. In psychoneuroendocrine research this is especially important in studies which investigate the effects of stress on cognitive or affective variables since these are vulnerable towards subtle changes in physical and cognitive demands. In the case of the TSST a control condition would be needed in order to demonstrate that observed effects are indeed caused by the stress response induced by the TSST and are not just secondary to the physical or cognitive demands of the task (e.g. giving a speech or calculating).

According to Shapiro and Morris (1978) placebo treatment is identical to the intended treatment, except its specific psychological or physiological effective factors. So, the appropriate control situation for the TSST must be equal to it except of its effective factors, namely the social evaluative component and the uncontrollability, according to the theory of Dickerson and Kemeny (2004). However, typical control conditions used for this treatment in past studies had often been quiescent and uneventful circumstances, in which the participants of the control group usually stayed alone in a room reading a magazine or completing questionnaires (e.g. Kirschbaum et al., 1993; Wolf et al., 2001; Domes et al., 2002, 2004; Nater et al., 2006, 2007a; Rohleder et al., 2006a). These control conditions differed from the TSST not only in their stressfulness, but also in the physical and cognitive load they impose on the participants. Those factors might influence neuroendocrine, affective and cognitive measures taken during or after the control condition. Body posture may be one factor that needs to be similar, since an orthostatic response may influence SNS parameters (Lake, 1979; Januszewicz et al., 1982; Goldstein, 1987; Carnethon et al., 2002). Thus, an appropriate placebo version of the TSST should require the participants to stand in an upright posture. Doing so, the physiological load of the participants of the control group would be comparable to that of the TSST group. Furthermore, the placebo version of the TSST should include tasks leading to a cognitive load comparable to the TSST, such as speaking aloud and/or performing mental arithmetic. In contrast to that, the participants must under no conditions perceive these tasks as stressful.

In our laboratories we have already started using a standardized placebo version of the TSST (e.g. Kuhlmann et al., 2005; Schoofs et al., 2008). We created a condition which is similar in physical and mental demand (speech and math task) to the TSST, but in which the stress inducing negative social evaluation component of the TSST is lacking. The participants of the placebo group are usually alone in a room and complete the tasks by themselves (see description below). Until now there is no neuroendocrine and psychological evaluation of the practicability of this standardized control condition of the TSST. Thus, the aims of the present set of two studies are as follows:

1. To evaluate a standardized placebo version of the TSST using neuroendocrine and psychometric stress measures.
2. To find out whether there is a difference in neuroendocrine parameters if an intercom is used to control the participants’ compliance during the placebo version.
3. To test for carryover effects within the use of crossover design with the TSST and its placebo version.

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