



Exogenous cortisol shifts a motivated bias from fear to anger in spatial working memory for facial expressions

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Summary

Studies assessing processing of facial expressions have established that cortisol levels, emotional traits, and affective disorders predict selective responding to these motivationally relevant stimuli in expression specific manners. For instance, increased attentional processing of fearful faces (attentional bias for fearful faces) is associated with fear and anxiety and diminishes after administration of the anxiolytic hormone testosterone. Conversely, attentional bias for angry faces has been associated with higher levels of approach motivation (e.g. anger) and testosterone, but lower levels of cortisol. This negative relation between cortisol levels and bias for angry faces was also seen in a test of biased working memory performance. However, previous research suggests that exogenous glucocorticoids acutely decrease fearful and inhibited behavior and increase aggressiveness.

Hypothesizing from these findings, the present study tested this spatial working memory for faces of various emotional expressions (neutral, happy, fearful, and angry) after double-blind, placebo-controlled administration of 40 mg cortisol in 18 healthy young men. It was predicted that cortisol would acutely attenuate memory bias for fearful expressions while increasing memory bias for angry expressions, in effect creating a shift in biased motivated memory from fear to anger. Results largely confirmed the hypotheses. This is the first causal evidence that cortisol differentially regulates spatial working memory for different facial expressions. Possible biological mechanisms are discussed.

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1. Introduction

This paper describes a study that was performed to causally investigate acute effects of cortisol on selective cognitive processing of facial expressions of emotion using an

experimental method probing biased spatial working memory. This was done to provide further information on the motivation-regulatory function of cortisol.

The hypothalamus–pituitary–adrenal (HPA) stress response is not limited to instances of physiological stress such as extraneous physical activity, it also occurs in response to motivationally relevant experiences. In humans, for example, psychological stressors such as the Trier social stress test (Kirschbaum et al., 1993), and panic induction (Strohle et al., 2000) can cause marked HPA responses. Even performance of experimental tasks involving perception of emotional faces or other emotional pictorial stimuli can modulate transient alterations in HPA activity (van Honk et al., 2000; Ellenbogen et al., 2006). Several affective disorders (anxiety disorders and depression) and related motivational traits are associated with prolonged alterations of circulating glucocorticoid (GC) levels and/or aberrations of motivational HPA responsivity and its negative feedback mechanisms. Analogue motivations in non-human primates and other animals are similarly related to HPA functioning (Kagan et al., 1987; Sapolsky, 1990; Brown et al., 1996; Strohle et al., 2000; Smider et al., 2002; Kalin, 2003; Pariante et al., 2004; Takahashi et al., 2005). By and large, stable elevation of GC levels can be considered to be involved in inhibited, avoidant motivation.

However, in various animal species and in humans, anticipatory GC rises are observed in situations of impending aggression and agonistic competition (Salvador, 2005; Summers et al., 2005). In various animal species, causal evidence has been obtained that both peripheral and central infusion of GCs can rapidly increase aggressive behavior (Brain et al., 1971; Poole and Brain, 1974; Hayden-Hixson and Ferris, 1991; Mikics et al., 2004). Sandi et al. (1996) report acute reduction of a fear response in rodents after peripheral GC administration. A few experimental studies have been performed in healthy human participants testing acute effects of cortisol on implicit measures of affective processes and on self-report measures of mood. Several of these studies support the notion of acute approach motivating effects or attenuation of fearful motivation (Buchanan et al., 2001; Reuter, 2002; Soravia et al., 2006; Tops et al., 2006), often in the absence of effects on self-reported mood. Thus, a picture emerges how prolonged elevated HPA activity is associated with avoidant, inhibited and fearful behavior, whereas acute and relatively short-term exogenous cortisol elevations may facilitate approach behavior, including aggression, and reduction of fear. Acute effects of GCs seem to cause a shift away from fear, toward approach motivation. This provides with a short-term psycho-endocrine feedback system restraining further cascading of the HPA stress response after its first anxiogenic initiation. In concert with facilitation of fearful responding after prolonged stress exposure, this would imply an adaptive system of fear regulation (Rosen and Schulkin, 1998; Schulkin et al., 2005).

Previous studies in our lab have shown relations between basal steroid hormone levels, approach and avoidance motivation, and implicit measures of selective memory and attention for facial expressions of threat. Biased cognitive processing (e.g., selective memory for, attention to, and perceptual processing of) emotionally relevant stimuli is central to most, if not all, forms of psychopathol-

ogy (Mogg and Bradley, 1998; Harvey et al., 2004). Also in healthy humans, relations between prevailing mood-states and such measures of implicit motivated behavior are reliably measured using a variety of experimental methods. In general, stimuli with motivationally important predictive validity, or stimuli which represent current cognitive concerns will be selectively attended and remembered better than neutral stimuli. Biased processing of human facial expressions, specifically expressions of threat, has been used successfully to probe implicit affective processes in psychoneuroendocrinological and psychopharmacological studies (Harmer et al., 2003, 2004; van Honk et al., 2005). Expression-specific emotional-cognitive processing can be observed: biased processing of angry faces has been reported for increased approach motivation, while biased processing of fearful faces is related to avoidant motivation (van Honk et al., 1998, 1999, 2001a, 2003, 2005; Mathews et al., 2003; Putman et al., 2004a; Fox et al., 2005; Putman et al., 2006). For instance, higher basal levels of cortisol predict reduced biased memory for the spatial location of angry facial expressions (Van Honk et al., 2003) and administration of testosterone reduces biased attention to fearful faces (van Honk et al., 2005).

The present study tested if a single administration of 40mg of cortisol acutely increases superior spatial working memory for angry facial expressions, as an implicit affective–cognitive measure of increased hostile, approach motivation. It was also hypothesized that this exogenous cortisol manipulation would reduce biased performance of fearful facial expressions as an implicit measure of decreased fearful, avoidant motivation. In effect, we thus hypothesize a shift from greater biased processing of fear-related cues toward greater biased processing of anger-related cues. These predictions are based on assumptions of fear-reducing and approach motivation-facilitating effects of acute cortisol administration as discussed above.

2. Methods

2.1. Participants

Participants were 20 healthy, non-smoking young men recruited from campus. All were drug free, had no history of psychiatric, endocrine or neurological illness, and agreed to refrain from use of alcohol for at least two days prior to testing. Mean age for the 18 participants whose data for the memory task allowed analysis (see results section below) was 20.3, ranging from 18 to 23 years. Participants received payment for participation in the study. Only male participants were tested to exclude possible confounding influences of menstrual cycle related endocrine variance. The study was approved by the local institutional review board in accordance with the declaration of Helsinki and all participants provided informed consent.

2.2. Materials

2.2.1. Stimuli and software

Stimuli were oval cut-outs of gray-scaled photographs of neutral, happy, fearful, and angry faces from eight actors (four males and four females) from the Karolinska Directed

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