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Stress and reward: Long term cortisol exposure predicts the strength of sexual preference

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HIGHLIGHTS

- We measured *effort expended to view erotic images of women versus men.*
- This heterosexual preference declines with self-reported anhedonia.
- It increases with long term exposure to endogenous cortisol.

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ABSTRACT

Healthy individuals tend to consume available rewards like food and sex. This tendency is attenuated or amplified in most stress-related psychiatric conditions, so we asked if it depends on endogenous levels of the 'canonical stress hormone' cortisol. We unobtrusively quantified how hard healthy heterosexual men would work to consume erotic images of women versus men and also measured their exposure to endogenous cortisol in the prior two months. We used linear models to predict the strength of sexual preference from cortisol level, after accounting for other potential explanations. Heterosexual preference declines with self-reported anhedonia but increases with long term exposure to endogenous cortisol. These results suggest that cortisol may affect reward-related behavior in healthy adults.

1. Introduction

Glucocorticoid hormones (GC) – *cortisol* in humans and *corticosterone* in rodents – are released from the adrenal gland in a characteristic daily cycle under central nervous control [36]. They are best known as the canonical "stress hormones" [33]: they are released in response to punishments – actual or anticipated challenges to homeostasis. While GCs modulate punishment-related behaviors such as startle and inhibition [10,69], GCs are unlikely to mediate primary defensive responses. Rather, they may be more compensatory, protecting the organism from its own primary stress response [39]. In fact, GCs are often seen as a component of the endogenous "reward system" together with opioids, endocannabinoids, and *dopamine* (DA) [39,49]. For example, GCs are readily secreted in response to food and drug rewards [49] at similar concentrations to those seen in response to stressors. Experimental GC manipulations also potently modify reward-related behaviors, as elaborated below. Finally, at physiological levels, they have positive reinforcing effects, for a review see [49]. For example, animals will learn to make operant responses which self-administer GC intravenously [48]. Such findings make them relevant to the understanding of reward-related psychiatric symptoms: anhedonia (loss of pleasure or lack of reactivity to pleasurable stimuli), hyperhedonia, addiction, eating, and gambling disorders. Yet there is no work to date on the role of long term systemic cortisol exposure on reward processing in humans. Here we review the evidence that chronic GCs influence reward processing and introduce a new behavioral assay to assess whether trait cortisol (basal levels of endogenous cortisol) can predict how hard healthy "non-stressed" subjects will work for natural rewards.

In non-stressed rat populations, chronic experimental suppression of endogenous glucocorticoids (via adrenalectomy) diminishes preference for sweet saccharin rewards [8]. This effect is specifically mediated by a reduction of GC: GCs also increase the motivation to drink sweet water after a period of carbohydrate withdrawal [8]. GCs are also critical

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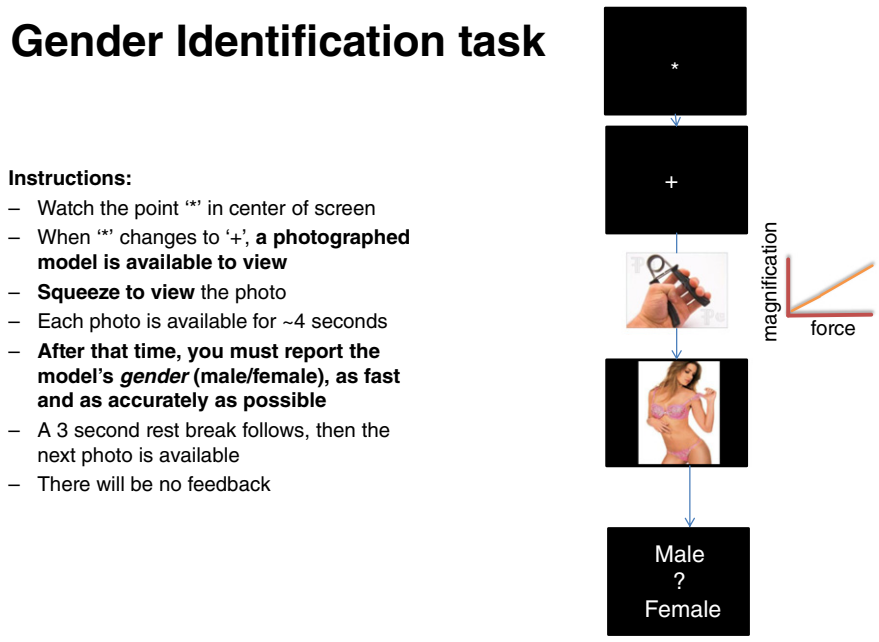

Fig. 1. The behavioral task. Instructions to subjects (left) and a time-line of one trial (right).

for the responses of rodents to rewarding drugs. Suppression of glucocorticoids, e.g. by adrenalectomy, again reduces behavioral responses to chemical rewards like morphine, amphetamine and cocaine [19,40] and decreases the work animals will exert to self-administer [39], whereas exogenous replacement of GC reverses this effect [8]. Furthermore, it has been suggested that under no-stress conditions, GCs may increase responsiveness to sexual rewards [61]. Consistent with this assumption, adrenalectomy reduces preferences for a (sexual) partner in monogamous male prairie voles, an effect reversed by GC replacement [20]. These results suggest that cortisol permits and/or drives reward-based behaviors. Puzzlingly, chronic treatment with GC leaves male rat sexual motivation unaffected [24,53] (despite reduced sexual performance [24]).

There is minimal human research into cortisol effects on reward-related behavior in healthy, non-clinical human populations [52,70]. It is not known whether basal differences in long-term cortisol exposure explain an individual's preference for natural reward. We aim to investigate this by measuring reward consumption behavior and long term systemic exposure to cortisol. We focus on objective behavioral assays [10,26,27,51,72] because behavioral and non-behavioral (questionnaire) measures of reward processing are often incongruent and therefore likely tap into different phenomena. Problems with subjective report per se include focusing illusions [34], framing effects [18], social conformity [2] and normality implications set by the questionnaire format [63]. In addition, it is often unclear how questionnaires connect to the reward protocols used in animal studies.

For ease, we focus on visually presented sexual rewards which animals will also work for [17]. While male subjects perform an unrelated task, we tracked the muscular effort they expended to magnify or 'approach' rewarding visual stimuli in real time (Fig. 1). Here, strong preferences for one class of stimuli are seen as relatively higher exertion (Fig. 2). Assuming that larger, more clearly visible, erotic images of females are more rewarding for male subjects, effortful magnification can be seen as analogous to approaching and consuming food or sexual rewards [45]. The strength with which subjects exerted muscular effort can therefore be taken as a measure of how strongly they prefer one image to another. Focusing on real-time viewing of available images, our task measures *consumption* preference in isolation from other aspects of reward processing (see Materials and methods). This is important because reward processing can be parsed into functionally distinct components[1] [6,71].

Our task thus measures consumption preferences without requiring participants to choose between alternatives, to act in the absence of the reward (i.e. to mentally *simulate* upcoming or abstract rewards at the time of acting), to learn or predict reward value [50] or to wait for temporally delayed rewards [25,28]. In this way we attempt to isolate the determinants of simple consumption preference per se, while excluding explanations based on high-order cognition (e.g. decision-making deficits).

Based on these considerations we measured individual differences in long term (prior two months) endogenous cortisol, and hypothesized that increased cortisol exposure predicts increased preference for the consumption of sexual rewards. We also expected that self-reported anhedonia predicts diminished preference for these same reward stimuli.

2. Materials and methods

2.1. Subjects

Thirty six male undergraduates (18–32 years old, median 21) were recruited by email from the University of Zurich, Switzerland. Five subjects were excluded: two lacked sufficient hair for the cortisol analysis, one had clinical-range stress-related symptoms (score of 21 in Beck's Depression Inventory, indicating moderate depression), one subject showed a behavioral pattern indicative of possible homosexual orientation (see Supplementary data), and one was a statistical outlier (Cook's distance [13] was >1 in the regression below). The study was approved by the local review board and all subjects provided written informed consent.

2.2. Behavioral measures

Fig. 1 outlines the behavioral task (see also Supplementary data). The task comprised 80 trials, with 10 male and 10 female pictures presented 4 times each, i.e. $80 = 10 \times 2 \times 4$. Trials occurred in a completely

[1] Correspondingly there is a toolbox of behavioral measures in animals, including unconditioned responses (orofacial taste reactions to palatable liquids presented intraorally [5]), choice behavior (effort-related T-mazes [58]) and progressive ratio [31].