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Amygdala activity to fear and anger in healthy young males is associated with testosterone

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Summary Neuroimaging studies have documented modulation of the activity of the amygdala — a key node in the neural network underlying emotion perception and processing, and one that has also been associated with regulating aggression — by exogenous testosterone. However, results on the impact of normal range testosterone levels on explicit emotion recognition as a prerequisite for social interaction and amygdala activation in healthy young males are missing.

Hence, we performed functional MRI at 3 T in a group of 21 healthy males during explicit emotion recognition with a protocol specifically optimized to reliably detect amygdala activation. We observed similar amygdala activation to all emotions presented without any effect of gender of poser or laterality. Reaction times to fearful male faces were found negatively correlated to testosterone concentration, while no significant effects emerged for other emotions and neutral expressions. Correlation analyses revealed a significant positive association between testosterone levels and amygdala response to fearful and angry facial expressions, but not to other expressions. Hence, our results demonstrate that testosterone levels affect amygdala activation and also behavioral responses particularly to threat-related emotions in healthy young males. We conclude that these findings add to our understanding of emotion processing and its modulation by neuroendocrine factors.

1. Introduction

Converging evidence has shown that testosterone levels are associated with basic social abilities, e.g., facial mimicry as one component of empathic behavior (Hermans et al., 2006a), mood and selective attention to angry faces (Van

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Honk et al., 1999), and also moderation of the reinforcing qualities of angry faces (Wirth and Schultheiss, 2007). While animal research has unequivocally demonstrated the connection between elevated testosterone levels and increased aggressiveness (e.g., Lumia et al., 1994; Melloni et al., 1997) in human studies only correlational evidence has been reported (e.g., Dabbs et al., 1995; Archer, 2006). Regarding the possible anxiolytic effect of testosterone, this phenomenon has been replicated many times and in a large variety of animal species (e.g., Aikey et al., 2002). Although there is evidence for antidepressant effects in hypogonadal depressive patients after testosterone treatment (e.g., Wang et al., 1996), clear reductions in fear after testosterone administration or treatment have rarely been reported for humans (Van Honk et al., 2005; Hermans et al., 2006b).

The special role of the amygdala in the processing of threat-related stimuli, in particular anger and fear is well documented (e.g., Adolphs, 2002). Consequently, it has been argued to be strongly involved in the pathways controlling aggression, and most neuroimaging studies have consistently observed amygdala activation to angry facial expressions (e.g., Whalen et al., 2001).

Recently, several neuroimaging studies have shown a modulating effect of testosterone on amygdala activation: Van Wingen et al. (2008a) used an emotion matching task and administered a single dose of testosterone to middle-aged healthy females. This modulated amygdala activation, leading to a higher reactivity comparable with the one of young, healthy females. Also, applying exogenous testosterone to healthy young females who were presented with angry faces in a passive viewing task, Hermans et al. (2008) observed stronger amygdala activation in subjects to whom higher testosterone doses had been administered.

Studies investigating possible association of testosterone levels with explicit emotion recognition, another basic prerequisite for social interaction, and the underlying amygdala activation are totally missing. Hence, we investigated whether normally distributed testosterone levels in healthy young males exert an influence on explicit emotion recognition and amygdala reactivity. We performed functional magnetic resonance imaging (fMRI) using an explicit emotion recognition paradigm in healthy young males. Based on previous results from our group (e.g., Habel et al., 2007; Derntl et al., 2008a), we hypothesized amygdala activation to all emotions presented. Moreover, we hypothesized a significant positive association between testosterone levels and amygdala reactivity in healthy males especially to threat-related stimuli as shown by previous fMRI studies in healthy females (Hermans et al., 2008; Van Wingen et al., 2008a) and behavioral data (Van Honk et al., 1999; Wirth and Schultheiss, 2007). In light of assumptions that males respond more strongly to male faces (cf. Mazurski et al., 1996), we also investigated this aspect by presenting both female and male faces.

2. Materials and methods

2.1. Sample

Twenty-one right-handed healthy males aged 21—33 years (mean age 25.1 years, S.D. = 3.5) were enrolled in the study. Participants were all students (mean education 17.9 years, S.D. = 3.2) and were recruited by advertisements at the University of Vienna and the Medical University of Vienna, Austria. The study was approved by the ethics committee of the Medical University of Vienna and written informed consent was obtained from all subjects prior to the examination.

The presence of psychiatric disorders (according to DSM IV) was excluded on the basis of the German version of the Structured Clinical Interview for DSM (SCID, Wittchen et al., 1997) conducted by experienced clinical psychologists. The usual exclusion criteria for MRI were also applied and all participants had a negative drug screening.

All subjects performed above average according to norms on several neuropsychological tasks taken from the computerized neuropsychological test battery (Gur et al., 1992) engaging nonverbal intelligence, cognitive flexibility, visual learning and memory. No subject was alexithym, measured with the Toronto Alexithymia Scale 20 (Bagby et al., 1994). All tests were presented with an Apple MacIntosh G3 Powerbook using Powerlab software (System General, Milpitas, CA, USA).

Blood samples were taken on the day of fMRI measurements and only males without any hormone treatment were included to prevent any influences of external hormone administration. Assays were analyzed by the Institute for Laboratory Diagnostics of the Medical University of Vienna, Austria, using an electrochemiluminescence-immunoassay (ECLIA, Johnson et al., 1993). The intra-assay accuracy was over 90% (i.e., coefficient of variation was 4—8%) and the sensitivity of each assay was 0.2 ng/ml.

2.2. Functional tasks

We applied the same explicit emotion recognition task as described in detail elsewhere (Derntl et al., 2008a). Briefly, the stimulus material consisted of 72 color photographs of facial expressions portraying an equal number of the five basic emotions (anger, disgust, fear, happiness and sadness) as well as neutral expressions. Subjects were instructed to choose the correct emotion from two verbal possibilities presented on the left and right of the image, by pressing the corresponding button of a response box using the right hand. One of the options was correct and the other was selected at random from all other choices. Emotional facial expressions were presented for a maximum of 5 s with a variable interstimulus interval (ISI) ranging from 12 to 18 s (during which subjects viewed a scrambled face with a central crosshair). Responses triggered immediate progression to the next ISI. Stimuli were projected onto a screen and viewed by the participants via a mirror mounted on the head coil. The presentation of images, recording of responses and acquisition of scanner triggers (one per repetition time) was achieved using the Presentation software package (Neurobehavioral Systems Inc., Albany, CA, USA).

2.3. Behavioral data analysis

The behavioral data acquired during scanning (recognition accuracy and reaction time) were analyzed with repeated measures ANOVAs, with emotion and gender of poser as within-subjects factor. Greenhouse—Geisser corrected