ORIGINAL ARTICLE

Differential modulation of impulsive behavior by loneliness and testosterone in adolescent females

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Abstract

OBJECTIVE: Adolescence is characterized by increases in loneliness, impulsiveness and circulating testosterone levels. We investigated the relationship between these characteristics in adolescent females.
METHODS: For this purpose, we measured impulsivity and loneliness by means of a Go/No-go task and the UCLA loneliness scale, respectively. Testosterone levels in saliva were measured by Enzyme-Linked Immunosorbent Assay (ELISA).
RESULTS: The results showed that testosterone and loneliness have a positive relevance to impulsivity in adolescent females, whereas there was no relationship between loneliness and testosterone levels.
CONCLUSIONS: These results suggest that testosterone and loneliness modulate impulsivity via distinctive pathways.

INTRODUCTION

Adolescence is a period of physical, psychological and social transition from childhood to adulthood (Sebastian *et al.* 2010). One of the characteristic behaviors of adolescents is a high social interaction. Adolescents spend more time with peers (see Csikszentmihalyi & Larson, for review), place greater value on peers' approval, advice and opinions (Brown 1990) and are more concerned about maintaining peer relationships (Parkhurst & Hopmeyer 1988), which enable them to be independent from their parents. As peer relationships become more important during adolescence, the potential consequences of rejection by peers, including loneliness, become more severe. A review of related research has shown that the prevalence of loneliness peaks during adolescence (Heinrich & Gullone 2006).

Another characteristic of adolescent behavior is impulsivity. Adolescents have long been described as excessively prone to rash and impulsive behavior, as exemplified by drug abuse, unintentional injuries (especially car accidents), and unprotected sexual activities (Arnett 1992). Impulsivity is also regarded as a core symptom of psychiatric disorders, including conduct disorders, eating disorders, and addiction, which onset in adolescence (Moeller *et al.* 2001). The onset of eating disorders peaks between 14 to 18 years (Phelps & Bajorek 1991), and most forms of addictive behavior (e.g. smoking, drinking) increase rapidly in adolescence (SAMHSA 2004). Additionally, previous research using behavioral tasks (e.g., Go/No-go tasks) have shown that adolescents were more impulsive than children or adults (Somerville *et al.* 2011).

Maturation of the reproductive system during adolescence results in elevated levels of gonadal

steroid hormones. In addition to secondary sexual characteristics influencing the physical body appearance, gonadal hormones contribute to the development of neural function by binding to androgen and estrogen receptors in the brain (Casey *et al.* 2010). The elevation of these hormones during adolescence have been shown to sculpt and remodel cortical and limbic circuits, and are related to characteristic behaviors in adolescence (Giedd *et al.* 1999; Lenroot & Giedd 2006).

The aim of the present study is to investigate the relationships between loneliness, impulsivity and testosterone levels among adolescents. In this research, we investigated these relationships by focusing on adolescent females because the need for peer acceptance reaches a peak at age 15–16 in females (Kloep 1999) and because endogenous plasma testosterone is related positively with young females with impulsive behavior (Bjork *et al.* 2001) or bulimia nervosa (Sundblad *et al.* 1994). Furthermore, there have been many reports of correlations of salivary testosterone with various female behaviors (López *et al.* 2009; van Anders & Watson 2006, 2007; van Anders *et al.* 2007; Hamilton & Meston 2010; Hamilton *et al.* 2009; Oliveira *et al.* 2009; Pollet *et al.* 2011; Stanton *et al.* 2011). Therefore, we measured impulsivity, loneliness and salivary testosterone levels in adolescent females by means of a Go/No-go task, the UCLA loneliness scale and Enzyme-Linked Immunosorbent Assay (ELISA) method, respectively, to investigate the relationships among these factors.

METHODS

Participants

A total of 36 healthy female adolescents aged between 15 to 17 years (mean age 16.1 ± 0.72 years) participated in the present study. None of the participants used hormonal contraceptives or medications that affect sex steroids. The participants were recruited from two high schools in different geographical areas of Nagasaki prefecture in Japan, which are representative of a range of socioeconomic status backgrounds. All participants provided written informed consent prior to the start of the experiment. The experimental protocol was conducted in accordance with the Declaration of Helsinki. The present study was approved by the Ethics Committee of the Nagasaki University Graduate School of Biomedical Sciences.

Measures of testosterone levels in saliva

Saliva samples were collected from each participant between 12 p.m. and 1 p.m. on the day of the experiment (15–30 min before lunch), by having them spit through a straw into a small polypropylene tube. Saliva samples were frozen and stored at −80 °C in the laboratory. Testosterone was assayed in saliva duplicates using an ELISA technique (Salimetrics, State College, USA), with each sample being analyzed in duplicate. The average intra-assay coefficient of variation (CV) was 4.5%. In the present study, we did not control for menstrual cycle phase for each participant, because a previous study has indicated that these accordant but small effects do not need to be controlled unless the menstrual cycle itself is of interest (Dabbs 1990).

Measures of loneliness

In order to assess the loneliness of each participant, we used the UCLA loneliness scale (revised), a 20-item self-administered questionnaire measuring general feelings of social isolation, loneliness, and dissatisfaction with one's social interactions (Russell 1996). Participants were asked to rate how often they felt the way described by the items on a scale ranging from 1 (never) to 4 (often). The UCLA scale has been shown to have high reliability (alpha = 0.94) and is widely used. High scores reflect a high degree of loneliness. We used the Japanese version to assess subjective loneliness of all participants in the experiment (Moroi 1991).

Measures of impulsivity: The Go/No-go task

Participants performed a behavioral task of the Go/No-go type, which has been widely used as a measure of impulsivity and the validity of which has been shown by many studies (LeMarquand *et al.* 1999; Nomura *et al.* 2006). On Go/No-go task, participants are instructed to make responses on Go trials as quickly as possible but to withhold responses on No-go trials. Participants learned by trial and error to press a button for Go stimuli and not to press for No-go stimuli, all of which are consisted of a random set of ten two-digit numbers (one half are Go stimuli and the rest are No-go stimuli) (LeMarquand *et al.* 1999; Nomura *et al.* 2006). After the first 30 trials as a practice session, participants continued to perform the last 70 trials as an experimental session. Correct responses were rewarded with a consonant tone and presentation of the word "Hit" on the computer screen. Incorrect responses were punished by a dissonant tone and presentation of the word "Error".

The number of commission errors (CER; inappropriate responses to No-go stimuli) and omission errors (OER; inappropriate responses to Go stimuli) were summed separately across the 70 trials. To eliminate the effect of total errors within participants, commission errors indices were calculated according to the following equation and were used as a measure of impulsivity.

$$\text{CER index} = (\text{CER} - \text{OER})/(\text{CER} + \text{OER}) \times 100$$

When CER indices are positive, the values indicate that CER were included at a higher rate than OER, regardless of total number of errors.

RESULTS

Pearson's correlation analysis was conducted to examine the relationships between salivary testosterone levels, loneliness and the CER index. As shown in

Figure 1A, the salivary testosterone level was significantly correlated with the CER index (r (36)=0.352, p<0.05). The loneliness score was also significantly correlated with the CER index (r (36)=0.330, p<0.05; Figure 1B). However, there was no significant correlation between salivary testosterone level and loneliness score (r (36)=0.152, *n.s.* Figure 1C).

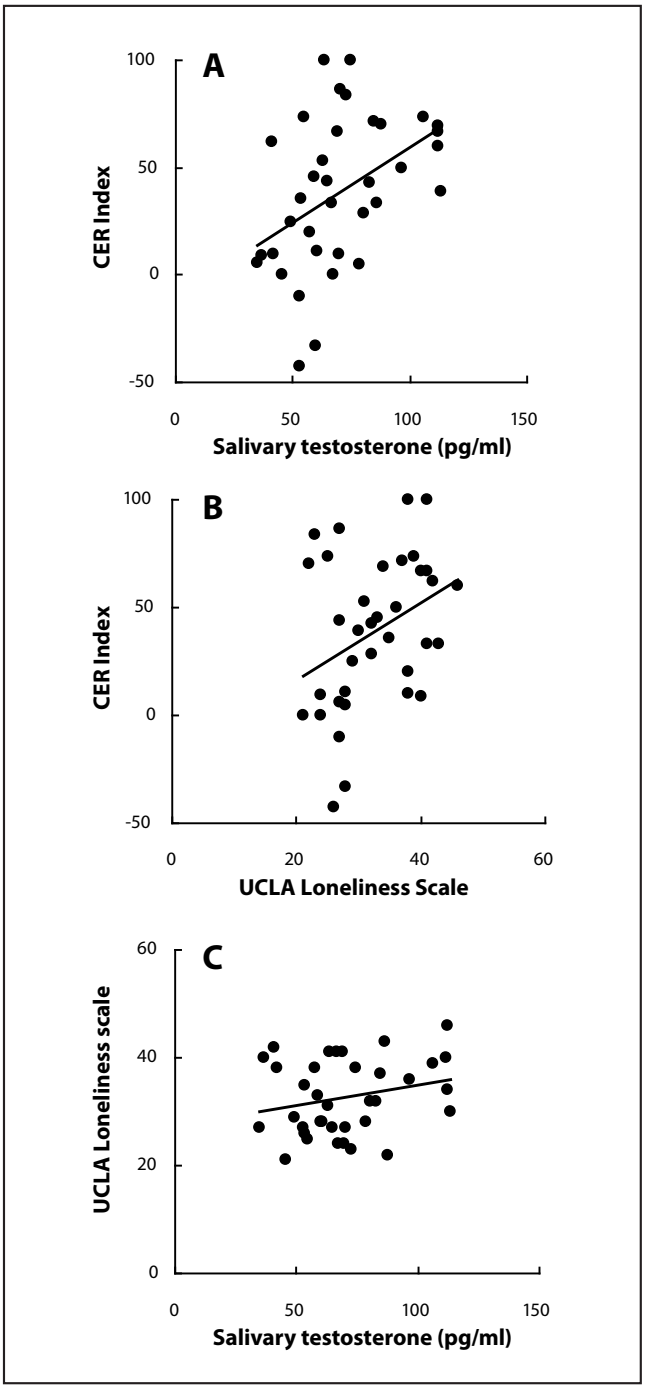

Fig. 1. Relationship between the salivary testosterone levels, impulsivity and the UCLA loneliness score (**A**: Testosterone levels and CER index, **B**: Loneliness score and CER index, **C**: Testosterone levels and Loneliness score)

DISCUSSION

In the present study, we investigated the relationships between loneliness, impulsiveness and salivary testosterone levels, which are characteristic features in adolescent females. The results showed that both testosterone and loneliness had positive relevance respectively to impulsivity in adolescent females, whereas there was no correlation between loneliness and salivary testosterone levels. These results suggest that adolescent females with high testosterone levels are more impulsive than females with low testosterone levels, and that lonely females are more impulsive than social females. On the other hand, there was no correlation between salivary testosterone level and loneliness, suggesting that testosterone and loneliness modulate impulsivity via distinctive pathways.

To assess the impulsiveness of adolescent females, we used a Go/NoGo task, which is widely used to measure impulsiveness (LeMarquand *et al.* 1999; Nomura *et al.* 2006). Bjork *et al.* (2001) used a similar method to assess impulsivity for adult females and compared it with blood testosterone levels, which showed a positive relationship between blood testosterone levels and impulsivity. However, the subjects in their study were aged 32 to 55, despite the fact that testosterone levels in adult females change with age (Davison *et al.* 2005). In contrast, the age of the participants in the current study were limited to 15~17 years. Our current results were consistent with those in the previous study that confirmed the validity of a Go/NoGo task to measure impulsivity and salivary testosterone level as a good indicator of circulating testosterone levels. In light of the current and previous studies, we speculate that impulsivity is modulated by testosterone level in women from adolescence to menopause.

On the other hand, adolescence is a specific age period, when testosterone levels are remarkably increased and impulsive behaviors often observed (Arnett 1992). These two adolescent characteristics are well known but the relationships between them have not been investigated directly. The current study found that impulsivity is dependent on testosterone levels in adolescent females, and this finding might be linked to the symptoms of mental disorders. Eating disorders, which are particularly common in adolescence females, show impulsive symptoms such as binge eating, followed usually by vomiting and/or by taking laxatives, diuretics or excessive exercise (Phelps & Bajorek 1991). Furthermore, a previous report indicated that the testosterone level was linked positively to eating disorders (Sundblad *et al.* 1994), suggesting that testosterone levels are also involved in pathological impulsivity.

In the present study, we could not clarify any target brain sites of testosterone action, but the amygdala is a candidate region. Many of the biological actions of testosterone and other androgens are mediated by androgen receptors (ARs), which were abundantly

expressed in the amygdala (Rubinow & Schmidt 1996). Testosterone-dependent amygdala activation may cause hyperactivation of the striatal system (Crews & Boettiger 2009). Thus, striatal hyperactivation was observed during reward processing, when adolescents were required to assess an incentive cue, but showed elevation during reward anticipation (Geier *et al.* 2010), which suggests that adolescents may have limited capacity to assess potential reward outcomes and have exaggerated reactivity when anticipating reward compared with adults. These behavioral characteristics seem to lead adolescence impulsivity (Galvan 2010).

A positive correlation was found between loneliness and impulsivity in adolescent females. It is well known that the prevalence of loneliness peaks during adolescence (Heinrich & Gullone 2006). Furthermore, severe loneliness often results in depressive moods (Cacioppo *et al.* 2006; Cacioppo *et al.* 2010), which have been proven to trigger impulsive behaviors (Marlatt & Gordon 1985; Sinha 2009). It is, therefore, reasonable to conclude that loneliness modulates impulsivity in adolescent females.

The current study did not clarify the neural mechanism underling how loneliness modulates impulsivity in adolescent females. Considering the fact that social rejection brings about loneliness, ventrolateral prefrontal cortex (vlPFC) and/or dorsal anterior cingulate cortex (dACC) can be considered as candidate regions. In a brain imaging study using a virtual ball-tossing game task, it was found that vlPFC has a negative and dACC has a positive correlation with negative emotion induced by social rejection (Eisenberger *et al.* 2003; Masten *et al.* 2009). Furthermore, previous studies using a Go/NoGo task showed that the vlPFC and dACC play a crucial role in impulsiveness in adults (Menon *et al.* 2001; Watanabe *et al.* 2002). Together with the previous study, the present results suggest the possibility that decreased activity in vlPFC and increased activity in dACC induced a negative mood such as loneliness, leading to higher impulsivity.

In conclusion, the present results showed that testosterone and loneliness have a positive relevance to impulsivity in adolescent females, whereas there is no relationship between their loneliness and testosterone levels. These results suggest that testosterone and loneliness were involved in impulsivity with distinctive pathways. Although we did not investigate directly the neural mechanism underlying this effect, future studies that combine the present experimental paradigm with neurophysiological indicators of VLPFC activity using brain imaging techniques will be fruitful in further elucidating mechanisms underlying impulsivity as feature of adolescent behavior.

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