Development of Risk Taking: Contributions from Adolescent Testosterone and the Orbito-frontal Cortex

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Abstract

■ The role of puberty in the development of risk taking remains poorly understood. Here, in a normative sample of 268 participants between 8 and 25 years old, we applied a psycho-endocrine neuroimaging approach to investigate the contribution of testosterone levels and OFC morphology to individual differences in risk taking. Risk taking was measured with the balloon analogue risk-taking task. We found that, corrected for age, higher endogenous testosterone level was related to increased risk taking in boys (more explosions) and girls (more money earned). In addition, a smaller medial OFC volume in boys and larger OFC surface area in girls related to more risk taking. A mediation analysis indicated that OFC morphology partly mediates the association between testosterone level and risk taking, independent of age. Mediation was found in such a way that a smaller medial OFC in boys potentiates the association between testosterone and risk taking but suppresses the association in girls. This study provides insights into endocrinological and neural underpinnings of normative development of risk taking, by indicating that OFC morphology, at least partly, mediates the association between testosterone and risk-taking behavior. ■

INTRODUCTION

Adolescence, which involves the transition between childhood and adulthood, is often described as a period of increased risk taking and sensation seeking (Burnett, Bault, Coricelli, & Blakemore, 2010; Figner, Mackinlay, Wilkening, & Weber, 2009; Crone, Bullens, van der Plas, Kijkuit, & Zelazo, 2008). During adolescence, individuals move away from the safe parent environment: They start to actively explore their social environment, and they develop intimate peer relations, which eventually help them to obtain mature social goals (Steinberg, 2008). Thus, there is a natural tendency to explore and take risks, which leads to learning and discovery but can sometimes also lead to risky and dangerous behaviors (Dahl, 2004). A key question is to understand the biological causes of this period of vulnerability.

An intriguing recent line of research has demonstrated important links between the steroid hormone testosterone and individual differences in risky behavior. For example, in male and female adults, enhanced endogenous levels of testosterone contribute to increased interpersonal dominance, aggression, and risky behavior (for reviews, see Stanton & Schultheiss, 2009; van Honk et al., 2004). In addition, increased endogenous levels of testosterone (Stanton, Liening, & Schultheiss, 2011) as well as pharmacologically increased levels of testosterone (Goudriaan et al., 2010) are associated with higher risk taking. This leads to the question whether natural fluctuations in testosterone levels, which occur during puberty, are associated with higher risk taking. It is well documented that puberty involves a steep increase in testosterone levels that is most prominent in boys but is also present in girls (Grumbach, 2002). Initial evidence for this potential relation between testosterone levels and risk taking in adolescence comes from normative studies showing that increased testosterone levels in boys (and to some extent in girls) are associated with risk-taking tendencies, assessed with self-report questionnaires (de Water, Braams, Crone, & Peper, 2013; Vermeersch, T'Sjoen, Kaufman, Vincke, & Van Houtte, 2010; Vermeersch, T'Sjoen, Kaufman, & Vincke, 2008). A study directly testing this relation with an experimental risk-taking task is still lacking.

A candidate brain region that is thought to modulate the relation between testosterone and risk taking is the medial OFC: The medial OFC is involved in value-based decision making (for a review, see Wallis, 2012) and exploratory behavior (Daw, O'Doherty, Dayan, Seymour, & Dolan, 2006). Higher endogenous levels of testosterone were associated with less engagement of the medial OFC when controlling impulses (Mehta & Beer, 2010), and administration of testosterone leads to decreased functional connectivity between the OFC and the amygdala (Bos, Hermans, Ramsey, & van Honk, 2012; van Wingen, Mattern, Verkes, Buitelaar, & Fernandez,

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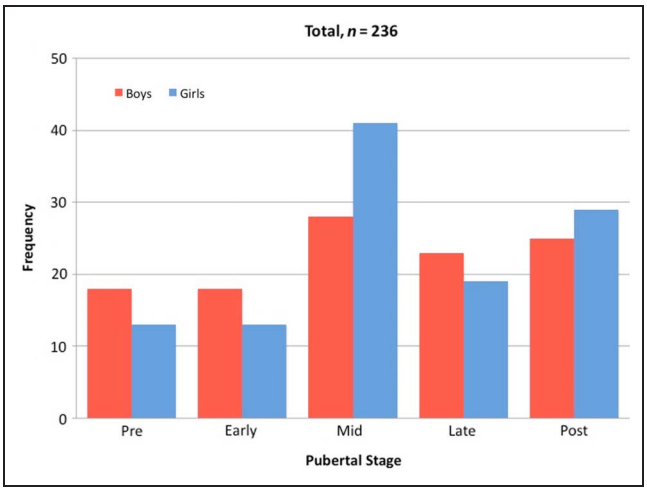

Figure 1. Pubertal stage distribution across the sample. Pubertal stage was based on the Petersen Developmental Stage, divided into category scores. Within each pubertal group, there were at least 30 participants.

2010). In addition, the OFC is critically implicated in risk taking in adolescence, for example, Fukunaga, Brown, and Bogg (2012) recently showed robust ventromedial PFC activity when participants chose to continue inflating the balloon (risky option). Moreover, this region is also active when taking "wheel of fortune" risks (Van Leijenhorst et al., 2010) and is highly active in adolescence.

It has previously been argued that brain areas underlying risky behavior are being structurally "shaped" by pubertal hormones (Peper & Dahl, 2013), possibly predisposing to higher sensitivity to sensation seeking and/or exploratory behavior (Crone & Dahl, 2012). These prior findings made us hypothesize that the link between endogenous levels of risk taking during adolescence may be dependent on the relative structural maturation of the OFC, an area of the brain known to develop structurally until early adulthood (Shaw et al., 2008).

In this study, we used the Balloon Analogue Risk Task (BART; Lejuez et al., 2002) as a measure of risk taking. In this task, participants have the opportunity to inflate virtual balloons to increase potential monetary reward, but each pump concurrently increases the risk that the balloon will explode and that all earnings for that trial will be lost (Lejuez et al., 2002). At any point, participants could decide to cash out to collect the reward. The BART has predictive validity to real-world risk taking and has been administered in a wide variety of populations, including healthy developing children and adolescents (Aklin, Lejuez, Zvolensky, Kahler, & Gwadz, 2005). A sample of 268 participants, equally distributed among ages 8–25 years and with a relative oversampling around pubertal age and an equal number of men and women, completed the BART and performance was related to (1) general pubertal development, (2) testosterone levels, and (3) medial OFC morphology. We hypothesized that, compared with same-aged peers, advanced pubertal development and heightened testosterone production would be related to higher risk taking. We expected that OFC morphology would mediate the association between testosterone levels and risk-taking behavior, such that increased testosterone levels would be related to relatively late structural OFC development and thereby increased sensitivity to risk-taking behavior (Peper & Dahl, 2013).

METHODS

Participants

A total number of 268 participants were enrolled in the study (131 boys) between 8 and 25 years old. Of these 268 participants, a total number of 236 (115 boys = 49%) successfully completed the neuroimaging session, hormonal sampling as well as behavioral testing. Mean age of this final group was 14.3 years (*SD* = 3.9 years), and it was ensured that, within each pubertal group (prepuberty, early puberty, midpuberty, late puberty, and postpuberty), there was an *n* of at least 30 (Figure 1). We oversampled at age 12–13 years in girls and 13–14 years in boys, corresponding to midpuberty. This selection allowed us to test for age versus puberty effect by including participants before, within, and after puberty, with most variation within puberty. Children were recruited from elementary schools and high schools in the Netherlands, and young adults were recruited from the Leiden University and surrounding community. All participants had normal intelligence (mean = 109.6; *SD* = 10.5) approximated using block design and similarities of the Wechsler Intelligence Scale for Children-III for children up to 16 years old and of the WAIS-IV for 16 years old and above (Table 1). Participants were free from any history of psychiatric, endocrinological, or neurological illnesses, screened by an interview. The internal review board from the Leiden University approved the study. Informed consent was obtained from all participants, and additional informed

Table 1. Demographic Characteristics of the Sample (Means [*SD*])

	Boys (n = 115)	*Girls (n = 121)*
Age (years)	14.5 (4.0)	14.1 (3.9)
PDS	3.0 (1.4)	3.3 (1.3)
Testosterone (pmol/L)	221.6 (197.1)	19.3 (13.3)**
Z testosterone	0.034 (1.0)	0.033 (1.0)
BART explosions	11.5 (3.8)	10.6 (3.7)*
BART money earned (in €)	8.6 (3.6)	7.9 (3.6)*
Estimated IQ	110.5 (10.9)	108.9 (10.2)

The PDS is 1–5. Estimated IQ is based on the Wechsler Intelligence Scale for Children-III subscales similarities and block design (<17 years old) and WAIS-IV for young adults.

*$p < .05$.

**$p < .0001$.

consent was obtained from the parents of children under the age of 17 years.

Pubertal Measures

Puberty Developmental Scale (PDS)

A self-report questionnaire containing questions on secondary sexual characteristics was administered to children and adolescents (up to 18 years old). At a 4-point scale, participants had to indicate whether a physical characteristic (1) had not yet started to develop, (2) was showing the first signs, (3) was showing very clear development, or (4) had already finished developing (Carskadon & Acebo, 1993). Puberty category scores were subsequently calculated and were based on body hair growth, voice change, and facial hair growth for boys and body hair growth, breast development, and menarche for girls, leading to five categories: prepubertal, early pubertal, midpubertal, late pubertal, and postpubertal.

Testosterone

Testosterone was determined in morning saliva samples. Boys and girls collected their saliva by passive drool at home, directly after waking up. Participants were instructed not to eat or brush their teeth before collecting saliva.

To control for hormonal fluctuations across the menstrual cycle, postmenarcheal girls collected saliva samples on the same day within the early follicular phase of the menstrual cycle (Day 7), when hormone levels (e.g., progesterone) are relatively low (Peper et al., 2013; Mihm, Gangooly, & Muttukrishna, 2011; Dorn, Dahl, Woodward, & Biro, 2006). Similarly, girls using oral contraceptives (n = 16) collected a saliva sample on the last day within their stopping period (Day 7). Girls using contraceptives without a stopping period, such as hormonal intrauterine devices (e.g., Mirena), were excluded from participating in this study. Compliance with saliva collection was ensured by reminding participants individually the day before they had to collect it. This reminder was either done by phone or by e-mail.

The saliva samples of boys and girls were assayed for testosterone levels at the Department of Clinical Chemistry of the Free University Medical Centre. The lower limit of detection was 4 pmol/L. Salivary T was determined by isotope dilution—online solid phase extraction liquid chromatography—tandem mass spectrometry (Peper et al., 2013). Intra-assay coefficients of variation were 11% and 4% at 10 and 140 pmol/L, respectively, and interassay coefficients of variation were 8% and 5% at 31 and 195 pmol/L, respectively (de Water et al., 2013).

BART

The BART task was adapted from Lejuez et al. (2002). On a computer screen, participants saw a small balloon, a balloon pump, a button with "total earned," a button with "earned on last balloon," and a cash (€€€) button. By mouse clicking on the pump, the balloon was inflated, and 0.05€ was gained for each pump. The total amount of collected money on each trial was stored in a temporary bank (not displayed on the screen). Participants could decide to stop inflating the balloon at any time and collect their money by clicking the €€€ button. Then, their money was transferred to the permanent bank (accompanied by a slot-machine sound), and the amount was displayed on the screen. When the balloon exploded, the computer played a "pop" sound, and the temporarily saved money on that trial was lost.

The BART consisted of 30 trials, including 10 orange, 10 yellow, and 10 blue balloons presented in a random fashion. Each color had a different probability of exploding, with an average explosion point of 4, 16, and 64, respectively (Lejuez et al., 2002). Participants were told that, at some point, each balloon would explode and that this explosion could occur as early as the first pump all the way up to the point at which the balloon had expanded to fill the entire computer screen. No information was provided on the diverse explosion probabilities of the balloons. Participants were instructed to gain as much money as possible.

The variables of interest on the BART were total number of explosions, total amount of earned money, and the adjusted number of pumps (i.e., accumulative pumps on trials on which the balloon did not explode; Lejuez et al., 2002). The variables "total amount of earned money" and "adjusted number of pumps" were highly correlated (correlation of .94 in our sample); therefore, we chose to report total amount of earned money and number of explosions only. Analyzing the blue balloons only yielded similar results.

Structural MRI

Acquisition

Scanning was performed on a 3-T Achieva whole-body scanner (Philips, Best, The Netherlands) at the Leiden University Medical Center. A high-resolution 3-D T1-FFE scan was obtained (repetition time = 9.760 msec, echo time = 4.59 msec, flip angle = 8°, 140 slices, 0.875 × 0.875 × 1.2 mm^3 voxels, field of view = 224 × 168 × 177 mm^3) with a total scan duration of 296 sec. All T1 scans were reviewed and cleared by a radiologist. MRI scans were individually checked on motion artifacts or other sources of signal loss.

Preprocessing and Measurement of OFC Morphology

Cortical reconstruction and volumetric segmentation was measured automatically using the publicly available software FreeSurfer version 5.0 (surfer.nmr.mgh.harvard.edu/; Fischl & Dale, 2000; Dale, Fischl, & Sereno, 1999;

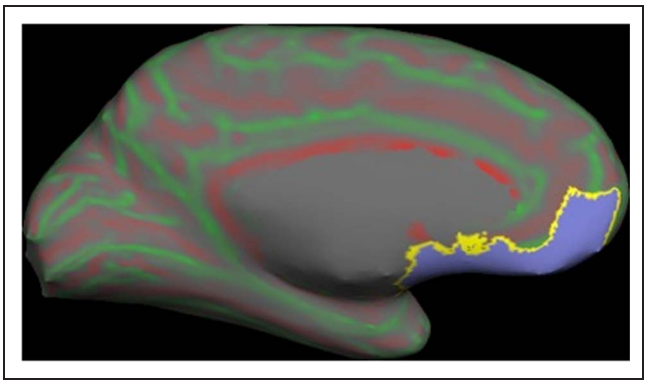

Figure 2. The medial OFC segment. Representative example of a left medial OFC labeled in purple (derived from the Freesurfer Desikan–Killiany atlas). OFC gray matter volume, cortical thickness, and pial surface area were extracted.

Fischl, Sereno, & Dale, 1999). Details of the surface-based cortical reconstruction and subcortical volumetric segmentation procedures have been extensively documented previously (Segonne et al., 2004; Dale et al., 1999; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999). Briefly, the FreeSurfer pipeline performs motion correction on the T1 images, automatically removes non-brain tissues (Segonne et al., 2004), transforms volumetric data to a common atlas, performs intensity normalization and topology correction (Segonne, Pacheco, & Fischl, 2007; Fischl et al., 2004; Fischl, Liu, & Dale, 2001; Sled, Zijdenbos, & Evans, 1998), and defines the boundaries of the gray/white matter and pial surface (Dale et al., 1999).

Medial OFC, as listed in the Desikan–Killiany atlas (Figure 2; Desikan et al., 2006), gray matter volume (in ml), cortical thickness (in mm), and pial surface area (further referred to as surface area, in mm^2) were automatically extracted. The OFC parcellation was averaged across hemispheres within participants. Intracranial volume was determined by a validated automated method known to be equivalent to manual intracranial volume estimation (Buckner et al., 2004). Finally, all segmentations were visually inspected for accuracy before inclusion in the group analysis.

Statistical Analyses

All variables were normally distributed, except for testosterone levels. These were log transformed. Because of the substantial sex difference in (log-transformed) testosterone level ($F = 128.8$, $p < .00001$), a Z transformation was applied: high scores on this testosterone distribution indicated high levels of testosterone relative to other individuals of the same gender (Mehta, Jones, & Josephs, 2008; Josephs, Sellers, Newman, & Mehta, 2006). All further analyses concerning basal levels of testosterone were carried out on these log-transformed, standardized scores of testosterone. Analyses with Z scores of testosterone were done within the whole sample and within each sex. The last method is preferred in puberty-related research given the difference in timing at which puberty emerges (approximately 1.5 years early for girls than boys; Shirtcliff, Dahl, & Pollak, 2009).

First, general patterns of puberty and sex effects on risk-taking behavior were investigated with an ANCOVA, using PDS and sex as independent factors, corrected for age and estimated intelligence quotient (IQ; Ashenhurst, Jentsch, & Ray, 2011). Second, stepwise regression analyses were carried out with number of explosions and total money earned as dependent variables. Independent variables that were entered in the model were Age, Sex, IQ, PDS, and Testosterone.

Third, to investigate whether testosterone was related to risk taking via the medial OFC and interrelations between OFC volume, OFC thickness, and surface area, testosterone and BART performance were investigated using partial correlations, corrected for age, IQ, and intracranial volume. In an attempt to dissociate variance related to BART explosions from BART total money earned, either one variable was added as a covariate.

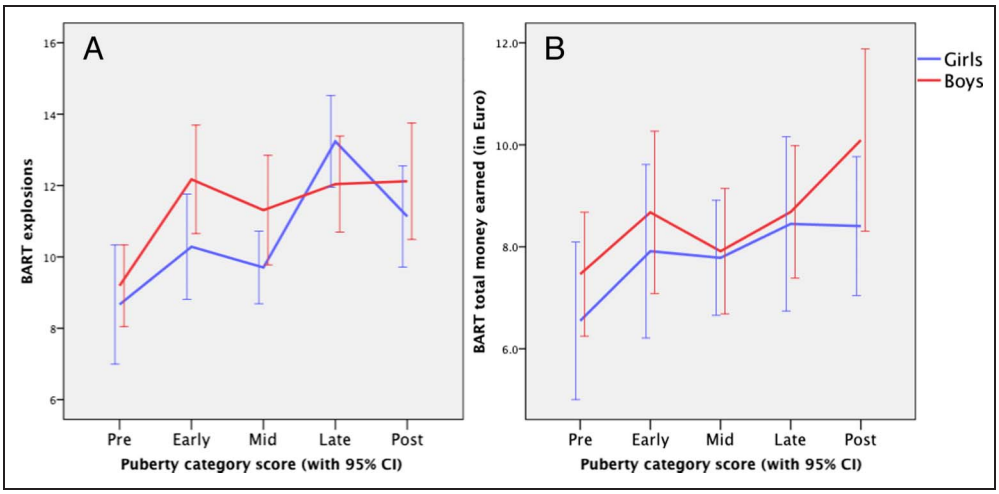

Figure 3. BART explosions (A) and total money earned (B) across different pubertal stages. There was a main effect of PDS on BART explosions (after correcting for age; $F = 4.25$, $p = .002$), mainly driven by girls. No PDS effect was found for BART total money earned.

Table 2. Regression BART Performance and Puberty Measures

BART Measure	*Factor*	*β*	*p*
Explosions			
All (n = 236)	**T**	**.28**	**<.0001**
	Sex	.12	.06
	IQ	−.10	.13
	Age	.08	.28
	PDS	.04	.61
Boys (n = 115)	**T**	**.34**	**<.0001**
	IQ	−.17	.06
	PDS	−.17	.25
	Age	−04	.78
Girls (n = 121)	**PDS**	**.26**	**<.006**
	IQ	−.12	.19
	T	.11	.35
	Age	.08	.67
Money Earned			
All	**Age**	**.24**	**<.0001**
	Sex	.09	.19
	IQ	−.05	.46
	T	.05	.55
	PDS	−.06	.58
Men	**Age**	**.29**	**.002**
	IQ	−.08	.36
	PDS	−.13	.44
	T	−.03	.82
Women	**T**	**.19**	**.06**
	Age	.07	.72
	PDS	−.04	.85
	IQ	.01	.96

Results of stepwise regression of BART measures, with independent factors: age, sex, PDS, testosterone (T), and IQ. NB. Results of the number of adjusted pumps are similar to the "total money earned" variable, and these results are omitted from the article.

An additional mediation analysis was performed to examine whether OFC morphology mediates the possible association between testosterone and risk-taking behavior. Using the bootstrapping method of Preacher and Hayes (Preacher & Hayes, 2004, 2008), the indirect effect of testosterone on risk-taking behavior (through OFC morphology) was tested for significance. A bootstrapped mediation analysis uses resampling of raw data to estimate the confidence intervals (CI) of the indirect effects, of which the mediation model consists. The mediation analysis was performed within each sex separately and again corrected for age, IQ, and intracranial volume.

RESULTS

Demographic Analyses

As expected, there were significant correlations between age and PDS in boys (r = .85, p < .00001) and girls (r = .86, p < .00001), between age and testosterone in boys (r = .74, p < .00001) and girls (r = .54, p < .0001), and between PDS and testosterone in boys (r = .78, p < .00001) and girls (r = .60, p < .00001).

Puberty and Testosterone Effects on BART Performance

The ANCOVA showed a main effect of PDS on BART explosions, corrected for age and estimated IQ (F(4, 253) = 4.25, p = .002; Figure 3). This main effect indicated that

Table 3. Correlations of BART Performance, Medial OFC Morphology, and Testosterone Levels in Boys (A) and Girls (B)

	BART TE	*BART Ex*	*T*
Boys			
1. BART (TE)[a]			
2. BART (Ex)[a]			
3. T[a]		**.23**	
4. OFC vol[b]		**−.23**	**−.25**
5. OFC CT[b]			
6. OFC SA[b]			**−.24**
Girls			
1. BART (TE)[a]			
2. BART (Ex)[a]			–
4. T[a]	**.19***		
6. OFC vol[b]			**−.19***
7. OFC CT[b]	**−.24**		
8. OFC SA[b]			**−.22**

BART (TE) = total amount of money earned on BART; BART (Ex) = total number of explosions on BART; T = testosterone (Z value, log transformed); OFC vol = gray matter volume of medial OFC; OFC CT = cortical thickness of medial OFC; OFC SA = surface area of the medial OFC.

All correlations in bold are p < .05.

[a]Corrected for age and IQ.

[b]Corrected for age, IQ, and intracranial volume.

*p = .06.

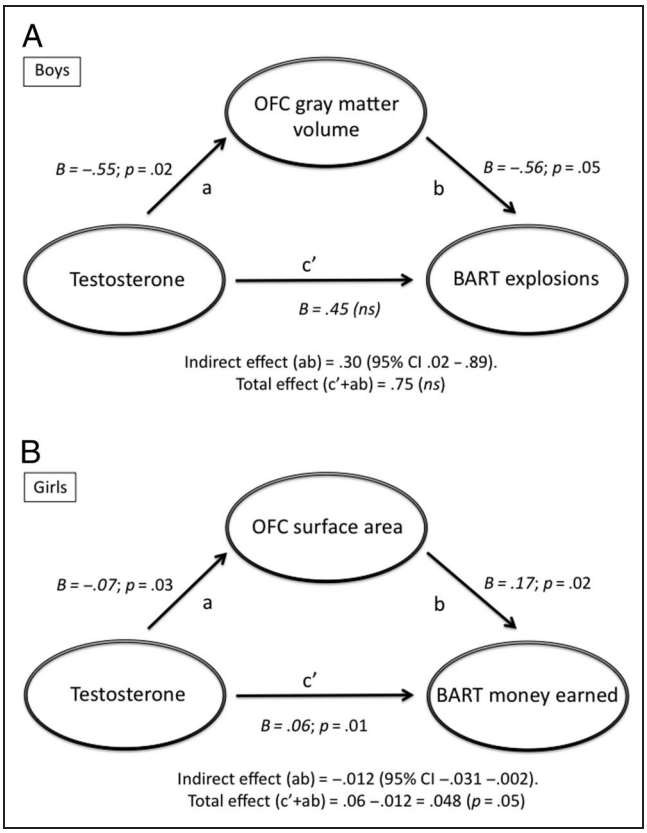

Figure 4. Mediation between testosterone and risk taking through the OFC in boys (A) and girls (B). Mediation analyses between independent variable (testosterone level) and mediator (OFC; a), between mediator and dependent variable (risk taking; b), and their indirect effect (ab) and direct effect (c′). Significance of the indirect effects was determined using bootstrapping analysis (Preacher & Hayes, 2004, 2008).

BART explosions increased with advancing puberty levels. No effect of PDS was found on BART money earned.

Stepwise regression analyses including age, sex, PDS, and testosterone as predictors and IQ as covariate revealed that individual differences in the total number of explosions on the BART were only explained by testosterone levels ($p < .001$; Table 2): Higher testosterone levels were related to an increased number of explosions. Moreover, a sex effect showed that boys had more explosions than girls at trend level ($p = .06$). When the sexes were analyzed separately, the association between testosterone and BART explosions was significant only in boys ($p < .0001$), but not in girls ($p = .35$). In girls, PDS was the best predictor of BART explosions ($p = .006$). The association between testosterone and BART explosions in boys remained significant after correcting for the total money earned.

The same regression analysis for total money earned on the BART showed that age was the only significant predictor in both the whole sample ($p < .0001$; Table 2) and in boys ($p = .002$) but not in girls separately. In girls, testosterone levels predicted increased amount of money earned at trend level ($p = .06$). This trend disappeared after correcting for the number of explosions. There were no sex differences or effects of PDS on BART total money earned.

OFC Morphology, Testosterone, and BART Performance

Given the sex differences in effects reported above, the next set of analyses was performed for boys and girls separately. In this set of analyses, we explored the correlation with and moderating effects of OFC gray matter volume, thickness, and surface areas.

In boys, OFC gray matter volume was positively correlated with BART explosions ($r = .23$, $p < .05$). Furthermore, male testosterone levels correlated negatively with OFC gray matter volume ($r = -.25$, $p < .05$) and OFC surface area ($r = -.24$, $p < .05$; Table 3). There was no relation between BART total money earned and OFC morphology in boys. These relations were further examined using mediation analysis. The mediation analysis showed that there was mediation between testosterone levels in boys and BART explosions through OFC gray matter volume ($B = .30$; 95% CI [.02, .89]; Figure 4A),

Table 4. Main Findings

	Boys	*Girls*
Puberty and T	+T → +explosions	+Puberty → +money
		+T → +money[a]
OFC and T	+T → −OFC volume	+T → −OFC thickness
	−OFC → +explosions	+T → −OFC surface area
		−OFC → +money
Mediation	Smaller OFC volume potentiates the association between T and risk taking	Smaller OFC surface area suppresses the association between T and risk taking

T = testosterone. Puberty was assessed using the PDS scale. Correlations are corrected for age, (estimated) IQ, and intracranial volume.

[a]Trend.

such that higher testosterone levels were associated with a smaller OFC gray matter volume, and a smaller OFC gray matter volume was associated with more risk taking.

In girls, there were no relations between OFC morphology and BART explosions, but OFC cortical thickness was negatively correlated with BART total money earned ($r = -.24$; $p < .05$). In addition, higher levels of testosterone were related to a smaller OFC volume ($r = -.26$; $p < .05$) and a smaller OFC surface area ($r = -.25$; $p < .05$). Mediation analysis again showed evidence for a significant mediating effect of OFC surface area on the association between testosterone and BART total money earned ($B = -.02$; 95% CI [−.03, −.01]; Figure 4B). Higher testosterone levels were associated with a smaller OFC surface area, and a smaller OFC surface area was related to less total money earned.

DISCUSSION

The current findings show that, in a normative sample of 236 participants between 8 and 25 years old, testosterone levels and OFC morphology modulate risk taking across pubertal development (Table 4). That is to say, in boys and, to a lesser extent, in girls, corrected for age, higher testosterone levels were associated with increased risk taking. In boys, this was associated with a mediating role of smaller OFC gray matter volume, which may suggest that OFC morphology amplifies risk taking, whereas in girls, this was associated with a mediating role of a larger OFC surface area that was found to suppress risk taking.

This study provided direct evidence for the role of pubertal hormones in the development of risk taking. As hypothesized, testosterone was a predictor for risk taking in boys and girls, when age effects were controlled. These findings are consistent with prior studies demonstrating a relation between adolescent testosterone and self-reported risk-taking tendencies (de Water et al., 2013; Vermeersch et al., 2008, 2010).

It should be noted that the relation between testosterone levels and risk taking was associated with more explosions in boys but more money earned in girls. Therefore, in boys, higher testosterone may lead to more sensation seeking (the thrill of pumping the balloon further). In girls, however, higher testosterone may lead to more long-term advantageous risk taking (more money earned).

Overall, these measures (explosions and money earned) were correlated, so it is unclear whether they can be dissociated. In a first attempt, adding total money earned as a covariate to the analyses on number of explosions did not change the results in boys, possibly indicating relative independent behavioral constructs. In girls, however, both variables seem to be intertwined. Therefore, based on the current data, we cannot state that higher testosterone in girls is associated with more long-term advantageous risk taking. Nonetheless, an intriguing question for future research is whether testosterone may have different effects on types of risk taking in boys and girls (Overman et al., 2004).

The relation between testosterone and the medial OFC was also investigated. Although effects of testosterone on brain morphological development were found to be different in boys and girls (Bramen et al., 2012), in this study, male and female testosterone levels were both correlated with smaller OFC morphology (gray matter volumes and surface area, respectively). The current findings fit with studies on functional connectivity of the OFC (with the amygdala), which decreases with higher levels of testosterone (Bos et al., 2012; van Wingen et al., 2010). Indeed, a smaller brain volume or surface area relates to less structural or functional connections from/to that specific brain area (van den Heuvel & Sporns, 2011).

Interestingly, the association between risk taking and testosterone levels was mediated by OFC morphology. However, mediation between testosterone and risk taking via the OFC varied by risk-taking "parameter" (explosions vs. money earned), morphological parameter (brain volume/cortical thickness vs. surface area), and sex. In boys, higher testosterone is associated with a smaller OFC volume, which is associated with more risk taking (explosions). In girls, higher testosterone is associated with a smaller OFC surface area, and smaller OFC surface area is associated with less risk taking (money earned). The rather complicated associations in girls are the result of inconsistent mediation (MacKinnon, Fairchild, & Fritz, 2007); inconsistent mediation occurs when the direct effect between the dependent (BART performance) and independent variable (testosterone) is positive, whereas the indirect effect through the mediator (OFC) is negative (MacKinnon et al., 2007). Indeed, the OFC volume seems to act as a suppressor variable in girls, which would be in line with the idea that testosterone inhibits OFC-mediated regulatory control of impulsivity/reward sensitivity (Schutter & van Honk, 2004).

To explain the OFC-mediated associations between testosterone and risk taking, we compared our data with earlier literature on the structural development of the adolescent brain. These studies show, with a few focal exceptions, that an increase of surface area and decrease of volume/thickness of the cortex are the general trend (Raznahan et al., 2011; White, Su, Schmidt, Kao, & Sapiro, 2010; Shaw et al., 2008). Therefore, our data might suggest that, in boys, a relative mature OFC potentiates the relation between testosterone and risk taking, but a relative mature OFC in girls suppresses the relation between testosterone and risk taking. From a developmental perspective, this mechanism shows functional comprehensibility by considering risk taking as an "adaptive" adolescent behavior: More testosterone (or advanced pubertal development) leads to risk-taking/exploration behavior, whereas a relative immature OFC suppresses this adaptive behavior. Speculatively, it might be argued that, in boys, a relative immature OFC is advantageous (less explosions), but in girls, a relative immature OFC is disadvantageous (i.e.,

less money earned). This hypothesis needs further investigation, however, using a longitudinal design and clear separation of both "types" of risk taking.

Several studies suggest that internally fluctuating sex steroid levels contribute to the neural reorganization within the developing brain (Peper, Hulshoff Pol, Crone, & van Honk, 2011; Blakemore, Burnett, & Dahl, 2010; Sisk & Zehr, 2005). The exact neuronal mechanisms, however, of how testosterone affects risk taking through OFC morphology remain unclear. Possibly, testosterone directly influences OFC morphology, as receptors for androgens such as testosterone are found in the OFC (Finley & Kritzer, 1999). Alternatively, indirect effects of testosterone on neurotransmitter systems within the pFC such as the serotonin system (Handa, Hejna, & Lorens, 1997) or the dopamine system (Aubele & Kritzer, 2012) can also modulate individual differences in reward-related risk-taking behavior. These hypotheses should be investigated in future research.

Several limitations should be considered when interpreting these results. First, sex differences in the association between testosterone and risk taking might be because of the enhanced natural variation in testosterone levels in boys compared with girls. These differences may have resulted in PDS being a stronger predictor of BART performance in girls compared with testosterone differences. It might also be argued that testosterone can be more reliably measured in boys because of higher natural variation (i.e., effect relative to error) leading to larger effect sizes in boys. Alternatively, because of higher levels of bio-available testosterone, the male brain might be more susceptible to the effects of endogenous levels of testosterone. Given the smaller variation in testosterone in girls, PDS may be a better indicator of pubertal development, which is, in girls, associated with a range of other hormonal change as well. This also seems the case with respect to the initiation of alcohol use in adolescence; this type of risk taking was associated with testosterone in boys but to general pubertal development in girls (de Water et al., 2013).

Second, although this study provided evidence for the role of the OFC in mediating the effects of testosterone on risk taking, future longitudinal studies are needed to show whether the development of the OFC (or connections from/to the OFC) has a protective effect on the development of risk taking.

To conclude, our study provides the first evidence that increased levels of testosterone contribute to increased risk taking and that this association is partly driven by medial OFC morphology. A relative mature OFC in girls seems to suppress this association, whereas a relative immature OFC in boys seems to enhance the association. Our study sheds light on the specific contribution of hormonal changes, versus general age effects, vis-à-vis the development of neural systems involved in motivational tendencies toward sensation-seeking behavior. This knowledge is relevant to obtain a better understanding of the neuro-maturational underpinnings to affective changes during adolescent development.

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