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Intelligence and salivary testosterone levels in prepubertal children

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Abstract

Background: Hormones are one of the regulatory systems influencing brain-cognition interactions and subsequent emotions and behavior in humans and animals. Sex hormones have been found to influence brain structures prenatally, so as to prepare targeted neuronal circuits for activation during and after puberty. Testosterone is believed to affect cognition and thinking in humans as well as between-sex differences in cognitive abilities. *Aim:* The aim of this paper was to investigate associations between testosterone and different levels of intelligence in young prepubertal children of both sexes.

Methods: Two hundred and eighty four prepubertal children of both sexes between 6 and 9 years of age provided saliva samples. Of these, 107 were intellectually gifted (IQ above 130), 100 children of average intelligence—randomly chosen from general population (IQ between 70 and 130), and 77 children mentally challenged (IQ less than 70).

Results: Our results have revealed the differences in salivary testosterone levels in boys grouped according to IQ, intellectually gifted and mentally challenged boys having lower salivary testosterone levels than their peers characterized by average intelligence proposing the common biological characteristic of minority IQ groups on both ends of the Gauss curve. In girls, no differences in salivary testosterone levels were found among IQ groups.

Conclusions: Our findings are the first that present the relationship between testosterone and the broad range of general IQ in childhood. The boys of average intelligence had significantly higher testosterone levels than both mentally challenged and intellectually gifted boys, with the latter two groups showing no significant difference between each other. The functional implications of the brain-cognition interactions remain to be fully explored with regard to the internal milieu influencing neural substrate.

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1. Introduction

All human characteristics are a product of an interaction between the genes and the environment during the course of ontogenesis of an individual. But what makes one person smarter than another one? Recent studies focus more on general

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cognitive capacities in an attempt to find the factor which could provide biological foundations for a set of cognitive capacities which men and women share (Spelke, 2005). A body of evidence suggests that intelligence is significantly influenced by genetic factors (Plomin & Spinath, 2004). Other evidence indicates that gifted children are born with atypical brains, which implies that giftedness is the product of biological factors (Winner, 1996, 2000). According to Haier, Siegel, Tang, Abel, and Buchsbaum (1992) and Haier, Jung, Yeo, Head, & Alkire, 2004) intelligent performance is a function of efficient use of the brain substrate. This was supported by EEG findings by Jaušovec (2000). In his experiments, highly intelligent individuals showed less

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mental activity and more cooperation between the brain areas activated in specific problem solving than the average intelligent individuals did. Brain anatomy or modulatory effect of neurohormones on particular anatomical substrates was widely accepted (Simerly, 2005). Martin-Loeches, Muñoz-Ruata, Martinez-Lebrusant, and Gómez-Jarabo (2001) reported on the EEG analysis in children with intellectual disability. They found frontal lobes, especially the prefrontal regions to be affected regardless of the etiology of mental disability. Taking recent research into account it is reasonable to suppose that the associative cortex of the frontal lobe plays a fundamental role in the implementation of the integrated cognitive function (Duncan, 2005; Duncan et al., 2000; Fuster, 2005).

Hormones as mediators of gene effects control indirectly the development of human body and brain, with subsequent consequences on behavior and cognitive functions. A number of published studies documenting the relationship between testosterone and human intellectual performance have indicated that testosterone exerts its effects neuroanatomically by influencing the organization of the developing brain, modifying cognitive pattern within the limits of genetic predisposition (Geschwind & Galaburda, 1985; Gouchie & Kimura, 1991; O'Boyle et al., 2002).

During adolescence testosterone levels dramatically increase in boys. During this period the activation of preformed brain structures leads to sexually dimorphic physical behavioral and cognitive effects. Even transient fluctuations in testosterone levels during adulthood may change cognitive performance (Hampson & Kimura, 1992; Hausmann, Slabbekoorn, Van Goozen, Cohen-Kettenis, & Güntürkün, 2000; Celec, Ostatnikova, Putz, & Kudela, 2002). Many researchers relate hormonal replacement therapy in older subjects to cognitive benefits with different outcomes (Janowski, 2006; Josephs, Newman, Brown, & Beer, 2003).

It is believed that testosterone does not directly excite or inhibit a neuron but rather influences the expression of genes that code for enzymes or receptors involved in neurotransmission. Thus, testosterone is able to modulate the degree to which a neuron responds to an incoming input and indirectly influences the transmitter mechanisms in the brain (Fink, Sumner, McQueen, Wilson, & Rosie, 1988). It is also probable that there exist some testosterone effects on the formation or loss of synaptic connections, or on other cellular growth processes that affect function of the nerve tissue. (LeVay, 1993; Lustig, 1996).

Data suggesting that early androgen exposure on specific neuronal systems is crucial in brain morphologic differentiation of particular target neurons or neuronal networks have been accumulated. Steroids may have direct trophic effects on target cells or indirect growth effects mediated via neuronotrophic mediators secreted locally by steroid sensitive neuronal or glial cells. Another possibility is the active inhibition of neurotransmitters or neuropeptides. This organizational effect permanently influences the brain structures which are prepared for neuromodulatory effects during life (MacLusky, Bowlby, Brown, Peterson, & Hochberg, 1997).

Up to the present time, prenatal effects of testosterone on general intelligence in prepubertal children have not been sufficiently investigated. In the past, papers were published reporting above average intelligence in children whose mothers were treated with androgenic progestins during pregnancy or who themselves had higher testosterone levels due to endocrine disorders (Ehrhardt & Money, 1967; McGuire & Omenn, 1975; Perlman, 1973). Most results were obtained from studies monitoring females with congenital adrenal hyperplasia (CAH), a genetic disorder that causes an overproduction of adrenal androgens beginning prenatally and affecting cognition in females (Hines et al., 2003; Resnick, Berenbaum, Gottesman, & Bouchard, 1986). On the other hand, there appeared some other studies showing no significant difference in IQ after intrauterine exposure to sex hormones (Baker & Ehrhardt, 1974; Reinisch & Karow, 1977).

Studying the contribution of testosterone to cognitive development is very difficult. Direct measurement of testosterone in developing fetus during sensitive periods has ethical constraints and further follow-up postnatal studies would be needed to determine prenatal testosterone effect. Finegan, Bartleman, and Wong (1989) had performed a study in this area based on measuring testosterone levels in the amniotic fluid and assessing cognitive performance in childhood. They found increased testosterone levels in human males in comparison to human females in their umbilical cords between gestation weeks 16 and 18, and that girls with higher amniotic testosterone levels had a faster performance in mental rotation. There were no significant findings in boys.

In the study conducted by Grimshaw, Sitarenios, and Finegan (1995) in normal healthy children testosterone was measured in amniotic fluid and associated with mental rotation performance when they were 7 years old. Girls with higher amniotic testosterone levels had faster performance on mental rotation tasks than girls with lower testosterone levels. There were no significant relations among boys. Jacklin, Wilcox, and Maccoby (1988) determined testosterone levels from umbilical cord blood samples at birth and related them to spatial imagination at 6 years. They reported negative relationship between testosterone and spatial imagination with no sex differences. Inconsistent results could be explained by methodological limitations and small sample size, most cognitive parameters did not show large sex differences and sample size was very small (Cohen-Bendahan, van de Beek, & Berenbaum, 2005).

It has been already suggested that the prepubertal period mirrors intrauterine hormonal influence and this gives us a unique opportunity to look for a correlation between testosterone and intelligence. However, only a few studies have been published associating hormones with general intelligence during childhood.

Azurmendi et al. (2005) recently reported a relationship between general intelligence and testosterone levels in a general population of pre-school children. Besides other results, significant negative correlations were found between vocabulary subtest and testosterone levels in children of both sexes and positive relationships between fluid intelligence and testosterone in boys. Other researchers concentrated on studying the relationship between testosterone levels and mathematical giftedness (Benbow, 1986, 1987, 1988). Hassler and Birbaumer (1988) and Hassler (1991) had proposed hormonal basis for musical talents, finding negative association between creative musical talent and testosterone levels in adolescents.

In our follow-up study relating salivary testosterone levels and general intelligence (Ostatníková et al., 2000) we observed lower testosterone levels in intellectually gifted children in comparison to children from general population. The higher scores in intelligence tests in our gifted subjects were associated with lower levels of salivary testosterone. Kirkpatrick, Campbell, Wharry, and Robinson, (1993) determined salivary testosterone levels in prepubertal children with and without learning disabilities. They have found significantly higher salivary testosterone levels among disabled children in comparison with age-matched sample of children without learning disabilities.

The concept of gene–environment interaction is difficult to apply in studies of human development. Simple additive model suggesting that the phenotype is the sum of environmental and genetic effects is far from the real gene–environment interaction (Gottesman & Hanson, 2005).

The aim of the present study was to compare salivary testosterone levels in prepubertal children divided according to their general IQ into mentally disabled, average and intellectually gifted boys and girls.

2. Methods

In our study were determined the salivary testosterone levels in preadolescent children of both sexes who had different levels of intellectual ability. The youngest child was 6 years old and the oldest was 9 years old. Among 284 subjects, there were 113 girls and 171 boys. Of these, 107 children were intellectually gifted (78 boys and 29 girls) with a general IQ of at least 130 (mean IQ = 144.5). Their salivary testosterone levels were compared with the group of 100 children of average intelligence (43 boys and 57 girls) from the general population (mean IQ = 104.5), and 77 mentally challenged children (50 boys and 27 girls) whose IQ was lower than 70 (mean IQ = 61.0). Intellectually gifted children were those attending the special school for intellectually gifted learners founded in Bratislava, Slovakia in 1998. Admission criterion for being accepted to this kind of special school was general intelligence score of IQ 130 and more. Average intelligence children were gathered from randomly chosen elementary school and intellectually disabled children were those attending special schools for children with learning disabilities. Our approach to intellectually disabled children was highly ethical. Those parents who agreed with the participation of their children either did not know about the nature of the mental problem or were not willing to release the medical record. Children with Down syndrome were not included because of xerostomia; they were not able to provide us with their saliva. No autistic child participated in our study because of complicated IQ assessment and its interpretation.

General intellectual ability was assessed by standardized general intelligence test (WISC) in all three groups of children (Wechsler, 1974). The complete test assessing general intelligence was administered and evaluated by trained professional psychologist individually to each child in one session during morning hours (between 8.00 and 11.00 a.m.) lasting up to 1 hr, 3–6 months prior to saliva sampling. Performance and verbal scores were determined separately besides the complete assessment.

The vast majority of Slovak population is of white Caucasian race. We have excluded 24 non-Caucasian children (9 girls and 15 boys) from our study to avoid possible racial differences in testosterone levels, as certain racial differences were found in adrenal androgen excretion and sex hormone-binding globulin levels (Abdelrahaman, Ragavan, Baker, Weinrich, & Winters, 2005).

Testosterone levels were determined in saliva, since saliva contains biologically active fraction of the hormone and its sampling is non-invasive and stress-free. Saliva was taken once in amount of 4 ml within 2 weeks in autumn, between 9.00 and 11.00 a.m. to control the influence of circadian and seasonal biorhythms of testosterone production (Butler et al., 1989; Dabbs, 1990).

The subjects were asked to clear their mouth and then a sugarless fruitflavored chewing gum was given to each of them as a salivation stimulant. Saliva accumulated in the base of the mouth and was collected directly into sterilized test tubes. Contamination with food debris was avoided by rinsing the mouth with water and by delaying the collection for 5 min after rinsing to prevent sample dilution. Absence of blood contamination was checked by salivary blood contamination kit (Salimetrics LLC, State College, PA, USA). Each child provided two 2 ml samples of saliva for analysis. The interval between two samples was 40–50 min. Samples of saliva were frozen and left at -20 °C until analyzed. Parental consent was obtained prior to testing.

2.1. Radioimmunoassay (RIA)

Saliva including control samples or blank (bi-distilled water), 1.0 ml each, were traced with [³H]testosterone (Radiochemical Center, Amersham, UK, 1200 dpm/sample), and extracted in duplicate with diethyl ether (4 ml) in glass tubes with stopper. The aqueous phase was left frozen in solid carbon dioxide, organic phase was decanted and ether was evaporated to dryness. The extracts were dissolved in ethanol (500 µl), 100 µl of which was removed for determination of the losses during extraction, while the rest was evaporated again and taken for radioimmunoassay. A standard curve consisting of 0, 0.1, 0.2, 0.4, 0.8, 1.6, and 3.2 nmol/l testosterone in duplicate, was prepared. Antiserum (rabbit-anti-testosterone-3-CMO: BSA working dilution 1:100,000) and the tracer ([¹²⁵I] iodo-histaminyl-testosterone derivative, 15,000 cpm), 100 µl each, were added, the volume was adjusted to 300 µl with working buffer (20 mmol/sodium phosphate-saline containing sodium azide and BSA, 0.1% each) and the tubes were equilibrated with the room temperature for 1 hr or overnight at 4 °C. After incubation, dextran-coated charcoal suspension (0.025 and 0.25 g/100 ml, respectively, 1 ml) was added to each tube to separate the free fraction and the radioactivity of ¹²⁵I was measured in the supernatant using 12 channel gamma counter (Berthold, FRG). Results were calculated from the standard curve using a log-logit transformation, corrected for recovery and expressed as nmol testosterone per liter.

The analytical parameters of the method were as follows—Specificity: the only compounds that showed a significant cross-reaction were 5α -dihydrotestosterone (33.0%), 11 β -hydroxytestosterone, estradiol and androstenedione (0.1% each). Accuracy: the recovery of known amount (1–5 pg) of testosterone added to saliva (mean ± S.D.) was 101.4 ± 9.0% (*n* = 24). Sensitivity: the lowest analyzable amount of the sample detected with 95% probability was 1 pg. Precision: the variation between assays calculated from the results of a quality control run in each assay (*n* = 50) gave the value 0.220 ± 0.018 mol/l (coefficient of variation 8.2%). After the assay had been in routine use the results calculated from the recovery measured for each sample were compared with those calculated using the mean overall recovery for all previous assays. No significant differences were observed (regression analysis *r*=0.99, *y*=0.996*x*+0.02, and *n*=300).

2.2. Statistical analysis

The hormonal levels and IQ scores were analyzed using the Bonferoni modified unpaired *t*-test for independent datasets (for the analysis of sex differences) and One-way ANOVA with Tukey's post hoc test (for the analysis of differences between mentally disabled, control and gifted children). The level of significance of differences between groups was set to 0.05. Salivary testosterone levels were also analyzed using two-way ANOVA. Microsoft Excel 2000 and GraphPad Prism 4 were used for the statistical analysis. Data is presented as mean \pm standard deviation (S.D.).

3. Results

Our findings are the first to be presented in the whole range of IQ scores including intellectually gifted and mentally challenged children in relation to testosterone levels in prepubertal period of human life. Two-way ANOVA revealed that sex

Table 1	
Descriptive statistics of observed parameters in boys	

$IQ \le 70$	$71 \le IQ \le 130$	$IQ \ge 130$	
8.0 ± 0.8	7.7 ± 1.1	7.5 ± 1.2	
0.040 ± 0.010	0.069 ± 0.041	0.033 ± 0.010	
60.8 ± 8.4	101.1 ± 20.1	145.0 ± 8.7	
67.0 ± 7.6	103.3 ± 19.4	140.0 ± 11.4	
58.5 ± 7.6	98.8 ± 21.7	139.0 ± 1.2	
	$IQ \le 70$ 8.0 ± 0.8 0.040 ± 0.010 60.8 ± 8.4 67.0 ± 7.6 58.5 ± 7.6	IQ \leq 7071 \leq IQ \leq 1308.0 \pm 0.87.7 \pm 1.10.040 \pm 0.0100.069 \pm 0.04160.8 \pm 8.4101.1 \pm 20.167.0 \pm 7.6103.3 \pm 19.458.5 \pm 7.698.8 \pm 21.7	



Fig. 1. Salivary testosterone levels in nmol/l (mean + S.D.) in prepubertal boys and girls divided according to IQ (***p < 0.001).

(F = 11.7; p < 0.001), IQ-range group (F = 23.2; p < 0.001) and their interaction (F = 21.4; p < 0.001) significantly affect salivary testosterone levels. IQ-range group and sex explains 12% and 3% of the salivary testosterone variability, respectively.

In intellectually gifted and mentally challenged children, there were no differences found in salivary testosterone levels, or in general, verbal and performance IQ between sexes. In the average intelligence group, the difference in salivary testosterone levels between sexes was significant, boys having higher salivary

Table 2

Descriptive statistics of observed parameters in girls

testosterone levels than girls (t = 7.8; p < 0.001). Differences in IQ (general, verbal and performance) were not found.

The results of a comparison between girls in all groups showed no differences in salivary testosterone levels (F=0.4; p=0.70). In boys, salivary testosterone was statistically different between groups (F=36.6; p<0.001). The difference was found between mentally disabled and average boys (q=8.9; p<0.001) and between intellectually gifted boys and average boys (q=11.9; p<0.001). There were no differences between salivary testosterone levels of mentally challenged boys and salivary testosterone levels of intellectually gifted boys (Table 1 and Fig. 1). No significant correlation between salivary testosterone levels and IQ has been found neither in girls nor boys (Table 2 and Fig. 2).

4. Discussion

This study has focused on testosterone as one of the factors affecting brain physiology. The results demonstrate differences in salivary testosterone levels between boys with average intelligence and boys belonging to minority populations of intellectually gifted (IQ more than 130) and intellectually challenged (IQ less than 70). Both groups each comprise about 2% of the whole population.

We are unaware that there were any methodological problems in our study, respecting the biorhythms of testosterone production and all the children participating in the study were of pre-pubertal age so this allowed the exploration of the prenatal and early postnatal influence of testosterone on intelligence and sex differences. The main finding of this study was the higher salivary testosterone level in average intelligence boys in comparison with both minority population groups—mentally challenged boys and intellectually gifted boys. The results may give the impression that the average boys with significantly higher testosterone levels are those who are different. If so, one possible explanation might be the earlier maturation of average boys. Contrastingly, published data indicate that gifted boys

Girls	IO < 70	$71 \le IO \le 130$	IO > 130	
	25 + 0.2	75 + 11	75 + 10	
Age (years) Saliyary testosterone (nmol/l)	8.5 ± 0.8 0.038 + 0.007	7.5 ± 1.1 0.040 + 0.012	7.5 ± 1.2 0.040 ± 0.008	
General IO [IO points]	61.3 ± 7.0	107.0 ± 18.9	143.1 ± 9.4	
Verbal IQ [IQ points]	66.5 ± 6.5	104.6 ± 17.2	137.5 ± 11.7	
Performance IQ [IQ points]	58.7 ± 6.3	107.8 ± 20.3	137.8 ± 11.6	



Fig. 2. The relationship between the salivary testosterone levels in nmol/l and IQ in prepubertal boys and girls. Regression lines (thick solid), confidence (thin solid) and prediction (thin dashed) bands are shown.

are usually slow maturers (Waber, 1977). Puberty is a dynamic period of physical growth, sexual maturation and psychosocial achievement that generally begins between the ages of 8 and 14 (Pinyerd & Zipf, 2005). The age of onset varies, taking into consideration sex, ethnicity, health status, genetics, nutrition, and activity level and the launch of puberty itself is initiated by hormonal changes triggered by the hypothalamus. The results of our previous follow-up studies in a Slovak population of children (Ostatníková, Pastor et al., 2002) supported the general interpretation that salivary testosterone levels in pre-pubertal boys and girls are not substantially changed between the age of 6 and 9. An increase in the circulating levels of DHEA-S appears to be the first event which can be observed during adrenarche prior to clinical evidence of puberty. Azziz et al. (2004) have found that DHEA-S levels correlate positively with age in girls and the concentrations were found to be significantly increased at 9.1–10.0 years of age, so they do not interfere with testosterone levels prior to the onset of puberty. Puberty is triggered by multiple signals with a steroid dependent system providing fine control of gonadotropin secretion and sex hormone levels rise because of a decreased sensitivity to steroid negative feedback. Current opinion is that the rising sex hormone levels do not only activate, but also organize neural circuits during adolescence (Sisk & Foster, 2004) and that this has an influence on the development of cognition.

The free testosterone fraction that highly correlates with salivary testosterone levels (Granger, Schwartz, Booth, & Arentz, 1999) might be theoretically influenced by the levels of binding proteins in plasma. The levels of SHBG (sex hormone-binding protein) were proved not to be age-dependent within the period between the age of 5 and 9 (Abdelrahaman et al., 2005; Belogorosky & Rivarola, 1986) so the ratio of free to total testosterone is supposed to remain relatively stable in studied individuals. In accordance with the finding of stable SHBG levels it could be suggested that pre-pubertal boys in our study may differ in testosterone levels because of different sensitivity to testosterone that could be caused by mutations of the human androgen receptor gene. Analysis of the genetic polymorphism of the androgen receptor in future work could examine this possibility. The other important fact that should not be omitted is that testosterone affects the sensitive tissues not only as testosterone per se but also via its main metabolites dihydrotestosterone and estradiol (Federman, 2006). Even allowing for this, the androgen receptor is the principal mediator of the androgen effect in the frontal cortex and androgen levels modulate receptor density needed for full manifestation of neurotrophic androgen effects. Specific high affinity androgen binding sites were observed in prefrontal cortex in the developing rhesus monkey (Clark, MacLusky, & Goldman-Rakic, 1988). Expression of sex steroid receptors in several neocortical regions enables gonadal steroids to induce the morphologic changes in the central nervous system (MacLusky, Hajszan, Prange-Kiel, & Leranth, 2006). Testosterone levels may contribute to the regulation of androgen sensitivity. Clearly, the increased sensitivity of particular neurons to testosterone and enhanced metabolic turnover to estrogen could be a plausible hypothesis for the findings of lower testosterone levels in both gifted and intellectually challenged boys.

Several reports indicate that there exists an association between psychosocial development, including the development of learning abilities and salivary testosterone. Kirkpatrick et al. (1993) estimated salivary testosterone levels in pre-pubertal children with and without learning disabilities. They found higher testosterone levels in the learning disabled children in comparison with age-matched sample of children without learning disabilities. We did not have any information about the etiology of intellectual disability in the intellectually challenged children in our study. Current reports suggest that etiology of intellectual disability can be determined in only 40-60% with the diagnostic success biggest in the group with severe disability (Poplawski, 2003). Most of the intellectually challenged children in our study had mild to moderate intellectual deficiency. Intelligence is a general cognitive trait that involves abstract thinking and reasoning abilities. Mild retardation is commonly assumed to be caused by polygenic inheritance or general family environment, so it is more likely to run in families (Mackintosh, 1998). A recently published study (Burdick et al., 2006) suggests a region on chromosome 6p to be linked with variation in intelligence. The findings of our current study and also that of the research of Kirkpatrick et al. (1993) indicate that testosterone interacts with many other biological and non-biological factors that could lead to intellectual disability.

In the current study, sex differences in IQ (general, verbal and performance) were not found within the studied groups. That is in accordance with previous findings that human males and females from birth to adolescence do not differ in the specific cognitive abilities (Mackintosh, 1998). Research on cognitive development in human children provides evidence that scientific reasoning develops from a set of biologically based cognitive capacities that males and females share (Spelke, 2005).

While no difference was found in mean IQ between boys and girls, there was a difference in the proportion of boys and girls in the intellectually gifted group and also in the mentally disabled group: both groups contained more males than females. This is in accordance with findings of other researchers who observed greater variability in performance among boys (Lubinski & Humpreys, 1990; Hyde, Fennema, & Lamon, 1988). Hyde et al. (1988) and Benbow (1988) found more male than female pre-adolescents and adolescents in groups of above-average ability. Some sex differences in the occurrence of neurodevelopmental disorders have been reported with males more often showing several developmental disabilities, including severe mental retardation, language disorders, learning difficulties and others, irrespective of race and severity of disability (Flannery, Liederman, Daly, & Schultz, 2000; Liederman, Kantrowitz, & Flannery, 2005).

According to the well-known theory proposed by Geschwind and Galaburda (1985), gifted children might be exposed to higher testosterone levels in utero, with several consequences including giftedness, non-standard hemispheric specialization and handedness and also allergy occurrence. Our previous findings of higher allergy occurrence and lower percentage of right handedness in intellectually gifted children (Ostatníková, Laznibatová et al., 2002) supported this hypothesis and have led us to consider either lower postnatal maintenance of testosterone levels (through the negative influence of hypothalamic-pituitary-gonadal axis during prepubertal period in intellectually gifted children) or slower pre-pubertal development of these children as an explanation of their lower testosterone levels. Studies on mathematically gifted individuals confirmed a unique functional characteristic with bigger involvement of the right hemisphere in mental processing (O'Boyle, Alexander, & Benbow, 1991; O'Boyle et al., 2002) that would also indicate an effect of intrauterine testosterone on the right hemispheric development as proposed by Geschwind and Galaburda (1985).

Some recent studies on autistic children postulated a theory of there being a hyper-male brain in these children (Baron-Cohen, 2002) that would suggest the effect of higher testosterone levels during intrauterine development and lower postnatal maintenance of testosterone levels as was suggested in gifted children. Whilst the issue of the neurobiological basis of variation in intelligence remains unresolved, there are theoretical grounds for the hypothesis that at least fluid intelligence depends on cognitive processes that are mediated most prominently by the frontal lobes (Duncan, Burgess, & Emslie, 1995; Duncan et al., 2000; Fuster, 2005). Frontal cortical regions are among the neural networks that are under the influence of testosterone (Swerdloff, Wang, Hines, & Gorski, 1992). Gonadal steroids induce morphological changes in the neuronal system (growth, morphological differentiation or programmed apoptosis of particular groups of neurons) in topographically specific regions that contain androgen and estrogen receptors (De Bellis et al., 2001; MacLusky et al., 1997, 2006), having considerable impact on brain development and functioning. It is unlikely that genderdifferentiated biological features would arise independently of social influences. Equally, it seems implausible that all social influences would operate in ways apart from biological substrates.

The differences in cognitive abilities might reflect the variations in functional brain organization based on testosterone effect during early development (Geschwind & Galaburda, 1985). O'Boyle and Benbow (1990) found enhanced right hemisphere involvement and Singh and O'Boyle (2004) found enhanced interhemispheric collaboration and also the engagement of anterior cingulate cortex – regions typically involved in emotions – in gifted children. The recruitment of different brain regions with different androgen receptor expression and sensitivity could play role in feed back regulation of testosterone concentrations during prepubertal age in intellectually gifted and intellectually challenged children.

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References

- Abdelrahaman, E., Ragavan, S., Baker, L., Weinrich, M., & Winters, S. J. (2005). Racial difference in circulating sex homone-binding globulin levels in prepubertal boys. *Metabolism Clinical and Experimental*, 54, 91–96.
- Azurmendi, A., Braza, F., Sorozabal, A., García, A., Braza, P., Carreras, M. R., Muñoz, J. M., Cardas, J., & Sánches-Martín, J. R. (2005). Cognitive abilities, androgen levels, and body mass index in 5-year-old children. *Hormones and Behavior*, 48, 187–195.
- Azziz, R., Farah, L. A., Moran, C., Knochenhauer, E. S., Potter, H. D., & Boots, L. R. (2004). Early adrenarche in normal pubertal girls: A perspective study. *Journal of Pediatric Endocrinology and Metabolism*, 17(9), 1231–1237.
- Baker, S. W., & Ehrhardt, A. A. (1974). Prenatal androgen, intelligence, and cognitive sex differences. In R. C. Friedman, R. M. Richart, & R. L. VandeWiele (Eds.), Sex differences in behavior. New York: Wiley & Sons.
- Baron-Cohen, S. (2002). The extreme male brain theory of autism. *Trends in Cognitive Sciences*, 6(6), 248–254.
- Belogorosky, A., & Rivarola, M. A. (1986). Progressive decrease in serum sex hormone-binding globulin from infancy to late puberty in boys. *Journal of Clinical Endocrinology and Metabolism*, 63, 510–512.
- Benbow, C. P. (1986). Physiological correlates of extreme intellectual precocity. *Neuropsychologia*, 24(5), 719–725.
- Benbow, C. P. (1987). Possible biological correlates of precocious mathematical reasoning ability. *Trends in Neuroscience*, 10, 17–20.

- Benbow, C. P. (1988). Sex differences in mathematical reasoning ability in intellectually talented preadolescents. Their nature, effects and possible causes. *Behavioral and Brain Sciences*, 11, 169–232.
- Burdick, K. E., Lencz, T., Funke, B., Finn, Ch., Szeszko, P. R., Kane, J. M., Kucherlapati, R., & Malhotra, A. K. (2006). Genetic variation in DTNBP1 influences general cognitive ability. *Human Molecular genetics*, 15(10), 1563–1568.
- Butler, G. E., Walker, R. F., Walker, R. V., Teague, P., Riad-Fahmy, D., & Ratcliffe, S. G. (1989). Salivary testosterone levels and the progress of puberty in the normal boy. *Clinical Endocrinology*, *30*, 587–596.
- Celec, P., Ostatnikova, D., Putz, Z., & Kudela, M. (2002). The circalunar cycle of salivary testosterone and the visual-spatial performance. *Bratislavske Lekarske Listy*, 103, 59–69.
- Clark, A. S., MacLusky, N. J., & Goldman-Rakic, P. S. (1988). Androgen binding and metabolism in the cerebral cortex of the developing rhesus monkey. *Endocrinology*, 123(2), 932–940.
- Cohen-Bendahan, C. C. C., van de Beek, C., & Berenbaum, S. A. (2005). Prenatal sex hormone effects on child and adult sex-typed behaviour: Methods and findings. *Neuroscience and Behavioural Reviews*, 29, 353–384.
- Dabbs, J. M. (1990). Salivary testosterone measurements: Reliability across hours, days, and weeks. *Physiological Behaviour*, 48, 83–86.
- De Bellis, M. D., Keshavan, M. S., Beers, S. R., Hall, J., Frustaci, K., Masalehdan, A., Noll, J., & Boring, A. M. (2001). Sex differences in brain maturation during childhood and adolescence. *Cerebral Cortex*, 11(6), 552–557.
- Duncan, J. (2005). Frontal lobe function and general intelligence: Why it matters. Cortex, 41, 215–217.
- Duncan, J., Burgess, P., & Emslie, H. (1995). Fluid intelliegence after frontal lobe lesions. *Neuropsychologia*, 33(3), 261–268.
- Duncan, J., Seitz, R. J., Kolodny, J., Bor, D., Herzog, H., Ahmed, A., Newell, F. N., & Emslie, H. (2000). A neural basis for general intelligence. *Science*, 289, 457–460.
- Ehrhardt, A. A., & Money, J. (1967). Progestin-induced hermaphroditism: IQ and psychosexual identity in a study of girls. *Journal of Sexual Research*, *3*, 83–100.
- Federman, D. D. (2006). The biology of human sex differences. *The New England Journal of Medicine*, 354, 1507–1514.
- Finegan, J. A., Bartleman, B., & Wong, P. Y. (1989). A window for the study of prenatal sex hormone influences on postnatal development. *Journal of Genetic Psychology*, 150(1), 101–112.
- Fink, G., Sumner, B. E. H., McQueen, J. K., Wilson, H., & Rosie, R. (1988). Sex steroid control of mood, mental state and memory. *Clinical and Experimental Pharmacology and Physiology*, 25, 764–775.
- Flannery, K. A., Liederman, J., Daly, L., & Schultz, J. (2000). Male prevalence for reading disability is found in a large sample of Black and White children free from ascertainment bias. *Journal of the International Neuropsychological Society*, 6(4), 433–442.
- Fuster, J. M. (2005). The cortical substrate of general intelligence. *Cortex*, *41*, 228–229.
- Geschwind, N., & Galaburda, A. M. (1985). Cerebral lateralization: Biological mechanisms, associations and pathology I. A hypothesis and program for research. Archives of Neurology, 42, 428–459.
- Gottesman, I. I., & Hanson, D. R. (2005). Human development: Biological and genetic processes. Annual Review of Psychology, 56, 263–286.
- Gouchie, C., & Kimura, D. (1991). The relationship between testosterone levels and cognitive ability patterns. *Psychoneuroendocrinology*, 16, 323– 334.
- Granger, D. A., Schwartz, E. B., Booth, A., & Arentz, M. (1999). Salivary testosterone determination studies of child health and development. *Hormones and Behavior*, 35, 18–27.
- Grimshaw, G. M., Sitarenios, G., & Finegan, J. A. (1995). Mental rotation at 7 years: Relations with prenatal testosterone levels and spatial play experiences. *Brain and Cognition*, 29, 85–100.
- Haier, R. J., Jung, R. E., Yeo, R. A., Head, K., & Alkire, M. T. (2004). Structural brain variation and general intelligence. *Neuroimage*, 1, 425–433.
- Haier, R. J., Siegel, B. V., Tang, C., Abel, L., & Buchsbaum, M. S. (1992). Intelligence and changes in regional cerebral glucose metabolic rate following learning. *Intelligence*, 16, 415–426.

- Hampson, E., & Kimura, D. (1992). Sex differences and hormonal influences on cognitive functions in humans. In J. B. Becker, S. M. Breedlove, & D. Crews (Eds.), *Behavioral endocrinology* (pp. 357–401). Cambridge: MIT Press.
- Hassler, M. (1991). Maturation rate and spatial, verbal, and musical abilities: A seven-year-longitudinal study. *International Journal of Neuroscience*, 58, 183–198.
- Hassler, M., & Birbaumer, N. (1988). Handedness, musical abilities and dichaptic and dichotic performance in adolescents, a longitudinal study. *Developmental Neuropsychology*, 4, 129–145.
- Hausmann, M., Slabbekoorn, D., Van Goozen, S. H. M., Cohen-Kettenis, P. T., & Güntürkün, O. (2000). Sex hormones affect spatial abilities during the menstrual cycle. *Behavioral Neuroscience*, 114, 1245–1250.
- Hines, M., Fane, B. A., Pasterski, V. L., Mathews, G. A., Conway, G. S., & Brook, C. (2003). Spatial abilities following prenatal androgen abnormality; targeting and mental rotation performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology*, 28, 1010–1026.
- Hyde, J. S., Fennema, E., & Lamon, S. J. (1988). Gender differences in mathematics performance: A meta-analysis. *Psychological Bulletin*, 107, 139– 155.
- Jacklin, C. N., Wilcox, K. T., & Maccoby, E. E. (1988). Neonatal sex-steroid hormones and cognitive abilities at six years. *Developmental Psychobiology*, 21, 567–574.
- Janowski, J. S. (2006). Thinking with your gonads: Testosterone and cognition. *Trends in Cognitive Sciences*, 10(2), 77–82.
- Jaušovec, N. (2000). Differences in cognitive processes between gifted, intelligent, creative and average individuals while solving complex problems: An EEG study. *Intelligence*, 28(3), 213–237.
- Josephs, R. A., Newman, M. L., Brown, R. P., & Beer, J. M. (2003). Status, testosterone, and human intellectual performance: Stereotype threat as status concern. *Psychological Science*, 14(2), 158–163.
- Kirkpatrick, S. W., Campbell, P. S., Wharry, R. E., & Robinson, S. L. (1993). Salivary testosterone in children with and without learning disabilities. *Psychology and Behavior*, 53, 583–586.
- LeVay, S. (1993). The sexual brain. Cambridge, Massachusetts: The MIT Press.
- Liederman, J., Kantrowitz, L., & Flannery, K. (2005). Male vulnerability to reading disability is not likely to be a myth: A call for new data. *Journal of Reading Disabilities*, 38(2), 109–129.
- Lubinski, D., & Humphreys, L. G. (1990). A broadly based analysis of mathematical giftedness. *Intelligence*, 14, 327–355.
- Lustig, R. H. (1996). In vitro models for the effects of sex hormones on neurons. Annals of the New York Academy of Sciences, 784, 370–380.
- Mackintosh, N. J. (1998). IQ and human intelligence (pp. 182–189). Oxford University Press.
- MacLusky, N. J., Bowlby, D. A., Brown, T. J., Peterson, R. E., & Hochberg, R. B. (1997). Sex and the developing brain: Suppression of neuronal estrogen sensitivity by developmental androgen exposure. *Neurochemical Research*, 22(11), 1395–1414.
- MacLusky, N. J., Hajszan, T., Prange-Kiel, J., & Leranth, C. (2006). Androgen modulation of hippocampal synaptic plasticity. *Neuroscience*, 138(3), 957–965.
- Martin-Loeches, M., Muñoz-Ruata, J., Martinez-Lebrusant, L., & Gómez-Jarabo, G. (2001). Electrophysiology and intelligence: The electrophysiology of intellectual functions in intellectual disability. *Journal of Intellectual Disability Research*, 45, 63–75.
- McGuire, L. S., & Omenn, G. S. (1975). Congenital adrenal hyperplasia. I. Family studies if IQ. *Behavior Genetics*, 5, 165–173.
- O'Boyle, M. W., Alexander, J. E., & Benbow, C. P. (1991). Enhanced right hemispheric activation in the mathematically precocious: A preliminary EEG investigation. *Brain andCognition*, 17, 138–153.
- O'Boyle, M. W., & Benbow, C. P. (1990). Enhanced right hemisphere involvement during cognitive processing may relate to intellectual precocity. *Neuropsychologia*, 28, 211–216.
- O'Boyle, M. W., Vaugham, D., Cunnington, R., Puce, A., Syngeniotis, A., & Egan, G. (2002). 3-Dimensional rotation in the mathematically gifted adolescents. An fMRI investigation. *NeuroImage*, 16, S673.
- Ostatníková, D., Laznibatová, J., Putz, Z., Maťašeje, A., Dohnányiová, M., & Pastor, K. (2000). Salivary testosterone levels in intellectually gifted and

non-intellectually gifted preadolescents: An exploratory study. *High Ability Studies*, *11*(1), 41–54.

- Ostatníková, D., Laznibatová, J., Putz, Z., Maťašeje, A., Dohnányiová, M., & Pastor, K. (2002). Biological aspects of intellectual giftedness. *Studia Psychologica*, 44, 3–12.
- Ostatníková, D., Pastor, K., Putz, Z., Dohnányiová, M., Maťašeje, A., & Hampl, R. (2002). Salivary testosterone levels in preadolescent children. *BMC Pediatrics*, 2, 5 (http://www.biomedcentral.com/content/pdf/1471-2431-2-5.pdf).
- Perlman, S. M. (1973). Cognitive abilities of children with hormone abnormalities: Screening by psychoeducational tests. *Journal of Learning Disabilities*, 6, 26–34.
- Pinyerd, B., & Zipf, W. B. (2005). Puberty—Timing is everything!. Journal of Pediatric Nursing, 20(2), 75–82.
- Plomin, R., & Spinath, F. M. (2004). Intelligence, genetics, genes, and genomics. Journal of Personality and Social Psychology, 86, 112–129.
- Poplawski, N. K. (2003). Investigating intelletual disability. A genetic perspective. Journal of Paediatrics and Child Health, 39, 492–506.
- Reinisch, J. M., & Karow, W. G. (1977). Prenatal exposure to synthetic progestins and estrogens: Effects on human development. *Archives of Sexual Behavior*, 6, 257–288.
- Resnick, S. M., Berenbaum, S. A., Gottesman, I. I., & Bouchard, T. J. (1986). Early hormonal influences on cognitive functioning in congenital adrenal hyperplasia. *Developmental Psychology*, 22, 192–198.

- Simerly, R. B. (2005). Wired on hormones: Endocrine regulation of hypothalamic development. *Current Opinion in Neurobiology*, 15, 81– 85.
- Singh, H., & O'Boyle, M. W. (2004). Interhemispheric interaction during global–local processing in mathematically gifted adolescents, average ability youth, and college students. *Neuropsychology*, 18(2), 371– 377.
- Sisk, C. L., & Foster, D. L. (2004). The neural basis of puberty and adolescence. *Nature Neuroscience*, 7(10), 1040–1047.
- Spelke, E. S. (2005). Sex differences in intrinsic aptitude for mathematics and science? A critical review. *American Psychologist*, 60(9), 950– 958.
- Swerdloff, R. S., Wang, C., Hines, M., & Gorski, R. (1992). Effect of androgens on the brain and other organs during development and aging. *Psychoneuroendocrinology*, 17, 375–383.
- Waber, D. P. (1977). Sex differences in mental abilities, hemispheric lateralization and rate of physical growth in adolescence. *Developmental Psychology*, 13, 29–38.
- Wechsler, D. (1974). Manual for the Wechsler intelligence scale for children—Revised. New York: Psychological Corporation.
- Winner, E. (1996). Gifted children. Basic Books. A Division of Harper Collins Publishers.
- Winner, E. (2000). The origins and ends of giftedness. *American Psychologist*, 55(1), 159–169.