Early Human Development (2006) **82**, 755–760

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/earlhumdev

Fetal testosterone and sex differences ☆

Rebecca Christine Knickmeyer [a,*], **Simon Baron-Cohen** [b]

[a] *Department of Psychiatry, University of North Carolina-Chapel Hill, CB #7160, 7023 Neurosciences Hospital, Chapel Hill, NC 27599–7160, USA*
[b] *The Autism Research Centre, Department of Psychiatry, University of Cambridge, Douglas House, 18b Trumpington Rd, Cambridge CB2 2AH, UK*

KEYWORDS:
Testosterone;
Sex differences

Abstract Experiments in animals leave no doubt that androgens, including testosterone, produced by the testes in fetal and/or neonatal life act on the brain to induce sex differences in neural structure and function. In this article, we argue that prenatal and neonatal testosterone exposure are strong candidates for having a causal role in sexual dimorphism in human behaviour, including social development.

Contents

Experiments in animals leave no doubt that androgens, including testosterone, produced by the testes in fetal and/or neonatal life act on the brain to induce sex differences in neural structure and function. In human beings, sex differences are apparent both in brain structures and cognitive skills [1,2]. In this article, we argue that prenatal and neonatal testosterone exposure are strong candidates for having a causal role in sexual dimorphism in behaviour.

1. Testosterone and the sexual differentiation of the brain

Endocrine (hormonal) systems are involved in every aspect of pregnancy, including implantation, formation of the placenta, maternal adaptation, embryonic and fetal development, parturition/birth, and fetal adaptation to life outside the

☆ The longitudinal studies of fetal testosterone and child development reviewed in this paper were carried out at the Autism Research Centre, University of Cambridge. This work was supported by the Nancy Lurie Marks Family Foundation. RCK was also supported by a British Government Overseas Research Studentship (ORS) and the Cambridge Overseas Trust. Portions of this work appeared in Knickmeyer and Baron-Cohen [42].

* Corresponding author. Tel.: +1 919 966 8990; fax: +1 919 966 8994.
E-mail address: rebecca_knickmeyer@med.unc.edu (R.C. Knickmeyer).

0378-3782/$ - see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.earlhumdev.2006.09.014

womb. Hormones have a range of functions involving reproduction, growth and development, maintenance of the internal environment and the production, use and storage of energy. Experiments in animals show that gonadal hormones are essential to the sexual differentiation of both the body and the brain. These include the androgens (e.g. testosterone, dihydrotestosterone), estrogens (e.g. estradiol, estrone, estriol) and progestins (e.g. progesterone).

Hormone effects are usually classified as *organizational* (those that are permanent and happen early in development) or *activational* (those that occur later in development, are transient, and are superimposed on the early organizational effects). These later hormonal actions are often essential to allow the tissue or organ in question to perform its function. For example, the tissues of the genetic male are organized prenatally for male adult reproductive behaviour. However, the male will not display such behaviour, unless adequate sex hormones are present in adulthood. This target article focuses primarily on organizational effects. However, the dichotomy between organizational and activational, although useful, is over-simplistic. When studying the organizational effects of hormones on the developing fetus, it is important to remember that later activational effects may be essential to the function in question. For some hormones such as estrogen the distinction is particularly problematic, as estrogen appears to exert 'organizational' effects for a very long period of time [3].

Organizational effects often occur during a sensitive (or critical) period. This is a specific period of time in which a tissue can be modified by environmental influences. They are adaptive, because development cannot be influenced outside the sensitive period, protecting the animal from disruptive influences. This means, for example, that circulating sex hormones necessary for adult sexual functioning do not cause unwanted alterations to tissues, even though the same hormones might have been essential to the development of those tissues. In contrast, if development is disrupted during the critical period, the relevant tissue may suffer extreme damage while the rest of the embryo remains essentially unaffected. Different behaviours can have different sensitive periods for development. For example, androgen exposure early or late in gestation has differential effects on male typical juvenile behaviours in the female rhesus macaque [4].

It has been recognised since the 1940s that castration of males during neonatal or prenatal life prevents the development of masculine genitalia, while prenatal or neonatal treatment of females with androgen masculinizes their genitalia [1]. Phoenix et al. [5] reasoned that similar experiments would affect the development of the brain producing differences in sex-typical behaviour. They exposed female guinea pig fetuses to testosterone and found that, as adults, these females showed more male and less female copulatory behaviours. Similar experiments have been conducted in a wide range of mammals, comparing castrated males, normal males, normal females, and females treated with androgen on a range of sexually dimorphic features. Castrated males usually show feminized neural development, cognition, and behaviour; while females treated with androgen show masculinized neural development, cognition, and behaviour. Fetal testosterone has been shown to affect the anatomy of the brain, including the hypothalamus, limbic system, and neocortex, [6], sexually dimorphic behaviour such as aggression and activity level and sexually dimorphic cognitive skills like spatial navigation [1,6].

Human beings also show sex differences in both brain structures and cognitive skills [1,2]. For example, males tend to outperform females on some spatial and mathematical tasks, while females are superior at some language tasks [2]. However, the effects of prenatal hormones on these skills have been difficult to study because it is patently unethical to manipulate hormone levels in human fetuses. Certainly the differentiation of the male and female phenotypes in the developing human fetus follows a similar pattern to that in other mammals, although exact timings vary by species. Gonadal hormones appear to play the primary role in this process [1,7] although direct genetic influences on sexual differentiation of the brain are increasingly recognised [8].

Under most circumstances the *genetic sex* of a human being is determined at the moment of conception by the presence of an X (female) or Y (male) chromosome in the fertilising sperm cell. The karyotype of the normal female is 46 XX and that of the normal male is 46 XY. Each is made up of 44 autosomes and 2 sex chromosomes. The male can be described as heterogametic, and the female as homogametic. There are few differences between the genes of males and females, except for the Y chromosome in the male (although the same genes may be expressed at very different levels in each sex). The critical gene for starting the process of phenotypic differentiation of the sexes is the Sry (sex related Y) gene, located on the Y chromosome. It is possible for the Sry gene to be translocated to another chromosome resulting in a child who may have a normal female karyotype, but develops as a phenotypic male. Studies of individuals who appear to be male but who have the XX karyotype confirm that this is because a section of the Y chromosome containing the Sry gene has been integrated into one of the X chromosomes. Experiments such as these isolated the Sry gene as critical for male gonadal development [7].

Genetically male and female fetuses have undifferentiated gonads during early development — i.e. there is no difference in their reproductive structures. Around week 6 of gestation, the Sry gene on the Y chromosome initiates testicular differentiation in the male. This is thought to be the major function of the Y chromosome. The Leydig cells of the testis are capable of testosterone synthesis by the end of week 8. Further development of the Leydig cells means that testosterone secretion is high between week 10 and week 20. Fetal synthesis of testosterone is probably controlled by human chorionic gonadotropin) and lutinizing hormone from the fetal pituitary. In addition males are exposed to testosterone from the fetal adrenals.

In the female, differentiation of the ovaries begins around week 7 of gestation. The fetal ovary is generally considered inactive until late in development [7] but may produce a small amount of estrogen [9]. The female fetus is also exposed to low levels of androgens. A small proportion may come from the fetal adrenals (a biproduct of the production of corticosteroids) and some comes from the maternal adrenals, ovaries and fat [10].

The secretions of the gonads determine the *phenotypic sex*. If male sex hormones and the appropriate receptors are present, the male genital phenotype will develop and, if sufficient male sex hormones or functioning receptors are not present (i.e. in females), the female genital phenotype will develop [7].

The gonadal hormones are also thought to be involved in the sexual differentiation of the brain, determining the *neuronal sex*, which refers to male- or female-type gonadotropin secretion, sexual orientation, gender role behaviour, and gender identity [7]. In animal models, the general critical period for sexual differentiation of the brain usually occurs when sex differences in serum testosterone are highest [6]. Therefore it is likely that this is an important period for masculinization of the brain in humans as well. The onset of testosterone biosynthesis occurs at about 9 weeks [7]. The maximal sex difference in serum levels occurs between week 12 and 18 (mean (sd) = 249 (93) ng/dL and mean (sd) = 29 (19) ng/dL for males and females respectively) [11]. Testosterone levels in males are initially elevated in response to placental human chorionic gonadotropin and remain high under the influence of lutinizing hormone. However, human chorionic gonadotropin and lutinizing hormone receptors may not appear until weeks 10–12 of gestation raising the possibility that the earliest secretion of fetal testosterone is controlled by other, unknown factors. Levels of both gonadotropins, lutinizing hormone and follicle stimulating hormone, are controlled by the hypothalamic gonadotropin releasing hormone pulse generator, which is insensitive to the negative feedback of gonadal sex steroids in early pregnancy. The pulse generator has matured by the third trimester and becomes sensitive to the high levels of estrogen and progesterone produced by the placenta. Levels of gonadotropins and of fetal testosterone fall [12]. After 24 weeks plasma testosterone levels are low (in the early pubertal range).

Although weeks 8 to 24 have been considered the most important in human sexual differentiation, this does not mean it is the only period for differentiation. Males are born with elevated testosterone levels (approximately 200 ng/dL), as a result of the sudden drop in inhibitory estrogen levels produced by the placenta. Testosterone rapidly decreases in the first day of life and then begins to rise again after the first week. Levels remain high for the first year of life, peaking around the 3rd to 4th months of life. Median levels are equivalent to those in the second stage of puberty (200–300 ng/dL) [12]; this is referred to as the neonatal surge. The function of the neonatal surge is not fully understood in humans, but is likely to be related to the preparation of tissue for subsequent androgen mediated growth. In monkeys, disruption of the neonatal surge is known to lead to disrupted testicular function at puberty [13]. As males have had a testosterone surge at this time, and females have not, the same amount of subsequent testosterone exposure will have very different effects on each sex. Females have a post-natal surge in estradiol production, which is thought to come from the ovaries. The post-natal surges in both sexes are stimulated by surges in gonadotropin levels [12].

During childhood the gonads are quiescent. The gonadotropin releasing hormone pulse generator is inhibited by the very low levels of sex steroids present. This feedback system is ten times more sensitive to sex steroids than the adult feedback mechanism. Puberty occurs when the sensitivity of the pulse generator drops and the hypothalamic–pituitary axis is released from inhibition. Levels of gonadotropins rise causing the gonads to enlarge, mature, and secrete increased amounts of gonadal steroids. The pubertal surge allows the secondary sexual characteristics to develop. By the end of this stage, the organism is prepared for reproduction [12]. In addition to these potential periods for steroid-induced sexual differentiation, sexual differentiation under direct genetic control can occur when no sex differences in testosterone are apparent [8].

This article focuses primarily on the prenatal stage of sexual differentiation. Testicular hormones, particularly testosterone, play a major role in this process. The default mammalian sex is female and, in the absence of very high levels of male sex hormones, female structures will develop. It has been assumed that no special hormonal environment is required for the formation of the female phenotype [7]. However, this traditional model is now being replaced by a more complex one which recognises that small amounts of ovarian hormones may be required for active feminization of the female brain [3]. Still, there are many stages, which must be successfully completed, in order for the male phenotype to develop, and these rely to a large extent on the existence of the right hormonal environment. This implies that there are a number of stages at which the normal development of the male could potentially be disrupted.

Not all animals have female as the default sex. In birds, for example, the default homogametic sex is male, and differentiation of the female depends on exposure to ovarian hormones. In mammals, fetuses are exposed to high levels of female hormones from the mother, so it is adaptive for the default sex to be female. In species which do not develop in the womb (i.e. egg layers) this reasoning does not apply, so having one sex as the default sex over the other does not necessarily confer the same advantages as in mammals. It is interesting to note that feminization of the brain in mammals by ovarian estrogen is thought to occur at a later period than masculinization (in female rats this may extend from the late neonatal to the pubertal period and perhaps even into adulthood) [3]. This would mean ovarian estrogen mediated feminization takes place after the individual is free from the maternal hormonal environment of the womb.

2. Human sex differences

The psychological study of sex differences has traditionally focused on spatial, mathematical, and verbal ability [2]. However, there is increasing interest in potential sex differences in social relationships. Several studies have shown a female advantage in reading nonverbal signals. A meta-analytic study by Hall [14] showed that females are on average better than males at interpreting body language, vocal tone, and facial expression. In a more recent study [15], women were better at attributing subtle mental states to a person, when interpreting the eye region of the face. However, not all studies show this effect [16]. Part of this variation may depend on the specific emotions being examined. For example, one study [17] showed that while females were better at identifying emotions overall, males were superior to females at recognising male anger.

Although a female superiority for language related skills is commonly accepted, actual results vary considerably across studies. This is not surprising given that language consists of a number of subsystems including phonology, morphology, the lexicon, semantics, syntax, pragmatics, and discourse. There are well-replicated female advantages for verbal memory, spelling ability and verbal fluency in adulthood, although females do not have a larger vocabulary than males [2]. Developmentally, a number of studies have reported greater

vocabularies and faster rates of language acquisition in girls [18].

Theory of Mind is the ability to make inferences about the intentions, beliefs, and emotions of other people in order to predict and explain their behaviour. Research into sex differences in theory of mind has been limited because many of the associated tests are not sensitive enough to detect subtle individual differences, such as sex differences [15]. There are several studies though that suggest that theory of mind may develop earlier in females, and that girls and women are on average better at making inferences about people's mental states and adjusting their behaviour accordingly [15,19,20]. These differences may arise, in part, from differences in social interest. Young girls even at 12 months old show a preference for dyadic interactions [21], spend more time watching a film of a face than a film of a car [22], and make more eye contact [23]. They are more interested in facial than spatial/mechanical stimuli even at birth [24].

3. Measuring fetal testosterone at amniocentesis

Both male and female fetuses produce some testosterone. In males the main source is the testes. Females are exposed to small amounts of testosterone from the fetal adrenal glands and from the maternal adrenals, ovaries and fat [10]. Testosterone can be measured in amniotic fluid collected during midtrimester amniocentesis. Testosterone is thought to enter the amniotic fluid via diffusion through the fetal skin in early pregnancy, and later from fetal urination. Although the exact correlation between testosterone levels in the fetal serum and the amniotic fluid is unknown, the maximal sex difference in amniotic testosterone between males and females occurs between weeks 12 and 18, closely paralleling peak serum levels [25]. In animal models, the general critical period for sexual differentiation of the brain usually occurs when sex differences in serum testosterone are highest [1]. Therefore it is likely that this is an important period for sexual differentiation of the human brain as well. This is supported by the study which found that only prenatal androgen exposure in the 2nd trimester related to adult gendered behaviour [26] and the study which found a relationship between gendered-play and testosterone in maternal blood during pregnancy at a mean gestational age of 16 weeks [27].

The first study to use this methodology was carried out by Finegan et al. [28]. They reported relationships with language comprehension, classification abilities, counting, number facts, and block building, but the results were not consistent with the predictions of androgen theory. This may be because the abilities studied did not show a sex difference in their, or other's, samples. Later studies by the same group have produced results more consistent with predictions. At age eight, girls with higher levels of amniotic testosterone performed a mental rotation task faster than girls with lower levels [29]. At age 10, girls with higher levels of amniotic testosterone showed a more masculine pattern of cerebral lateralization [30].

The amniocentesis design has several strengths. As with the measurement of testosterone in maternal blood, it involves quantitative measures of hormone levels and measures normal variability. The majority of studies showing that variations in fetal testosterone are related to gendered behaviour have used groups with large abnormalities in prenatal endocrine conditions due to genetic flaws or fetal exposure to synthetic progestins. Focusing on normal variation can be a weakness as well, as larger sample sizes may be needed to show an effect then in studies where exposure is very high. Sample sizes are generally smaller than in studies measuring maternal testosterone levels, because only a selection of women will be advised to have amniocentesis. However, amniocentesis is carried out routinely and children who underwent amniocentesis are far more common than those with prenatal endocrine conditions. For example, Addenbrooke's Hospital, which analyses amniocentesis samples from 6 hospitals in East Anglia UK, processes approximately 1000 samples a year. Amniocentesis takes place in mid-gestation, which is thought to be an important period for sexual differentiation of the human brain and, unlike studies using maternal blood, testosterone exposure can be measured in both boys and girls. A significant limitation of research using this method is that a truly random sample cannot be collected, since one can only include in a study those individuals who have decided/been advised to have an amniocentesis due to late maternal age or other factors that increase the risk of fetal abnormality.

In the next section we will review the results of a longitudinal study examining the relationship between amniotic testosterone, social development, and other traits relevant to autism.

4. The Cambridge Fetal Testosterone Project

This project is interested in the role of prenatal hormones in the development of autism. Although published prevalence rates for autism have increased significantly over the past decades, it is still a relatively rare condition. Autism spectrum conditions may occur as often as 1 in every 100 people [31]. Only a small proportion of pregnant women will be asked to undergo amniocentesis. To add to the difficulties, autism is seldom diagnosed before age 3, so there is a considerable lag between the time when an amniotic fluid sample is collected and a child is old enough for a diagnosis to be made with confidence. However, we can begin investigating possible links between fetal testosterone and autism spectrum conditions in a less direct way. It is increasingly suggested that autism is part of a spectrum of conditions that blend into the normal population. If autistic traits are continuously distributed in the population, then it is possible that factors that are related to variation in those traits in non-clinical groups are also important in the clinical population. At Cambridge University we have been following up a group of approximately 100 children whose fetal testosterone level had been measured in amniotic fluid. Their mothers had undergone amniocentesis in the Cambridge region between June 1996 and June 1997 and had given birth to the healthy singleton infants between December 1996 and December 1997.

The children were first seen at 12 months of age when the infants and parents were filmed and the amount of eye contact made by the infant to the parent was recorded. Eye contact is of major importance in normal social development [32]. Infants as young as 2 months of age spend more time looking at the eye region of the face than any other part of the face [33]. This may also be relevant to autism, which is

defined by marked social impairment, including abnormal eye contact [34]. Girls made significantly more eye contact than boys. The amount of eye contact varied quadratically with amniotic testosterone level when data from both sexes was examined together, and when the data for the boys was examined alone. This suggests that testosterone may shape the neural mechanisms underlying social development [23].

The children were next followed up 18 and 24 months after birth and their vocabulary size was assessed using the Oxford Communicative Development Inventory [35]. Girls were found to have a significantly larger vocabulary than boys at both ages [36],[40]. This replicates previous findings of a female advantage in language ability, but reveals this sex difference at the earliest point of development. Additionally, amniotic testosterone was an inverse predictor of vocabulary size when data from both sexes was examined together, but not within sex. The lack of a significant correlation between testosterone and vocabulary within each sex may reflect the sample size in that study. However, the significant correlation between testosterone and vocabulary when the sexes were combined suggests testosterone might be involved in shaping the neural mechanisms underlying communicative development.

The children were next followed up at 48 months. Their mothers completed the Children's Communication Checklist [37], a questionnaire assessing language, quality of social relationships and restricted interests. Amniotic testosterone was negatively correlated to quality of social relationships and directly correlated with restricted interests, taking sex differences into account. Testosterone was also positively correlated with restricted interests when boys were examined separately. Finally, testosterone was negatively correlated with systemizing at 8 years of age [38], but positively correlated with empathy at both 4 and 8 years of age [39,40]. These findings implicate testosterone in both social development and attentional focus [41].

Causal interpretations are, of course, unjustified from these correlational studies, but the results suggest that high levels of fetal testosterone could produce a behavioural profile relevant to that seen in autism.

Acknowledgements

We are grateful to the Nancy Lurie Marks Family Foundation for support during the period of this work. RK was also supported by a British Government Overseas Research Studentship (ORS) and the Cambridge Overseas Trust. SBC was also supported by the Medical Research Council (MRC) UK. We are grateful to Gerald Hackett, Kevin Taylor, Peter Raggatt, Svetlana Lutchmaya, Bonnie Auyeung, and Emma Chapman for their role in the Cambridge Fetal Testosterone Project.

References

[1] Hines M. Sexual differentiation of human brain and behavior. In: Pfaff D, Arnold A, Etgen A, Fahrbach S, Rubin R, editors. Hormones, brain and behavior. New York: Academic Press; 2002. p. 425-62.
[2] Kimura D. Sex and cognition. Cambridge, MA: The MIT Press; 1999.
[3] Fitch RH, Bimonte HA. Hormones, brain, and behavior: putatative biological contributions to cognitive sex differences. In: McGillicuddy-DeLisi A, DeLisi R, editors. Biology, society, and behavior: the development of sex differences in cognition. Greenwich: Ablex; 2002.
[4] Goy RW, Bercovitch FB, McBrair MC. Behavioral masculinization is independent of genital masculinization in prenatally androgenized female rhesus macaques. Horm Behav 1988;22: 552-71.
[5] Phoenix CH, Goy RW, Gerall AA, Young WC. Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. Endocrinology 1959;65:369-82.
[6] De Vries G, Simerly RB. Anatomy, development, and function of sexually dimorphic neural circuits in the mammalian brain. In: Pfaff D, Arnold A, Etgen A, Fahrbach S, Rubin R, editors. Hormones, brain and behavior. New York: Academic Press; 2002. p. 137-91.
[7] Grumbach MM, Hughes IA, Conte FA. Williams textbook of endocrinology. In: Larsen P, Kronenberg H, Melmed S, Polonsky K, editors. Williams textbook of endocrinology. 10th ed. Philadelphia: Saunders; 2003. p. 842-969.
[8] Arnold AP, Xu J, Grisham W, Chen X, Kim Y, Itoh Y. Minireview: sex chromosomes and brain sexual differentiation. Endocrinology 2004;145(3):1057-62.
[9] Smail PJ, Reyes FI, Winter JSD, Faiman C. The fetal hormonal environment and its effect on the morphogenesis of the genital system. In: Kogan S, Hafez E, editors. Pediatric andrology. Boston: Martinus Nijhoff; 1981. p. 9-19.
[10] Martin CR. Endocrine physiology. New York: Oxford University Press; 1985.
[11] Abramovich DR. Human sexual differentiation — in *utero* influences. J Obstet Gynaecol 1974;81:448-53.
[12] Fechner PY. The biology of puberty: new developments in sex differences. In: Hayward C, editor. Gender differences at puberty. Cambridge: Cambridge University Press; 2003. p. 17-28.
[13] Mann DR, Gould KG, Collins DC. Blockade of neonatal activation of the pituitary–testicular axis: effect on peripubertal luteinizing hormone and testosterone secretion and on testicular development in male monkeys. J Clin Endocrinol Metab 1989;68:600-7.
[14] Hall JA. Nonverbal sex differences: communication accuracy and expressive style. Baltimore: John Hopkins University Press; 1984.
[15] Baron-Cohen S, Jolliffe T, Mortimore C, Robertson M. Another advanced test of theory of mind: evidence from very high functioning adults with autism or Asperger Syndrome. J Child Psychol Psychiatry 1997;38:813-22.
[16] Gitter AG, Black H, Mostofsky B. Race and sex in the perception of emotion. J Soc Issues 1972;28(4):63-78.
[17] Rotter NG, Rotter GS. Sex differences in the encoding and decoding of negative facial emotions. J Nonverbal Behav 1988;12:139-48.
[18] Hyde JS, Linn MC. Gender differences in verbal ability: a meta-analysis. Psychol Bull 1988;104:53-69.
[19] Baron-Cohen S, O'Riordan M, Stone V, Jones R, Plaisted K. Recognition of faux pas by normally developing children and children with Asperger Syndrome or high functioning autism. J Autism Dev Disord 1999;29(5):407-18.
[20] Happe F. The role of age and verbal ability in the theory of mind task performance of subjects with autism. Child Dev 1995;66:843-55.
[21] Benenson JF. Greater preference among females than males for dyadic interaction in early childhood. Child Dev 1993;64:544-55.
[22] Lutchmaya S, Baron-Cohen S. Human sex differences in social and non-social looking preferences at 12 months of age. Infant Behav Dev 2002;25:319-25.
[23] Lutchmaya S, Baron-Cohen S, Raggatt P. Foetal testosterone and eye contact in 12 month old infants. Infant Behav Dev 2002;25:327-35.

[24] Connellan J, Baron-Cohen S, Wheelwright S, Ba'tki A, Ahluwalia J. Sex differences in human neonatal social perception. Infant Behav Dev 2001;23:113-8.
[25] Finegan JK, Bartleman B, Wong PY. A window for the study of prenatal sex hormone influences on postnatal development. J Genet Psychol 1989;150:101-12.
[26] Udry JR, Morris NM, Kovenock J. Androgen effects on women's gendered behaviour. J Biosoc Sci 1995;27:359-68.
[27] Hines M, Golombok S, Rust J, Johnston KJ, Golding J, Team tALSoPaCS. Testosterone during pregnancy and gender role behavior of preschool children: a longitudinal, population study. Child Dev 2002;73(6):1678-87.
[28] Finegan JK, Niccols GA, Sitarenios G. Relations between prenatal testosterone levels and cognitive abilities at 4 years. Dev Psychol 1992;28(6):1075-89.
[29] Grimshaw GM, Sitarenios G, Finegan J. Mental rotation at 7 years: relations with prenatal testosterone levels and spatial play experiences. Brain Cogn 1995;29:85-100.
[30] Grimshaw GM, Bryden MP, Finegan JK. Relations between prenatal testosterone and cerebral lateralization in children. Neuropsychology 1995;9:68-79.
[31] Baird G, Simonoff E, Pickles A, Chandler S, Loucas T, Meldrum D, Charman T. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). The Lancet 2006;368:210-5.
[32] Baron-Cohen S, Cross P. Reading the eyes: evidence for the role of perception in the development of a theory of mind. In: Davies M, Stone M, editors. The stimulation theory debate. Blackwells; 1995.
[33] Maurer D, Salapatek P. Developmental changes in the scanning of faces by young infants. Child Dev 1976;47:523-7.
[34] Swettenham J, Baron-Cohen S, Charman T, et al. The frequency and distribution of spontaneous attention shifts between social and non-social stimuli in autistic, typically developing and non-autistic developmentally delayed infants. J Child Psychol Psychiatry 1998;39(5):7747-53.
[35] Hamilton A, Plunkett K, Shafer G. Infant vocabulary development assessed with a British Communicative Inventory: lower scores in the UK than the USA. J Child Lang 2000;27(3):689-705.
[36] Lutchmaya S, Baron-Cohen S, Raggatt P. Foetal testosterone and vocabulary size in 18- and 24-month-old infants. Infant Behav Dev 2002;24:418-24.
[37] Bishop DVM. Development of the children's communication checklist (CCC): a method for assessing qualitative aspects of communicative impairment in children. J Child Psychol Psychiatry 1998;6:879-91.
[38] Auyeung B, Baron-Cohen S, Chapman E, Knickmeyer R, Taylor K, Hackett G. Foetal Testosterone and the Child Systemizing Quotient (SQ-C). Eur J Endocrinol in press.
[39] Chapman E, Baron-Cohen S, Auyeung B, Knickmeyer R, Taylor K, Hackett G. Fetal Testosterone and Empathy: Evidence from the 'Reading the Mind in the Eyes' Test. J Soc Neurosci in press.
[40] Knickmeyer R, Taylor K, Raggatt P, Hackett G, Baron-Cohen S. Fetal testosterone and empathy. Horm Behav 2006;49(3): 282-92.
[41] Knickmeyer R, Baron-Cohen S, Raggatt P, Taylor K. Foetal testosterone, social relationships, and restricted interests in children. J Child Psychol Psychiatry 2005;46(2):198-210.
[42] Knickmeyer R, Baron-Cohen B. Fetal testosterone and sex differences in typical social development and in autism. J Child Neurol 2006;21:825-45.