RELATIONSHIP BETWEEN SALIVARY TESTOSTERONE LEVELS AND EMPATHIZING/SYSTEMIZING IN SLOVAK BOYS WITH ASPERGER SYNDROME

Peter KRAJMER[1], Marian ŠPAJDEL[2,3], Peter CELEC[4,5,6], Daniela OSTATNÍKOVÁ[1]

[1]Institute of Physiology, Faculty of Medicine, Comenius University
Sasinkova 2, 813 72 Bratislava, Slovak Republic
E-mail: krajmerpeter@gmail.com

[2]Department of Psychology, Faculty of Arts, University of Trnava, Slovak Republic

[3]Institute of Normal and Pathological Physiology, Slovak Academy of Sciences
Bratislava, Slovak Republic

[4]Institute of Molecular Biomedicine, Faculty of Medicine, Comenius University
Bratislava, Slovak Republic

[5]Department of Molecular Biology, Faculty of Natural Sciences, Comenius University
Bratislava, Slovak Republic

[6]Institute of Pathophysiology, Faculty of Medicine, Comenius University
Bratislava, Slovak Republic

Abstract: The present study focused on the relationship between salivary testosterone levels and cognitive styles of empathizing and systemizing in children with Asperger syndrome (AS). Fifty AS boys from Slovakia in the range from 6 to 18 years participated in the research. The control group consisted of 79 age/sex-matched boys from primary and grammar schools. Participants were divided into a prepubertal and pubertal group. The measures of empathizing/systemizing as well as additional measures (intuitive physics and folk psychology) were used. The group of AS boys scored lower in empathizing measures compared to the control boys. The prepubertal AS group was more systemized than their control peers. Salivary testosterone levels were lower in AS group. The study found positive correlation between salivary testosterone and folk psychology, and revealed a negative correlation between salivary testosterone and intuitive physics in pubertal boys. These findings are discussed with reference to the "extreme male-brain" theory of autism.

Key words: testosterone, Asperger syndrome, autism, systemizing, empathizing

INTRODUCTION

Asperger syndrome (AS) is a chronic neurodevelopmental disorder belonging to the autism disorders spectrum. Hans Asperger, an Austrian pediatrician more than 50 years ago (1944) identified characteristic behavioral features in a group of young males. They included difficulties in social development and communication, social deficits, lack of empathy, narrow interests, one-way con-

versations and motoric clumsiness. The current diagnostic criteria (DSM-IV, 1994) describe AS as a qualitative impairment in social interaction, restricted repetitive and stereotyped patterns of behavior and impairment in social/occupational functioning. The key difference between AS and classic autism is the absence of language delay and the absence of delay in cognitive development. Patients with AS are also often fixated to constant daily routines and have circumscribed interests.

During the past two decades the spectrum of autism disorders has attracted growing attention and researchers have focused on studying the pathogenesis of its phenotypic characteristics (Kelemenová, Ostatníková, 2009 Kelemenová et al., 2010). Some theorists focused on cognitive deficits (Ozonoff et al., 1991; Russell et al., 1996; Robinson et al., 2009), others conceptualized autism as the inability to combine parts into a unit – a weak central coherence (Frith, 1989; Happé, 1997) or explored autism within the concept of the Theory of Mind (Baron-Cohen et al., 1985; Leslie, Frith, 1988; Happé, Frith, 1996).

Due to the uneven sex ratio in ASD [4:1 male : female (Rutter, 1978)] and due to even higher uneven sex ratio in AS [10:1 male : female (Gillberg, 1989)] theorists have started to explore the relationship between having ASD and being male (Baron-Cohen, Hammer, 1997; Knickmeyer et al.., 2006; Geier, Geier, 2007). According to the Extreme Male Brain (EMB) theory, autism was hypothesized as an extreme version of the male brain caused by high levels of prenatal testosterone. Testosterone affects brain maturation as well as postnatal cognition and behavior. Prenatal testosterone induces development of neural circuits for typically male behavior. This is generally called organizational effect of testosterone. After the peak of testosterone secretion during prenatal life (15th - 20th week of gestation) the hormone is less active (Geschwind, Galaburda, 1985; Auyeung et al., 2009). Previous studies found inverse correlations between fetal testosterone and the ability to read nonverbal communication, language abilities, eyes contact and peer relationships (Knickmeyer et al., 2005; Chapman et al., 2006; Whitehouse et al., 2010). At the same time the authors found positive correlations between fetal testosterone and autistic traits (Knickmeyer et al., 2006; Auyeung et al., 2009). In addition, increased levels of prenatal testosterone may cause excellent performance at systemizing skills (analyzing of objects and structures, collecting facts, excellent memory) in patients with AS and, in contrast, lack of empathy and communication deficits compared with the control group (Baron-Cohen et al., 2002).

The Theory of Mind is aimed at empathizing and systemizing skills. Empathizing is defined as the drive to identify emotions and thoughts in others and to respond to their mental states with an appropriate emotion. Empathizing allows one to predict another's behavior at an accurate level to improve so-

Acknowledgements: The authors are thankful to all children and their parents for participating in this study. Our thanks go to Dr. Kubranská, Dr. Lakatošová and Dr. Schmidtová for their help in collecting and analyzing saliva samples. Also thanks to Dr. Kusá and Dr. Halama for useful comments on the preliminary versions of the text. This study is a part of the interdisciplinary project titled "Autism – a Challenge for Integrative Medicine" carried out at the Institute of Physiology, Comenius University, Faculty of Medicine in Bratislava. This work was funded by grants MZSR 2006/22-UK-01, AV 4/0038/07, VEGA 1/0305/09, VEGA 2/0023/10, UK/116/2008, UK/430/2009.

cial interaction. Systemizing is defined as the drive to analyze and build systems, e.g. technical, natural, numeric, taxonomic, motor, and social. Systemizing allows the subject to predict and control such systems (Baron-Cohen, 2009). In the Extreme Male Brain (EMB) theory of autism Baron-Cohen proposed two fundamental cognitive styles, which are measured by the Empathizing Quotient (EQ) and the Systemizing Quotient (SQ). Male brain type is defined as S>E and female brain type as E>S. Individuals from autistic spectrum disorder (ASD) are considered as extremely systemized S>>E (Baron-Cohen, 2010, 1999).[1] Goldenfeld et al. (2005) in their study concluded that ASD arose from a cognitive deficit in empathizing. Wakabayashi et al. (2007) in adults and Krajmer et al. (2010) in children found that the ASD group scored higher on systemizing but lower on empathizing, compared with the controls. Bellow average empathy is a way to explain the social communication difficulties, whilst average or even above average systemizing is a way of explaining the narrow interests, repetitive behavior and resistance to change/ need for sameness among autistic individuals (Baron-Cohen, 2008).

As regards physiology of cognitive functioning, testosterone plays a particular role. Steroid hormones cross the blood-brain barrier and the androgen receptors are present in most areas of the human brain. Apart from its effect on sexuality, mood and aggressive behavior, testosterone levels have many effects on cognitive functions (spatial cognition and mathematical reasoning, working memory) (Williams et al., 1990; Alexander et al., 1997; Celec et al., 2002; Ostatníkova et al., 1996, 2007a). Postnatal testosterone influences brain structures during the life span. This effect is called activational (Geschwind, Galaburda, 1985). Circulating testosterone is known to have biorhytmic fluctuations with changing circadian levels (with peak levels in the morning and nadir in the evening) (Dabbs, 1990; Celec et al., 2002; Matchcock et al., 2007) and circannual variations with annual crest time in July even in prepubertal children (Bellastella et al., 1980, 1983).

Individual differences in hormone levels and their effects on cognitive abilities have been examined in healthy population. Reports differ on the relationship in individual fluctuations between and within testosterone levels and spatial performance. Celec et al. (2002) found mental rotation ability to mirror the circalunar fluctuations of testosterone. Significant differences between visual-spatial test performances during high-testosterone compared to low-testosterone phases were reported. On the other hand, Silverman et al. (1999) reported that mental rotation scores in healthy men was positively related to mean testosterone levels but not to diurnal testosterone fluctuations. Some studies failed to find associations between testosterone and perceptual and cognitive abilities (Alexander et al., 1997; McKeever et al., 1987; Halari et al., 2005). Hassler et al. (1992) reported that spatial performance was

[1] EMB is based on sex differences in brain when typical female brain is characterized by enhanced empathizing and typical male brain is characterized by enhanced systemizing. EMB theory suggests that women perform better on empathizing tasks and men perform better on visuospatial tasks that requires systemizing. ASD individuals score even lower than neurotypical males on empathizing. In contrast, on systemizing they score higher than males. Various studies confirmed these assumptions (Baron-Cohen et al., 2003, 2004).

associated with testosterone/estradiol ratio but not levels of testosterone and estradiol alone. Levels of testosterone in these studies were determined in saliva. Saliva is the ultrafiltrate of plasma and carries only the free form of testosterone, not bound to specific globulin nor to albumin. This free fraction can pass blood-brain barrier thus having its influence on specific areas in the brain that are associated with cognitive processes (Ostatníková et al., 1996).

Current literature provides comparisons in ASD group regarding plasmatic testosterone levels. Tordjman et al. (1997) examined patients with ASD relative to controls, and found that 1 in 3 pre-pubertal age children with ASD had significantly increased plasma testosterone levels relative to controls. Similarly, Geier and Geier (2006) found that prepubertal children with ASD had significantly increased dehydroepiandrosterone (DHEA) and serum testosterone levels relative to normal laboratory reference ranges. Studies of the relationship between salivary testosterone and cognition in autistic children are rare. Takagishi with coworkers (2010) found positive correlation between salivary testosterone levels and autistic features in healthy adults.

FOCUS OF THE STUDY

The role of testosterone in etiology of autism is under investigation. As mentioned above, the differences in salivary testosterone levels and allied characteristic cognitive styles between AS group and control group are supposed. This study aims to compare groups of prepubertal and pubertal boys with AS and age/sex-matched control children in psychological aspects of the EMB theory. The reason why the prepubertal and pubertal participants were studied separately is related to testosterone levels: concentrations of testosterone is relatively stable in prepubertal age, and dynamic changes with high variability occur in pubertal age (Ostatníková et al., 2000, 2002a, 2002b, 2007a). Testosterone levels affect not only physical appearance but also cognitive and behavioral characteristics as well.

Measures of cognitive styles of systemizing and empathizing were employed. Systemizing abilities were measured by the Systemizing Quotient (SQ) Questionnaire and Intuitive Physics Test. Empathizing abilities were measured by the Empathizing Quotient (EQ) Questionnaire and Folk Psychology Test. Higher extent of systemizing and lower extent of empathizing in boys with AS is hypothesized. To make this comparison relevant in the same groups, levels of salivary testosterone were examined as well.

METHODS

Participants

Participants included 50 boys with Asperger syndrome and 79 neurotypical boys with no history of autism. All children with suspected AS were diagnozed by trained clinicians as having Asperger syndrome according to standard DSM-IV diagnostic criteria (DSM-IV, 1994). Their IQ ranged from 93-128 on Wechsler Intelligence Scale WISC-III. They all attended standard national schools. Participants with Asperger syndrome were recruited by the local centers in various towns of Slovak Republic. They were all included anonymously into the research database at the Institute of Physiology of Comenius University, Faculty of Medicine, in Bratislava. Control group boys

were recruited from elementary and grammar schools. The boys were divided into two groups according to their age: prepubertal boys under the age of 10 (22 AS boys mean age 8.32; 31 control boys mean age 9.1) and pubertal boys over 10 years (28 AS boys mean age 13.71; 48 control boys mean age 14.83).

Informed consent signed by at least one parent of every single participant was obtained prior to testing.

Measures

All tests were developed at the Autism Research Centre, University of Cambridge and were used with the kind permission of Professor Baron-Cohen (Baron-Cohen et al., 2004, 2003, 2001, 1997) and met the standard psychometric criteria. The primary instruments used in this study were the adapted Slovak translations of the EQ and SQ Questionnaires, Reading the Mind in the Eyes Test and Intuitive Physics Test (Ostatníková, 2007b). Each participant completed four psychological tests measuring empathizing, systemizing, intuitive physics and folk psychology (Reading the Mind in the Eyes Test). Six participants were excluded from the sample because they were not collaborative.

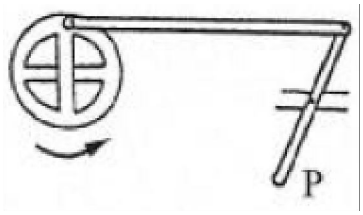
a) *Systemizing* as an ability to analyze systems was assessed by SQ (systemizing quotient). SQ was designed to test the EMB theory of autism. This instrument measures an individual's interest in systems across the different classes of systems. Example of SQ item: *When I am walking in the country, I am curious about how the various kinds of trees differ*.

b) *Empathizing* as an ability to understand and respond appropriately to other's emotions and thoughts was assessed by the EQ (empathizing quotient). The EQ scale was designed to have a clinical application and be sensitive to lack of empathy as a feature of psychopathology. Example of EQ item: *I can easily tell if someone else is interested or bored with what I am saying.*

Both questionnaires consist of 60 items. 40 of them are tapping empathy/systemizing and 20 are control items. Each item is scored by 2, 1 or 0 points, thus, the maximum score is 80 and minimum is 0 points. The participants indicated how strongly they agree with each statement by checking one of 4 options: 'definitely agree', 'slightly agree', 'slightly disagree', or 'definitely disagree'.

Whilst systemizing and empathizing abilities in the EQ and SQ tests are based on subjective self-report, the Intuitive Physics Test and Folk Psychology Test (Reading the Mind in the Eyes Test) were added to the test battery because they were developed to assess systemizing and empathizing in a performance-related way.

c) *Intuitive Physics Test* - comprises higher-level understanding of physical causality. This refers to skills relating to mechanics and understanding how things work. Intuitive Physics Test contains 20 problems from everyday real world experience of the physical-causal world with 4 given solutions. The subject had to choose one of the possible solutions. One point is scored for correct answer, thus, the maximum is 20. Higher scores on Intuitive Physics Test may reveal interest in the correctness and regularity of various systems. Item example: *If the wheel rotates as shown, P will: a) move to the right and stop, b) move the left and stop, c) move to and fro, d) none of the* above



d) *Folk Psychology* - comprises higher-level social intelligence. This includes being able to judge how an agent is expressing basic emotions. Folk Psychology was assessed by Reading the Mind in the Eyes Test which contains 36 photographs of the eye region of the face. The subject was asked to pick one out of 4 given descriptions that fitted the feeling expressed in the pictured eyes. One point is scored for a correct answer, thus, maximum is 36. Lower score, i.e. unrecognized emotions in the eyes, may indicate a problem in social functioning. Item example: *a) reminiscing, b) happy, c) friendly, d) angry.*

Saliva sampling

Levels of testosterone were determined in saliva as a non-invasive stress-free method. Due to circadian fluctuations (Hrnčiar, 1982; Dabbs, 1990) and circannual fluctuations (Bellastella et al., 1980, 1983; Ostatníková et al., 1995; Celec et al., 2002) of testosterone levels, all sampling was done between 9.00 and 11.00 a.m. in June/July 2009. The subjects gathered 2-4 ml of saliva into a Salivette test tube. Soon after sampling the test tubes with saliva were frozen until the time of analysis. Concentration of testosterone in saliva was determined using a commercially available ELISA kit (DRG Diagnostic, Marburg, Germany).

The present study was approved by The Ethical Committee of the Faculty of Medicine, Comenius University and carried out in accordance with the Ethical Codex of World Health Organization.

RESULTS

The measures of central tendency and variance for testosterone levels and the Psychological Test raw scores are in Table 1. The differences between the boys with AS and boys from the control group were computed separately in the prepubertal and pubertal group, using the Mann-Whitney U-test. A nonparametric test was chosen because the distribution of variables across the groups was not Gaussian.

Lower salivary testosterone levels in boys with AS (compared to the control group) were found both in the prepubertal group ($p = 0.036$) and pubertal group ($p < 0.001$).

In the prepubertal group, boys with AS had significantly higher raw SQ score than boys from the control group ($p = 0.001$). In the Folk Psychology Test (Reading the Mind in the Eyes Test) boys with AS performed significantly worse than boys from the control group ($p = 0.010$). No significant differences in empathizing and Intuitive Physics were found ($p = 0.864$; $p = 0.789$).

In the pubertal group, boys with AS scored significantly lower in empathizing and in the

Table 1. Group differences in testosterone levels and psychological measures (SQ, EQ, Intuitive Physics Test, and Folk Psychology Test) in AS (n = 50) and control (n = 79) groups

Group		**Testosterone (pmol/l)**	**SQ**	**EQ**	**Intuitive Physics**	**Folk Psychology**
		Median (CI 95%)	Median (CI 95%)	Median (CI 95%)	Median (CI 95%)	Median (CI 95%)
Prepubertal	AS	41.6 (36.8-90.1)	39.5 (35.0-43.0)	31.0 (26.0-35.0)	8.0 (7.0-10.0)	14.5 (8.0-16.0)
	Control	91.2 (80.9-102.1)	31.5 (27.0-36.0)	31.0 (28.0-34.0)	8.5 (6.0-10.0)	18.0 (16.0-19.0)
	U sig.	127 0.036	119 0.001	262 0.864	257 0.789	149 0.010
Pubertal	AS	86.6 (54.9-114.1)	39.0 (31.0-41.0)	29.0 (25.0-31.0)	12.0 (10.0-13.0)	16.0 (13.0-18.0)
	Control	234.6 (204.5-284.7)	33.0 (29.0-37.0)	41.0 (36.0-43.0)	11.0 (10.0-12.0)	23.0 (22.0-25.0)
	U sig.	202 <0.001	516 0.272	226 <0.001	553 0.497	133 <0.001

Folk Psychology Test than boys from the control group ($p < 0.001$; $p < 0.001$). No significant differences between boys with AS and control boys were found for systemizing ($p = 0.272$) and Intuitive Physics ($p = 0.497$).

In addition, relationships between testosterone and scores in the psychological test were analyzed. Correlations between testosterone and psychological measures were calculated separately in the group of prepubertal and pubertal boys. Positive relationship between testosterone levels and Folk Psychology Test was found, but in pubertal children only ($r = 0.23$; $p = 0.044$). Moreover, negative relationship between testosterone and Intuitive Physics Test was found ($r = -0.24$; $p = 0.041$) in the same group (Figure 1). Other relationships were not significant.

DISCUSSION

In the present paper we examined the differences between Slovak Asperger boys and a control group coming from generally healthy age-matched population using various psycho-physiological parameters. Particularly, we focused on the relationship between salivary testosterone levels and performance on relevant psychological tests (EQ, SQ, Intuitive Physics, Folk Psychology). We expected a higher extent of systemizing and higher levels of salivary testosterone in ASD children. Our focus was based on the EMB Theory of autism.

The hypothesis that the population with AS has higher levels of salivary testosterone based on previous studies (Tordjman et al., 1997; Geier, Geier, 2006; Auyeung et al., 2009) was not supported. The hypothesis

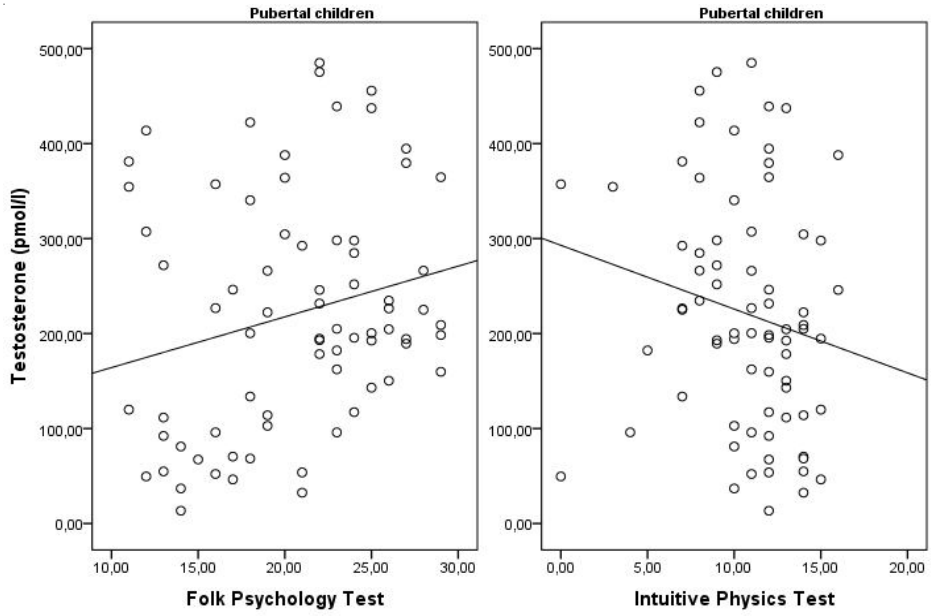


Figure 1. Relationship between testosterone and Folk Psychology Test, and between testosterone and Intuitive Physics Test in the pubertal group of AS (n = 28) and control group of pubertal boys (n = 48)

arises from psychological assumptions of poor emotional development, on one hand, and strong drive to systemizing, on the other hand, both influenced by prenatal levels of testosterone. However, boys with AS in our study had lower levels of salivary testosterone than controls.

We assume that AS children's higher levels of prenatal testosterone turned to be lower due to postnatal negative feedback setup of hormonal hypothalamo-pituitary-gonadal axis regulation. Moreover, it should be taken into consideration that lowered testosterone levels in AS group might be caused by stress during testing. Stress is known to reduce testosterone levels (Chatterton et al., 1999; Schultz et al., 1996; Zitzmann et al., 2001). Children with AS were in situation of social distress when saliva samples were taken individually by a researcher, while in the control group stress was diminished by a friendly atmosphere in known places. Even masticating the swab raised the discomfort in children with AS. Control boys provided saliva samples in a classroom with their peers and may have perceived the procedure less stressful. Collective saliva sampling was needed in the AS group as well, but due to a very individual and particular approach to these boys, it was impossible. Findings that even in gifted as well as mentally challenged chil-

dren lower levels of testosterone were observed, compared to the controls, are remarkable (Ostatníková et al., 2000, 2007a).

The interpretation of Asperger syndrome as a deficit in empathizing (Goldenfeld et al., 2005) was verified by measures of empathizing abilities in both groups of boys. Pubertal boys with AS scored lower in EQ in comparison with controls. The fact that in the prepubertal group there were no differences in EQ may suggest that empathizing, as the characteristic cognitive style, becomes evident in pubertal children and adults. Nevertheless, in the nonverbal test "Reading the Mind in the Eyes", boys with AS scored lower than control boys in both groups, which is in line with previous findings (Baron-Cohen et al., 1997, 2001) and may reflect their social roughness and inability to decode the emotions from the eyes of other people.

Systemizing as the characteristic cognitive style in ASD people has been manifested only in prepubertal boys. Boys with AS scored higher than their control peers. Based on the Extreme Male Brain Theory (Baron-Cohen et al., 2005), it could be suggested that children with AS in our study have a masculinized brain because of the higher levels of prenatal testosterone. This predisposition is supposed to enable boys with AS to operate better with systems. In consequence, even prepubertal children with AS outperformed the control boys in the SQ Test. The pubertal group of boys with AS had a tendency to score higher than the controls but not significantly. On the other hand, an increased performance in the control boys in SQ was discovered. Performance of AS boys seemed to have stabilized since prepuberty.

The Intuitive Physics measure showed no differences between the groups. Factor IQ could play a role in this task (Baron-Cohen et al., 2001). Boys from our research had probably similar IQ values (average or above-average intelligence is the criterion for AS diagnosis), therefore, the Intuitive Physics Test did not discriminate sufficiently. Current literature does not provide evidence for a relationship between IQ and Intuitive Physics. It is in the focus of our future research.

Association between salivary testosterone and performance in psychological variables was found in pubertal group only. Negative correlation between salivary testosterone and Intuitive Physics Test indicate the relationship between testosterone and IQ. Such an inverse correlation has been reported in gifted children (Ostatníková et al., 2002a) and it serves as a basis for the hypothesis of optimal levels of testosterone for certain cognitive abilities. The optimal concentrations of salivary testosterone for male brain functions (logical, mathematical, visuospatial) (Ostatníková et al., 2000, 2007a) are supposed to be lower physiological male concentrations and higher physiological female concentrations. Gifted boys were found to have higher IQ but lower salivary testosterone levels. Boys from the control group had lower IQ but higher salivary testosterone levels (Ostatníková et al., 2000,2007a). Surprisingly, our study revealed a positive correlation between salivary testosterone levels and Reading the Mind in the Eyes Test. This finding suggests that the higher the levels of testosterone, the higher the children's score in Reading the Mind in the Eyes Test. With respect to the above mentioned bias caused by the testing situation and a very demanding approach to the AS children, we cannot state that there is a positive correlation between salivary testosterone levels and em-

pathy in general. Moreover, interpretation of salivary testosterone levels is very complicated. Boys with AS who took part in our study had normal levels of salivary testosterone in prepubertal and also in pubertal groups. However, boys from the control groups had increased salivary testosterone levels, relative to normal laboratory reference ranges. It would be very useful to also assess the levels of SHBG (sex hormone binding globulin), the protein that binds testosterone. Increased SHBG levels show lower levels of testosterone in saliva (Schmidtová, 2008). There are no published data about SHBG plasma levels in people with AS as compared to the normal population.

It is also possible that AS children have a more sensitive androgen receptor which mediates the effect of testosterone in particular tissue and cells. Thus, even lower testosterone levels could increase the effect (Manning et al., 2003). Moreover, we do not have plausible information about the expression of receptors in the brain specific areas. It is known that testosterone is converted to estradiol in one step reaction enabled by the enzyme aromatase and thus the effect of testosterone could be mediated by its metabolite estradiol (Federman, 2006; Lephart, 1996).

Summing up, the findings of our study showed that boys with AS have a deficit in empathizing, whereas, any differences between groups in systemizing were not pinpointed. As far as a negative relationship between salivary testosterone levels and Intuitive Physics Test is concerned, similarities between AS and gifted children could be considered. However, puberty is a turbulent period with high variability of testosterone levels, especially in boys (Di Luigi et al., 2006). Therefore, a huge sample of subjects is crucial for a reliable interpretation. Our study with children with AS is a pilot study in Slovakia. In future studies, we will focus on other physiological and psychological parameters in the Slovak autistic population.

Received October 5, 2010

REFERENCES

ALEXANDER, G.M., SWERDLOFF, R.S., WANG, C., DAVIDSON, T., McDONALD, V., STEINER, B., HINES, M., 1997, Androgen-behavior correlations in hypogonadal men and eugonadal men. Mood and response to auditory sexual stimuli. *Hormones and Behavior*, 31, 110-119.

AMERICAN PSYCHIATRIC ASSOCIATION, 1994, *Diagnostic and statistical manual of mental disorders* (4th edition). Washington DC: American Psychiatric Association.

ASPERGER, H., 1944, Die "Autistischen Psychopathen" im Kindesalter. *Archiv für Psychiatrie und Nervenkrankheiten*, 117, 76-136.

AUYEUNG, B., BARON-COHEN, S., ASHWIN, E., KNICKMEYER, R., TAYLOR, K., HACKETT, G., 2009, Fetal testosterone and autistic traits. *British Journal of Psychology*, 100, 1-22.

BARON-COHEN, S., 1999, The extreme-male-brain theory of autism. In: H. Tager-Flusberg (Ed.) *Neurodevelopmental Disorders*. MIT Press.

BARON-COHEN, S., 2009, Autism: the empathizing-systemizing (E-S) theory. *Annals of the New York Academy of Sciences*, 1156, 68-80.

BARON-COHEN, S., 2010, Empathizing, systemizing and the extreme male brain theory of autism. *Progress in Brain Research*, 186, 167-75.

BARON-COHEN, S., HAMMER, J., 1997, Parents of children with Asperger syndrome: What is the cognitive phenotype? *Journal of Cognitive Neuroscience*, 9, 548-555.

BARON-COHEN, S., KNICKMEYER, R.C., BELMONTE, M.K., 2005, Sex differences in the brain: Implications for explaining autism. *Science,* 310, 819-823.

BARON-COHEN, S., LESLIE, A.M., FRITH, U., 1985, Does the autistic child have a "theory of mind"? *Cognition*, 21, 1, 37-46.

BARON-COHEN, S., RICHLER, J., BISARYA, D., GURUNATHAN, N., WHEELWRIGHT, S.,

2003, The systemizing quotient: An investigation of adults with Asperger syndrome or high-functioning autism, and normal sex differences. *Philosophical Transaction of the Royal Society London. The Royal Society*, 02tb, 1-14.

BARON-COHEN, S., WHEELWRIGHT, S., 2004, The Empathy quotient: An investigation of adults with Asperger syndrome or High functioning Autism, and normal sex differences. *Journal of Autism and Developmental Disorders*, 34, 2, 163-175.

BARON-COHEN, S., 1997, Are children with autism superior at folk physics? In: H. Wellman, K. Inagaki (Eds.), *Children's theories. New direction for child development series*. Jossey-Bass Inc.

BARON-COHEN, S., 2008, *Autism and Asperger syndrome. The facts*. Oxford: University Press.

BARON-COHEN, S., WHEELWRIGHT, S., GRIFFIN, R., LAWSON, J., HILL, J., 2002, The exact mind: Empathising and systemizing in autism spectrum conditions. In: U. Goswami (Ed.), *Handbook of Cognitive Development* (pp. 491-508), Oxford: Blackwell.

BARON-COHEN, S., WHEELWRIGHT, S., SCAHILL, V., LAWSON, J., SPONG, A., 2001, Are intuitive physics and intuitive psychology independent? A test with children with Asperger syndrome. *Journal of Developmental and Learning Disorders*, 5, 47-78.

BELLASTELLA, A., De LUCA, R., MANGO, A., PICCOLO, C., FUSCO, F., D'ALESSANDRO, B., 1980, Annual variations in plasma testosterone levels in prepubertal subjects. *Bollettino-Societa Italiana Biologia Sperimentale*, 56, 2001-2005.

BELLASTELLA, A., CRISCUOLO, T., MANGO, A., PERRONE, L., SINISI, A.A., FAGGIANO, M., 1983, Circannual rhythms of plasma luteinizing hormone, follicle-stimulating hormone, testosterone, prolactin and cortisol in prepuberty. *Clinical Endocrinology (Oxford),* 19, 453-459.

CELEC, P., OSTATNIKOVA, D., PUTZ, Z., KUDELA, M., 2002, The circalunar cycle of salivary testosterone and the visual spatial performance. *Bratislavské Lekárske Listy*, 103, 59-69.

DABBS, J.M., 1990, Salivary testosterone measurements: Reliability across hours, days and weeks. *Physiology & Behavior*, 48, 83-86.

Di LUIGI, L., BALDARI, C., GALLOTTA, M.C., et al., 2006, Salivary steroids at rest and after a training load in young male athletes: Relationship with chronological age and pubertal development. *International Journal of Sports Medicine*, 27, 709-717.

CHAPMAN, E., BARON-COHEN, S., AUYEUNG, B., KNICKMEYER, R., TAYLOR, K., HACKETT, G., 2006, Fetal testosterone and empathy: Evidence from the empathy quotient (EQ) and "reading the mind in the eyes" test. *Social Neuroscience*, 1, 135-148.

FEDERMAN, D.D., 2006, The biology of human sex differences. *The New England Journal of Medicine*, 354, 1507-1514.

FRITH, U., 1989, Autism. Explaining the enigma. Oxford: Blackwell Publishing.

GEIER, D.A., GEIER, M.R., 2006, A clinical and laboratory evaluation of methionin cycle-transsulfuration and androgen pathway markers in children with autistic disorders. *Hormone Research*, 66, 182-188.

GEIER, D.A., GEIER, M.R., 2007, A prospective assessment of androgen levels in patients with autistic spectrum disorders: Biochemical underpinnings and suggested therapies. *Neuroendocrinology Letters*, 28, 565-573.

GESCHWIND, N., GALABURDA, A.M., 1985, Cerebral lateralization, biological mechanisms, associations and pathology: A hypothesis and a program for research. *Archives of Neurology*, 42, 428-459.

GILLBERG, I.C., GILLBERG, C., 1989, Asperger syndrome-some epidemiological considerations: A research note. *Journal of Child Psychology & Psychiatry*, 30, 631-638.

GOLDENFELD, N., BARON-COHEN, S., WHEELWRIGHT, S., 2005, Empathizing and Systemizing in males, females, and autism. *Clinical Neuropsychiatry*, 2, 1-8.

HALARI, R., HINES, M., KUMARI, V., MEHROTRA, R., WHEELER, M., NG, V., SHARMA, T., 2005, Sex differences and individual differences in cognitive performance and their relationship to endogenous gonadal hormones and gonadotropins. *Behavioral Neuroscience*, 119, 104-117.

HAPPÉ, F., 1997, Central coherence and theory of mind in autism: Reading homographs in context. *British Journal of Developmental Psychology*, 15, 1-12.

HAPPÉ, F., FRITH, U., 1996, The Neuropsychology of autism. *Brain*, 119, 1377-1400.

HASSLER, M., GUPTA, D., WOLLMANN, H., 1992, Testosterone, estradiol, ACTH and musical, spatial and verbal performance. *International Journal of Neuroscience*, 65, 45-60.

HRNČIAR, J., IZAKOVIČ, V., LANGER, P., LICHARDUS, B., et al., 1982, *Klinická endokrinológia*, Martin: Osveta.

CHATTERTON, R.T., DOOLEY, S.L., 1999, Reversal of diurnal cortisol rhythm and suppression of plasma testosterone in obstetric residents on call. *Journal of the Society for Gynecological Investigation,* 6, 50-54.

KELEMENOVÁ, S., OSTATNÍKOVÁ, D., 2009, Neuroendocrine pathways altered in autism. Special role of reelin. *Neuroendocrinology Letters*, 30, 429-436.

KELEMENOVÁ, S., FICEK, A., CELEC, P., SCHMIDTOVÁ, E., OSTATNÍKOVÁ, D., 2010, Polymorphisms of candidate genes in Slovak autistic patients. *Psychiatric Genetics*, in press.

KNICKMEYER, R.C., BARON-COHEN, S., 2006, Fetal testosterone and sex differences in typical social development and in autism. *Journal of Child Neurology*, 21, 825-845.

KNICKMEYER, R.C., BARON-COHEN, S., RAGATT, P., TAYLOR, K., 2005, Foetal testosterone, social relationship and restricted interests in children. *Journal of Child Psychology and Psychiatry*, 46, 198-210.

KRAJMER, P., JÁNOŠÍKOVÁ, D., ŠPAJDEL, M., OSTATNÍKOVÁ, D., 2010, Empathizing, Systemizing, Intuitive physics and Folk psychology in boys with Asperger syndrome. *Activitas Nervosa Superior Rediviva*, 52, 1, 57-61.

LESLIE, A.M., FRITH, U., 1988, Autistic children's understanding of seeing, knowing and believing. *British Journal of* D*evelopmental Psychology*, 6, 316-324.

LEPHART, E.D., 1996, A review of brain aromatase cytochrome P450. *Brain Research Review*, 22, 1-26.

MANNING, J.T., BUNDRED, P.E., NEWTON, D.J., FLANAGAN, B.F., 2003, The second to fourth digit ratio and variation in the androgene receptor gene. *Evolution and Human Behavior*, 24, 399-405.

MATCHCOCK, R.L., DORN, R.D., SUSMAN, E.J., 2007, Diurnal and seasonal cortisol, testosterone and DHEA rhythms in boys and girls during puberty. *Chronobiology International*, 24, 969-990.

McKEEVER, W.F., RICH, D.A., DEYO, R.A., CONNER, R.L., 1987, Androgens and spatial ability: Failure to end a relationship between testosterone and ability measures. *Bulletin of the Psychonomic Society,* 21, 465-468.

OSTATNÍKOVÁ, D., PUTZ, Z., MATĚJKA, P., ORSZÁGH, M., 1995, Kolísanie hladiny testosterónu v slinách mužov a žien v priebehu roka. *Praktická Gynekológia*, 2, 45-48.

OSTATNÍKOVÁ, D., CELEC, P., PUTZ, Z., HODOSY, J., SCHMIDT, F., LAZNIBATOVÁ, J., KUDELA, M., 2007a, Intellingence and salivary testosterone levels in prepubertal children. *Neuropsychologia*, 45, 1378-1385.

OSTATNÍKOVÁ, D., LAZNIBATOVÁ, J., DOHNÁNYIOVÁ, M., 1996, Testosterone influence on spatial ability in prepubertal children. *Studia Psychologica*, 38, 237-245.

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, 41-54.

OSTATNÍKOVÁ, D., LAZNIBATOVÁ, J., PUTZ, Z., MAŤAŠEJE, A., DOHNÁNYIOVÁ, M., PASTOR, K., 2002a. Biological aspects of intellectual giftedness. *Studia Psychologica*, 44, 3-12.

OSTATNÍKOVÁ, D., PASTOR, K., PUTZ, Z., MAŤAŠEJE, A., DOHNÁNYIOVÁ, M., HAMPL, R., 2002b, Salivary testosterone levels in preadolescent children. *BMC Pediatrics,* 2, 5 (http://www.biomedcentral.com/content/pdf/1471-2431-2-5.pdf).

OSTATNÍKOVÁ, D., 2007b, Web: www.autismresearchcentre.com/tests/default.asp

OZONOFF, S., PENNINGTON, B.F., ROGERS, S.J., 1991, Executive function deficits in high-functioning autistic individuals: Relationship to theory of mind. *Journal of Child Psychology and Psychiatry,* 32, 7, 1081-1105.

RUSSELL, J., JARROLD, C., HENRY, L., 1996, Working memory in children with autism and with moderate learning difficulties. *Journal of Child Psychology and Psychiatry,* 37, 6, 673-686.

ROBINSON, S., GODDARD, L., DRITSCHEL, B., WISLEY, M., HOWLIN, P., 2009, Executive functions in children with Autism Spectrum Disorders. *Brain and Cognition*, 71, 362-368.

RUTTER, M., 1978, Diagnosis and definition of childhood autism. *Journal of Autism and Child Schizophrenia*, 8, 139-161.

SCHMIDTOVÁ, E., 2008, Testosterone – effects, metabolism and genetic determination. *Československa Fysiologie*, 57, 61-75.

SCHULZ, P., WALKER, J.P., PEYRIN, L., SOULIER, V., CURTIN, F., STEIMER, T., 1996, Lower sex hormones in men during anticipatory stress. *Neuroreport*, 25, 3101-3104.

SILVERMAN, I., KASTUK, D., CHOI, J., PHILIPS, K., 1999, Testosterone levels and spatial ability in men. *Psychoneuroendocrinology,* 24, 813-822.

TAKAGISHI, H., TAKAHASHI, H., YAMAGISHI, T., SHINADA, M., INUKAI, K., TANIDA, S., MIFUNE, N., HORITA, Y., HASHIMOTO, H., YANG, Y., KAMEDA, T., 2010, Salivary testosterone levels and autism-spectrum quotient in adults. *Neuroendocrinology Letters,* 31, 837-841.

TORDJMAN, S., FERRARI, P., SULMONT, V., DUYME, M., ROUBERTOUX, P., 1997, Androgenic activity in autism. *American Journal of Psychiatry*, 154, 1626-1627.

WAKABAYASHI, A., BARON-COHEN, S., 2007, Empathizing and systemizing in adults with and without autism spectrum conditions: Cross-cultural stability. *Journal of Autism and Developmental Disorders,* 37, 1823-1832.

WHITEHOUSE, A., MAYBERY, M., HART, R., MATTES, E., NEWNHAM, J., SLOBODA, D., STANLEY, F., HICKEY, M., 2010, Fetal androgen exposure and pragmatic language ability of girls in middle childhood: Implications for the Extreme male brain theory of Autism. *Psychoneuroendocrinology*, in press.

WILLIAMS, C.L., BARNETT, A.M., MECK, W.H., 1990, Organizational effects of early gonadal secretions on sexual differentiation in spatial memory. *Behavioral Neuroscience*, 104, 84-97.

ZITZMANN, M., NIESCHLAG, E., 2001, Testosterone levels in healthy men and the relation to behavioral and physical characteristics: Facts and constructs. *European Journal of Endocrinology*, 144, 183-197.

KORELÁCIE MEDZI HLADINAMI SALIVÁRNEHO TESTOSTERÓNU A EMPATIZÁCIOU/SYSTEMIZÁCIOU U SLOVENSKÝCH CHLAPCOV S ASPERGEROVÝM SYNDRÓMOM

P. Krajmer, M. Špajdel, P. Celec, D. Ostatníková

Súhrn: Štúdia je zameraná na vzťah medzi hladinami salivárneho testosterónu a empatizáciou/systemizáciou v populácii chlapcov s Aspergerovým syndrómom (AS). Do výskumného sledovania bolo zaradených 50 probandov s Aspergerovým syndrómom z celého Slovenska, vo vekovom intervale od 6 do 18 rokov. Kontrolnú skupinu tvorilo 79 probandov, ktorí boli študentmi základných škôl a gymnázií. Probandi boli rozdelení podľa veku na predpubertálnu a pubertálnu skupinu. Boli použité nasledovné metódy – test SQ/EQ, test Intuitívnej fyziky, test Ľudovej psychológie a boli zmerané hladiny salivárneho testosterónu. Chlapci s AS dosiahli nižšie skóre v testoch empatizácie v porovnaní s kontrolnou skupinou. Vyššie skóre v teste SQ dosiahla len predpubertálna skupina chlapcov s AS. Chlapci s Aspergerovým syndrómom mali nižšie hladiny salivárneho testosterónu v oboch vekových kategóriách. V pubertálnej skupine sme zistili pozitívnu koreláciu medzi hladinami salivárneho testosterónu a testom ľudovej psychológie, ale naopak negatívnu koreláciu medzi hladinami salivárneho testosterónu a testom intuitívnej fyziky. Výsledky sú interpretované z pohľadu teórie autizmu ako „extrémne mužského mozgu“.