

## CLINICAL STUDY

## 2D:4D finger ratio in Slovak Autism Spectrum Disorder population

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**Abstract:** Previous studies have revealed that autism may arise as the result of exposure to high concentrations of prenatal testosterone. Ratio of second and fourth digits (2D:4D) is usually used as a proxy for prenatal testosterone. In this study, 2D:4D in 56 boys with ASD and in 32 control boys was measured. We found that the 2D:4D in ASD boys were lower than the ratio in control boys. These findings are discussed with reference to the “extreme male - brain” theory of autism. Results achieved in this interdisciplinary research are valuable in further biological and psychological approaches in neurocognitive research and diagnostics of children from ASD (Tab. 1, Ref. 38). Full Text in free PDF [www.bmj.sk](http://www.bmj.sk).

Key words: autism, finger ratio, testosterone.

**Abbreviations:** ASD – Autism Spectrum Disorders, AS – Asperger syndrome, T – Testosterone, 2D:4D – Second-to-fourth digit length ratio, AR – Androgen receptor, CAH – Congenital adrenal hyperplasia, ADHD – Attention-Deficit-Hyperactivity Disorder

Autism spectrum disorders (ASD) are pervasive developmental disorders that include autism, Asperger syndrome and atypical autism. Characteristically, this category of disorders is associated with severe and pervasive impairment in several areas of development including social interaction and communication skills (1). Each of these disorders has specific diagnostic criteria described by American Psychiatric Association (2).

Pathogenesis of phenotypic characteristics of ASD has been conceptualized from various aspects (3, 4, 5). Current studies focused on neurobiological aspects and relate autism to prenatal testosterone (6, 7, 8) because it is strongly sex-dependent condition (male to female sex ratio, 4:1 in autism and 10:1 in children with Asperger syndrome (9, 10)). Simon Baron-Cohen (11) postulated “Extreme male brain” theory and considered autism as

an extreme version of the male brain. His research group hypothesized that exposure to very high levels of testosterone in utero might lead to problems with communication and empathy often seen in autism (12).

2D:4D has been found as a reliable marker for prenatal testosterone (13), which causes prolongation of the fourth digit relative to the second digit. It is known that prenatal androgens affect digit ratio (14). The right hand digit ratio was suggested to be more sensitive to prenatal testosterone (15, 16). 2D:4D ratio is sexually dimorphic. The value of 2D:4D is lower in men and within each sex lower 2D:4D ratio points to the higher intrauterine androgen levels. Finger ratio is associated likewise with other sex-related variables and conditions. Manning et al (17) reported on correlation between 2D:4D ratio and variations in the androgen receptor (AR) gene. Men with high sensitivity to the androgen receptors have lower (i.e. more masculine) 2D:4D ratio. Lower number of CAG repeats in gene for androgen receptors was found in autistic individuals (14). There are reports on the association between the 2D:4D ratio and handedness, lower 2D:4D ratio, indicating higher prenatal testosterone exposure, was found in left-handers compared to right-handers (18, 19). Falter et al (20) reported that in both sexes the 2D:4D ratio was negatively related to targeting accuracy and high prenatal testosterone levels was associated with superior performance in a male-favoring task. Congenital adrenal hyperplasia (CAH) was reported to be associated with high prenatal T levels. Males and females with CAH had lower values of 2D:4D compared to control groups (21, 22). Significantly lower 2D:4D ratios was found in males with Asperger syndrome (AS) and ADHD (Attention-Deficit-Hyperactivity Disorder) compared to males with anxiety disorder (female-linked disorder) (8). On the other hand, in girls with autistic features a strong association with low 2D:4D ratio is reported (23). Previous studies found negative correlations

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between fetal testosterone and the ability to read nonverbal communication, language abilities, eyes contact, peer relationships – abilities that should show female superiority (24, 25, 26). Others found positive correlations between fetal testosterone levels and autistic traits (27, 28). Manning et al (6) found lower 2D:4D ratios in AS children compared to their control peers, moreover in children with autism 2D:4D ratios were even lower than in children with AS. At the same time, increased levels of prenatal testosterone may cause above-average performance in systemizing skills (analysing of objects and structures, collecting facts, excellent memory) in patients from Autism spectrum disorders (ASD) and in contrast might underpin the lack of empathy and communication deficits (29). However, findings of Bloom et al (30) and Putz et al (31) are different from those of previous authors, they hypothesize finger bone immaturity as a factor causing error in 2D:4D ratio measurement. Unclear reliability of 2D:4D as a predictor of sex-related traits has been found.

Referring to previous studies, our work aims to compare 2D:4D ratios (as indicators of prenatal T) between ASD group and sex/age-matched control group.

### Subjects and methods

Our sample consisted of 56 boys with ASD (20 boys with AS, 36 boys with autism) and 32 normally developing boys. All boys with autism or AS had previously been diagnosed by trained clinicians as having autism or Asperger syndrome according to standard DSM – IV diagnostic criteria (2). Participants with autism and Asperger syndrome were recruited by the local centers in various towns of Slovak Republic (Bratislava, Dubnica, Žilina, Zvolen, Trnava, Košice and Kremnica). They all were included anonymously into the research database at the Institute of Physiology of Comenius University in Bratislava. Their mean age was 11.2 (SD =1.92). Control group boys were recruited in elementary and grammar schools in Pezinok, Trstín and Galanta. Control boys mean age was 12.1 (SD =1.67). Informed consent from at least one parent of every single participant was obtained prior to testing.

2D:4D ratio is stable and fixed in early life. There is no evidence that the 2D:4D changes with age (32, 33). Therefore we compared digit ratios between our studied groups.

To determine digit ratio computer-assisted analysis was used (Autometric software (34)) that is more reliable than those methods using physical measurements, photocopies and printed scans (35, 36). Digital scan of ventral surface of the right hand was completed for each participant. Eight autistic children were scared to place the hand on the scanner and they had to be excluded because the images of their fingers were blurred. Measurements were made from the proximal crease at the base of the finger to the tip of the finger. Professionals who assessed the images were blind for the name and diagnosis of the child.

### Results

The mean values of digit ratios were compared using the t-test for independent samples in the statistical software SPSS.

**Tab. 1. Mean values of 2D:4D ratios for both groups.**

	Group	n	Mean	Std. deviation
2D:4D right hand	Controls	32	.9519	.02904
	ASD	56	.9346	.02784

ASD = Autism spectrum disorders, 2D:4D = second-to-fourth digit ratio, n = number of probands

The main result of this paper is that 2D:4D right hand digit ratios showed significantly lower values for ASD group compared to control group [ $t(85) = -2.74$ ;  $p = 0.008$ ] (Tab. 1).

### Discussion

The current study has provided the first direct comparison of second-to-fourth digit ratios between Slovak autistic population and sex/age-matched control group. 2D:4D ratios are associated with prenatal T levels (13, 14). In line with previous studies (6, 8), we hypothesised lower 2D:4D digit ratios in ASD group compared to controls and our assumptions have been mainly confirmed.

Boys from ASD group had lower 2D:4D digit ratio than the control group. This finding reflects higher prenatal testosterone levels in ASD children (6, 7, 13, 33, 37, 38).

Computer-assisted analysis (Autometric software (34)) used in our experiment has showed that our results are reliable compared to other studies. The mean ratios for both groups are comparable with studies using electronic vernier callipers (6, 7, 8).

We are aware of the fact that our sample is small to generalize our results but it is in focus of our future research to collect more data. The hypothesis of the extreme male brain 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 T (24, 27, 28). Therefore searching for further psycho-physiological correlates is needed.

### References

1. Manning-Courtney P, Brown J, Molloy CA, Reinhold J, Murray D, Sorensen-Burnworth R, Messerschmidt T et al. Diagnosis and treatment of autism spectrum disorders. *Curr Probl Pediatr Adolesc Health Care* 2003; 33: 283–304.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* (4th edition). Washington DC: American Psychiatric Association, 1994.
3. Baron - Cohen S, Leslie AM, Frith U. Does the autistic child have a „theory of mind“? *Cognition* Oct 1985; 21 (1): 37–46.
4. Ozonoff S, Pennington BF, Rogers SJ. Executive function deficits in high-functioning autistic individuals: relationship to theory of mind. *Journal of child psychology and psychiatry*. 1991; 32 (7): 1081–1105.
5. Happé F. Central coherence and theory of mind in autism: reading homographs in context. *Brit J Develop Psychol* 1997; 15: 1–12.
6. Manning JT, Baron-Cohen S, Wheelwright S, Sanders G. The 2nd to 4th digit ratio and autism. *Develop Med Child Neurol* 2001; 43: 160–164.

7. Lutchmaya S, Baron-Cohen S, Ragatt P, Knickmeyer R, Manning JT. 2nd to 4th digit ratios, fetal testosterone and estradiol. *Early Human Develop* 2004; 77: 23–28.
8. De Bruin EI, Verheij F, Wiegman T, Ferdinand RF. Differences in finger length between males with autism, pervasive developmental disorder – not otherwise specified, ADHD, and anxiety disorders. *Dev Med Child Neurol* 2006; 48: 962–965.
9. Rutter M. Diagnosis and definition of childhood autism. *J Autism Child Schizophr* 1978; 8: 139–161.
10. Gillberg IC, Gillberg C. Asperger syndrome – some epidemiological considerations: a research note. *J Child Psychol Psychiatr* 1989; 30: 631–638.
11. Baron-Cohen S. The extreme – male – brain theory of autism. In: Tager-Flusberg H (Ed). *Neurodevelopmental Disorders*. MIT Press. 1999.
12. Baron-Cohen S, Hammer J. Parents of children with Asperger syndrome: What is the cognitive phenotype? *Journal of Cognitive Neuroscience* 1997; 9 (4): 548–555.
13. McIntyre MH. The use of digit ratios as markers for perinatal androgen action. *Reprod Biol Endocrinol* 2006; 26: 4–10.
14. Breedlove MS. Minireview: Organizational hypothesis: instance of the fingerpost. *Endocrinology* 2010; 151, in press.
15. Williams TJ, Pepitone ME, Christensen SE, Cooke BM, Huberman AD, Breedlove NJ, Breedlove TJ et al. Finger-length ratios and sexual orientation. *Nature* 2000; 404: 233–250.
16. Csatho A, Osváth A, Biscák E, Karádi K, Manning J, Kállai J. Sex role identity to the ratio of second to fourth digit length in women. *Biol Psych* 2002; 62: 147–156.
17. Manning JT, Bundred PE, Newton DJ, Flanagan BF. The second to the fourth digit ratio and variation in the androgen receptor gene. *Evol Hum Behav* 2003; 24: 399–405.
18. Nicholls ME, Orr CA, Yates MJ, Loftus AM. A new means of measuring index/ring finger (2D:4D) ratio and its association with gender and hand preference. *Laterality* 2008; 13: 71–91.
19. Stoyanov Z, Marinov M, Pashalieva I. Finger length ratio (2D:4D) in left- and right-handed males. *Int J Neurosci* 2009; 119: 1006–1013.
20. Falter CM, Arroyo M, Davis GJ. Testosterone: Activation or organization of spatial cognition? *Biol Psychol* 2006; 73: 132–140.
21. Brown WM, Hines M, Fane B, Breedlove SM. Masculinized finger length ratios in human males and females with congenital adrenal hyperplasia. *Horm Behav* 2002; 42: 380–386.
22. Okten A, Kalyonku M, Yaris N. The ratio of second- and fourth-digit lengths and congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Early Hum Dev* 2002; 70: 47–54.
23. De Bruin EI, De Nijs PF, Verheij F, Verhagen DH, Ferdinand RF. Autistic features in girls from a psychiatric sample are strongly associated with a low 2D:4D ratio. *Autism* 2009; 13(5): 511–521.
24. Knickmeyer R, Baron-Cohen S, Ragatt P, Taylor K. Foetal testosterone, social relationship and restricted interests in children. *J Child Psychol Psychiatry* 2005; 46: 198–210.
25. Chapman E, Baron-Cohen S, Auyeung B, Knickmeyer R, Taylor K, Hackett G. Fetal testosterone and empathy: evidence from the empathy quotient (EQ) and „reading the mind in the eyes“ test. *Soc Neurosci* 2006; 1: 135–148.
26. Whitehouse A, Maybery M, Hart R, Mattes E, Newnham J, Sloboda D, Stanley F et al. Fetal androgen exposure and pragmatic language ability of girls in middle childhood: Implications for the Extreme male brain theory of Autism. *Psychoneuroendocrinology* 2010; article in press.
27. Knickmeyer R, Baron-Cohen S. Fetal testosterone and sex differences in typical social development and in autism. *J Child Neurol* 2006; 21: 825–845.
28. Auyeung B, Baron-Cohen S, Ashwin E, Knickmeyer R, Taylor K, Hackett G. Fetal testosterone and autistic traits. *Br J Psychol* 2009; 100: 1–22.
29. Baron-Cohen S, Wheelwright S, Griffin R, Lawson J, Hill J. The exact mind: empathising and systemizing in autism spectrum conditions. 491–508. In: Goswami U (Ed). *Handbook of Cognitive Development*. Oxford: Blackwell, 2002.
30. Bloom MS, Houston AS, Mills JL, Molloy CA, Hediger ML. Finger bone immaturity and 2D:4D ratio measurement error in the assessment of the hyperandrogenic hypothesis for the etiology of autism spectrum disorders. *Physiology and Behavior* 2010; 100: 221–224.
31. Putz D, Gaulin SJC, Sporter RJ, McBurney DH. Sex hormones and finger length: What does 2D:4D indicate? *Evolution and Human Behavior* 2004; 25: 182–199.
32. Malas MA, Dogan S, Evcil EH, Desdicioglu K. Fetal development of the hand, digits and digit ratio (2D:4D). *Early Hum Dev* 2006; 82: 469–475.
33. Manning JT, Scutt D, Wilson J, Lewis-Jones DI. The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. *Human Reproduction* 1998; 13: 3000–3004.
34. De Bruine LM. Autometric software for measurement of 2D:4D ratios. 2004; from <http://www.facelab.org/debruine/programs/autometric.php>
35. Allaway HC, Bloski TG, Pierson RA, Lujan ME. Digit ratios (2D:4D) determined by computer-assisted analysis are more reliable than those using physical measurements, photocopies and printed scans. *Amer J Human Biol* 2009; 21: 365–370.
36. Kemper CJ, Schwerdtfeger A. Comparing indirect methods of digit ratio (2D:4D) measurement. *Amer J Human Biol* 2009; article in press.
37. Voracek M, Dressler SG. Digit ratio (2D:4D) in twins: heritability estimates and evidence for a masculinized trait expression in women from opposite - sex pairs. *Psychol Rep* 2007; 100: 115–126.
38. Voracek M, Loibl LM. Scientometric analysis and bibliography of digit ratio (2D:4D) research, 1998–2008. *Psychol Rep* 2009; 104: 922–956.

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