Autism and fetal androgens: Commentary on Levy et al. (Lancet 2009; 374: 1627-38)

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The *Seminar* on autism by Susan Levy and colleagues¹ is an excellent source of current knowledge on this neurodevelopmental disorder of prenatal and postnatal brain development and highly useful for generalists. The well-known sex difference in the lifetime prevalence of autism, wherein boys and men exceed girls and women by a large margin, along with its obvious prenatal origins, together suggest a role of prenatal factors wherein males differ from females in the aetiology of autism.²

Prenatal androgens are one such early sexually differentiated factor. A now widely studied presumed retrospective biomarker for prenatal testosterone is the second-to-fourth digit ratio (2D:4D).³ Human 2D:4D is sexually differentiated (lower in males than in females), and sex and individual differences in 2D:4D emerge prenatally and are preserved during postnatal growth.³ Lower (male-typical) 2D:4D is associated with higher sensitivity to testosterone (i.e., functional polymorphisms in the androgen receptor gene) and a higher testosterone-to-estradiol ratio, as assayed from the amniotic fluid.³

Of note, children with autism or high-functioning autism (Asperger syndrome), as well as their unaffected first-degree relatives (siblings, mothers, and fathers), have conspicuously lower (hypermasculinised) 2D:4D than healthy general populations controls.⁴ This finding has been independently replicated in by now some ten further reports (reviewed elsewhere⁵). All in all, this points to a role of altered sex-hormone profiles, already arising in utero, in the pathways leading to the neurodevelopmental disorder autism.²

References

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