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The second to fourth digit ratio and variation in the androgen receptor gene

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Abstract

The second to fourth digit ratio (2D:4D) is sexually dimorphic, with lower mean values in males compared to females. It has been suggested that the sex difference in 2D:4D is determined prenatally, 2D:4D is negatively related to prenatal testosterone and positively to prenatal oestrogen, and that 2D:4D is a marker for levels of sex steroids during brain organisation. There is growing evidence that many sex-dependent behaviours are correlated with 2D:4D. However, there is no direct evidence for an effect of prenatal sex steroids on the digit ratio. The response to prenatal testosterone is dependent on the amount produced and the foetal sensitivity to the hormone. Variation in the X-linked androgen receptor gene (AR) determines sensitivity to testosterone. Alleles of AR with low numbers of CAG triplets respond to testosterone with high transactivational activity, while high numbers of CAG's are associated with increased insensitivity to testosterone. We show in a sample of 50 men (49 Caucasian subjects, 1 Caucasian/Chinese subject) that 2D:4D is a phenotypic correlate of AR structure. Right-hand 2D:4D was positively correlated with CAG number and individuals with low 2D:4D in their right hand compared to left hand had AR alleles with low CAG numbers. We discuss the implications of our findings for our understanding of the aetiology of 2D:4D, its relationships with sex-dependent behaviours, and the evolutionary implications of variation in 2D:4D and AR.

Keywords: [2D:4D](#), [Androgen receptor](#)

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PII: S1090-5138(03)00052-7

doi:10.1016/S1090-5138(03)00052-7

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