

M9. SEX-SPECIFIC FOXP1 AND FOXP2 EXPRESSION IN THE DEVELOPING MOUSE BRAIN AND ITS IMPACT ON VOCAL COMMUNICATION

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Background Men are more susceptible to neurodevelopmental diseases such as autism and language deficits than women however, the underlying factors remain unclear. FOXP1 is associated with autism, intellectual disability and speech and language deficits, while FOXP2 is exclusively involved in speech and language disorder. FOXP1 and FOXP2 together form heterodimers for transcriptional regulation.

Methods Generation of mouse models, Quantitative real-time PCR, Protein, antibodies and western blotting, Pup ultrasonic vocalization recordings, Immunofluorescence.

Results In this study, we analyzed Foxp1 and Foxp2 expression in the developing mouse brain and observed sex-biased expression of Foxp1 and Foxp2 in the striatum at embryonic day (E) 17.5 and postnatal day (P) 7.5. Since the striatum is implicated in social and vocal communication, we investigated isolation-induced ultrasonic vocalization in brain-specific Foxp1NesCre mice. Foxp1NesCre pups had strongly reduced ultrasonic vocalization and lacked the sex-specific call rate from wild type pups, indicating that Foxp1 is important for normal ultrasonic vocalization. In addition, Foxp1 expression was reduced in the striatum of brain-specific androgen receptor KO mice at E17.5 and P7.5, suggesting that androgens significantly contribute to the sex-specific differences in Foxp1 expression and sex-dimorphic ultrasonic vocalization.

Discussion Our findings demonstrate a spatio-temporal pattern of Foxp1 and Foxp2 expression at distinct stages in the developing mouse brain, directly or indirectly regulated by androgens. This regulation seems to mediate sex-specific differences in USV, commonly used as a readout for social behavior. The present study contributes to the understanding how testosterone may influence gene expression during human brain development, and helps to assess its impact on the etiology of social and communicative behavior in autism spectrum disorder.

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