**MEETING ABSTRACT**

**A18.3** Humanized Foxp2, a gene involved in language acquisition, alters dopamine levels, cortico-striatal synaptic plasticity and accelerates transitions from declarative to procedural learning

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What enables the human nervous system to acquire language and speech and which genetic candidates might have contributed to this capacity? Two human-specific amino acid substitutions in the transcription factor FOXP2 are outstanding candidates, given that they might have been positively selected during human evolution and given that FOXP2 is currently the only gene firmly linked to speech and language development. When these two substitutions are introduced into endogenous Foxp2 of mice (Foxp2hum), cortico-basal ganglia circuits are specifically affected. Here we show that humanized Foxp2 alters dopamine levels, learning and cortico-striatal synaptic plasticity. Foxp2hum mice learn stimulus–response associations faster than their wild-type littermates in situations in which declarative (i.e. place-based) and procedural (i.e. response-based) forms of learning could compete. Striatal districts known to be differently related to these two modes of learning are affected differently in the Foxp2hum mice, as judged by measures of dopamine levels, gene expression patterns, and synaptic plasticity, including an NMDA receptor-dependent form of long-term depression. These findings suggest that dopamine-processing in cortico-basal ganglia circuits might be altered in mice with the humanized form of Foxp2 and raise the possibility that the humanized Foxp2 phenotype reflects a different tuning of corticostrital systems involved in declarative and procedural learning, a capacity potentially contributing to adapting the human brain for speech and language acquisition.

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