S61-4 Knockdown of DISC1 by in utero gene transfer disturbs postnatal dopaminergic maturation in the frontal cortex and leads to adult behavioral deficits

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Adult brain function and behavior are influenced by neuronal network formation during development. Genetic susceptibility factors for adult psychiatric illnesses, such as Disrupted-in-Schizophrenia-1 (DISC1), influence adult high brain functions, including cognition and information processing. Here we report the potential to generate an animal model via *in utero* gene transfer in order to address an important question how nonlethal deficits in early development may affect postnatal brain maturation and high brain functions in adulthood, which are impaired in various psychiatric illnesses, such as schizophrenia and mood disorders.

We show that transient knockdown of DISC1 in the pre- and peri-natal stages, specifically in a lineage of pyramidal neurons mainly in the prefrontal cortex, leads to selective abnormalities in postnatal mesocortical dopaminergic maturation and behavioral abnormalities associated with disturbed cortical neurocircuitry after puberty.

This technique can be utilized to develop novel animal models for various adult mental disorders, including schizophrenia and mood disorders, in which multiple risk factors play etiological roles during neurodevelopment.