Gene that helps adolescent minds mature identified

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A gene that controls the development of dopamine connections in the prefrontal cortex of the brain specifically during adolescence may have a role in susceptibility to psychiatric disorders, according to a study in mice published this week in *Translational Psychiatry*.

In humans, the risk of developing psychiatric disorders is considerably increased during adolescence, when significant developmental changes occur in the medial prefrontal cortex (mPFC), including the wiring of dopamine neurons. Previous research has indicated that a gene called *dcc* (*deleted in colorectal cancer*) may be involved in this process, but the mechanisms are unclear. Through electrophysiological, anatomical, and behavioral experiments in a mouse model expressing variable levels of *dcc*, Cecilia Flores and colleagues found that *dcc* is required for the development and normal function of the adult mPFC, and is implicated in the establishment of dopamine-neuron connections to...
this brain region specifically during adolescence. Behaviorally, mice with lower-than-normal levels of dcc show increased cognitive flexibility — the ability to make adaptive responses to a changing environment — along with more resilience when exposed to stressors.

Given that deficits in cognitive flexibility have been observed in dopamine-related psychopathologies associated with mPFC dysfunction, including schizophrenia and depression, the authors speculate that variations in DCC may influence predisposition to these disorders, and that lower levels of DCC may play a protective role through subtle changes in the development of mPFC connectivity. To this end, the authors measured DCC expression in postmortem brains of 30 patients with depression who committed suicide, as well as 35 age-matched sudden-death controls. DCC levels were 48% higher in suicide completers, suggesting that increased levels of DCC influence the development of psychiatric illness.

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