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NETRIN-1 RECEPTOR DEFICIENT MICE: A PHENOTYPE RESISTANT TO PSYCHOPATHOLOGY?

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Dysfunctions of the midbrain dopaminergic system are implicated in the psychopathology of schizophrenia and other disorders including drug addiction. Abnormalities in brain development play an etiological role in schizophrenia leading to altered dopaminergic function in adulthood and increased vulnerability to the effects of stimulant drugs. Netrins are proteins that organize neuronal connectivity during development and their receptors are highly expressed in dopaminergic neurons. We find that adult netrin-1 receptor deficient mice exhibit altered dopamine-related behaviors and show profound molecular and anatomical changes in dopamine systems that appear opposite to those observed in developmental animal models of schizophrenia or following chronic use of drugs of abuse. Significantly, the signs of this apparently 'protective' phenotype are not evident in pre-pubertal mice. We propose that variations in netrin-1 receptor function at critical periods in development could contribute to individual differences in susceptibility to psychopathology.

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