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# Developmental NMDA receptors are required for wiring of adult-born neurons into excitatory olfactory bulb circuit

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Adult-born neurons have a transient period of plasticity during their integration into the circuit, when glutamatergic NMDA receptors are required for neuronal survival and when neuronal survival and synaptic organization depend on sensory input. This transient plasticity may involve NMDA receptors containing GluN2B, the major subunit expressed at early developmental stages. Adult-born granule cells in the olfactory bulb may undergo NMDA receptors-dependent synaptic development in a mature circuit with strong and concerted synaptic activity different from new neurons in the developing cortex when NMDA receptors put a brake on developing glutamatergic synapses. We tested this hypothesis using retroviral single-cell ablation of GluN2B to directly compare matched birth-dated adult-born wild-type and neighboring GluN2B-deficient neurons in conditional knockout GluN2B mice.

The GluN2B-deficient neurons developed a normal dendritic morphology. However, neurons failed to mature glutamatergic transmission even though glutamatergic synapses had initially formed. In contrast to glutamatergic transmission, inhibitory synaptic transmission developed normally in GluN2B-deficient neurons, suggesting that inhibitory neurotransmission and initial morphological differentiation are regulated independently of glutamatergic synaptic input. Furthermore, GluN2B-deficient neurons did not respond to novel odor exposure and eventually died at later stages of their maturation. Survival could not be genetically rescued by over-expression of the mature subunit GluN2A after endogenous GluN2B depletion in adult-born neurons.
In summary, GluN2B-containing NMDA receptors that normally dominate during the critical period of adult-born neurons are not required for initial synaptogenesis, but necessary to mature glutamatergic synapses in adult-born neurons. For the maturation of glutamatergic synapses, adult-born neurons use NMDAR-dependent mechanisms opposite to those observed in new neurons in the developing brain.