Title:	The Regulation of NMDA Receptors at GABAergic Interneurons During Postnatal Development
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Abstract:	Brain development is marked by periods of enhanced brain plasticity, known as critical periods. The termination of critical periods requires the maturation of parvalbumin-positive interneurons (PV + INs). Several studies have linked the disruption of N-methyl D-aspartate receptors (NMDARs) in PV + INs during postnatal development to the pathophysiology of schizophrenia and autism spectrum disorders. Canonical NMDA receptors are hetero-tetramers with two GluN1 and two GluN2 subunits, which together form an ion channel. GluN2 subunits can be of four classes- GluN2A/B/C/D. NMDAR activation requires the simultaneous binding of the excitatory neurotransmitter glutamate, and a co-agonist, which can be glycine or D -serine. Recent studies by our lab have found that in adult mice, D -serine but not glycine is critical for maintaining the activity of NMDARs at PV INs in the late adolescent-young adult prefrontal cortex (PFC), and that loss of D -serine functions leads to the synaptic deficits observed in neuropsychiatric disorders such as schizophrenia. However, it is not known if the identity of the NMDAR co-agonist in these cells is developmentally regulated. Through this study, I aim to test the functions of D -serine and glycine as NMDAR co-agonists throughout postnatal development using the transgenic PV -tdTomato mice where PV INs are readily identifiable. Using selective enzymatic scavengers to block the function of either D -serine or glycine, I reveal that D -serine but not glycine gates NMDARs at the PFC PV INs at juvenile synapses (11-17 day old mice) . Strikingly, I also show that bath application of D -serine inhibits NMDA-EPSCs at PV+ in neonates (11-17 days-old) while it does increase the synaptic responses in mature synapses (45-70 days old). Finally, I test the hypothesis for a change in the composition of NMDARs subunits in PFC PV INs during development. Overall, this study helps in understanding the relative contribution of D -serine and glycine in the regulation of specific NMDARs at PV INs during postnatal development.
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