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2. Title
   Cognitive Remediation by Cholinergic Modulation in a Mouse Model of Schizophrenia

3. Period
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4. Summary
   Cognitive impairment in schizophrenia remains a major unmet medical need, for which no effective treatment has been established. Although cholinergic neurotransmission has been implicated, its optimal pharmacological modulation remains unclear. The present study aimed to elucidate the neural circuit mechanisms underlying cognitive deficits and to explore potential therapeutic strategies. Using a chronic phencyclidine (PCP) mouse model, we investigated the mechanisms by which chemogenetic activation of parvalbumin (PV)-positive interneurons in the prelimbic cortex (PL) improves cognitive impairment, employing local field potential (LFP) recordings and *in vivo* calcium imaging. This approach robustly increased PV interneuron activity and modulated gamma-band oscillations, with effects that appeared to depend on the disease state. In parallel, we examined the relationship between dopamine D2 receptor occupancy and extrapyramidal side effects, as well as their mitigation by anticholinergic agents. Consistent with clinical observations, these relationships were recapitulated in mice. However, the amelioration of side effects was observed only at doses that impaired cognitive function. Taken together, these findings highlight the importance of optimizing both circuit-level interventions and pharmacological conditions to achieve a balance between improving cognitive deficits and minimizing adverse effects.