# Cognitive dysfunction in new animal model for schizophrenia with suppression of presynaptic protein Piccolo in the prefrontal cortex of mice is involved in disturbance of neuronal network in the perirhinal cortex

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Schizophrenia, a severe psychiatric disorder, exhibits three major symptoms, including cognitive dysfunction. Piccolo, a presynaptic protein, plays a role in synaptic vesicle trafficking, and is suggested to be associated with several psychiatric disorders in the postmortem and GWAS analyses. We previously proposed that mice knocking down Piccolo in the prefrontal cortex (PFC-Piccolo-KD mice) were useful as an animal model for schizophrenia based on those face and predictive validities. In this study, we investigated the neuronal circuits that contribute to cognitive dysfunction in the new animal model.

We firstly confirmed the bidirectional connection between the PFC and ventral hippocampus (vHIP) via the perirhinal cortex (PRC) by using neuronal tracer. Cognitive dysfunction in the PFC-Piccolo-KD mice in the novel object and location recognition test was recovered by activation of the PFC-PRC circuit. Furthermore, mice knocking down Piccolo in the PRC showed impairment of cognitive memory, and its impairment was also ameliorated by activation of the PRC-vHIP circuit.

These findings suggest that disturbance of the PFC-PRC-vHIP neuronal network is involved in schizophrenia-like symptoms. Accordingly, improvement of disturbed PFC-PRC-vHIP network could be a therapeutic approach for cognitive dysfunction in schizophrenia.