1. No.
   2020Y011

2. Title
   Therapeutic Mechanisms by Nicotinic Neurotransmission for Cognitive Impairment in Mouse Model of Schizophrenia

3. Period
   2020-2022

4. Summary

   Current cognitive enhancers targeting various neurotransmitters, including acetylcholine, have been reported to have little or only very limited ameliorative effects on cognitive deficits in schizophrenia. The aim of this study is to identify the neural circuits responsible for cognitive deficits using an animal model of schizophrenia, and to search for effective therapeutic agents by targeting these neural circuits.

   Our results revealed that activation of parvalbumin positive inhibitory neurons in the prelimbic cortex using chemogenetics plays a key role in the improvement of cognitive deficits. Therefore, a compound known to activate these cells in *in vitro* studies were locally administered to the prelimbic cortex, but we observed no improvement. This result suggested the need to clarify *in vivo* the neural activity alterations induced by chemogenetics. In addition, we established an experimental system that simultaneously manipulates neural activity induced by chemogenetics and measures neural activity of parvalbumin positive neurons in the prelimbic cortex of awake mice *in vivo*.

   The results obtained in this study and the experimental system are expected to be useful for exploratory studies of the mechanisms by which modulation of nicotinic acetylcholine neurotransmission can ameliorate and then potentiate cognitive deficits.