The Possibility of Antipsychotic Drug Targeting Nicotinic Acetylcholine Receptor

○Shuntaro Kohnomi[1,2], Katsuya Suemaru[2], Hiromu Kawasaki[1], Tominari Choshi[3], Satoshi Hibino[3] and Hiroaki Araki[2]
([1]Dept. of Clin. Pharmacy, Okayama Univ., [2]Dept of Clin. Pharmacol. and Pharmaceutics, Ehime Univ., [3]Faculty of Pharmacy and Pharmaceutical Sci., Fukuyama Univ.)

Recently, nicotinic acetylcholine receptors (nAChR) were shown to be involved in the sensorimotor gating deficits in schizophrenia, therefore nAChRs are thought to be one of the therapeutic targets for schizophrenia. We have revealed in the experiments, the prepulse inhibition (PPI) in Wistar rats, that nicotine ameliorated the disruption of the PPI by apomorphine via α_7 nAChR.

Tropisetron (Trop), a 5-HT_3 serotonin receptor antagonist, is known to have affinity to α_7 nAChR as well. So we speculated that Trop also has the ameliorating effect on the sensorimotor gating deficits. In this study, we investigated whether Trop improves the disruption of the PPI induced by a dopamine receptor agonist apomorphine (Apo) or a glutamine NMDA receptor antagonist phencyclidine. Results revealed that Trop improved the disruption of the PPI induced by Apo dose-dependently, but not by phencyclidine. On the other hand, ondansetron, the 5-HT_3 serotonin receptor antagonist without affinity to α_7 nAChR, did not affected the disruption of the PPI induced by Apo. Moreover, ameliorating effect of Trop on the PPI was antagonized by mecamylamine, nonselective nAChR antagonist. These results indicated that the effect of Trop was involved in nAChR. We also investigated whether Trop was effective in the stereotyped behavior induced by Apo, however, Trop have not inhibited the behavior.

In these experiments, it was suggested that Trop was effective in the sensorimotor gating deficits, not in positive symptoms of schizophrenia.