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TAAR1 ligands as prospective neuroleptics: From D-neuron research

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Recent pharmacological studies has been shown the importance of trace amine-associated receptor, type 1 (TAAR1), a subtype of trace amine receptors, as a prospective target receptor for novel neuroleptics. The author introduces D-neuron (trace amine (TA)-producing neuron) research in psychiatric field. Although dopamine (DA) dysfunction is a well-known hypothesis of etiology of schizophrenia, its molecular basis has not yet been clarified. To explain this, modulating function of TAs on DA neurotransmission was noticed. The TAAR1 has a large number of ligands, including tyramine, β-phenylethylamine and methamphetamine that influence on human mental state. Reduced stimulation of TAAR1 on DA neurons in the midbrain ventral tegmental area (VTA) has been revealed to increase firing frequency of VTA DA neurons. Significant D-neuron decrease has been reported in the nucleus accumbens (Acc) of postmortem brains of patients with schizophrenia. This implies the decrease of TA synthesis and consequent TAAR1 stimulation reduction on terminals of midbrain VTA DA neurons, that leads to mesolimbic DA hyperactivity in schizophrenia. D-neuron decrease in Acc of postmortem brains, due to neural stem cell (NSC) dysfunction in the subventricular zone of lateral ventricle, might be pivotal in etiology of schizophrenia. The new "D-cell hypothesis (TA hypothesis)", in which D-neurons and TAAR1 are involved, is in agreement of recent reports showing effectiveness of TAAR1 ligands for schizophrenia model animals.

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