Cholinergic system in schizophrenia

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Past schizophrenia researches have focused first on dopamine and glutamate systems abnormalities. A more synthetic approach in schizophrenia research suggested the pathological changes in either the prefrontal cortex or temporal lobe that mainly are the consequence of neurotranschemical changes in multiple neurotransmitter systems. Some evidences such as high rate of smoking in schizophrenics and increased level of eicosanoid acetylcholine receptors (aCHRs) antibodies, lead the researchers to investigate the role of cholinergic system in schizophrenia. It has shown that nicotine administration have positive effects on sensory gating, positive symptoms, and cognitive deficits. Cholinergic innervations of brain (cortical and striatal regions) is very extensive. Acetylcholine (Ach) released from the cholinergic fibers of the basal forebrain, striatum, and the prefrontal cortex could act as an important role in cognition and emotion processing. The complexity of cholinergic system regarding its extensive projections, different receptors with various subunits, and distribution of its receptors make it difficult to describing its role in schizophrenia. This complexity is more prominent when try to correlate its relations with specific phenotypes in schizophrenic. However, recent studies in this filed open new avenues in front of researchers to understand more the pathophysiology of schizophrenia, and also developing new antipsychotics.

The most studied case of a cholinergic deficit in schizophrenia is abnormality in expression of e7 nicotinic receptor expression. Abnormality in the function of e7 nicotinic receptors can produce sensory-motor gating disturbances. Previous studies have shown that acetylcholinesterase inhibitors, which make higher synaptic levels of acetylcholine, can reduce the cognitive deficits of schizophrenia. Nicotinic and muscarinic Receptors are good targets for drug development in aim to lessen cognitive deficits in schizophrenia. Recently efforts were made to synthesis of new antipsychotic with agonistic activity on M1/M4 muscarinic receptors.

Key words: acetylcholine; cholinergic system, schizophrenia, e7 nicotinic receptor, M1/M4 muscarinic receptors

Intrapritoneally administration of 20 & 30% ethanol (3g/kg) affected rats’ spatial working memory

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Balance between excitatory and inhibitory neurotransmission is important for brain functions. Short-term alcohol consumption through alteration this balance depresses brain function. Some brain areas are more sensitive to alcohol, especially the neocortex, hippocampus and cerebellum. Previous findings suggested that alcohol disrupt spatial learning and memory in male rats. Working memory is an important cognitive process that is changed by alcohol consumption, moreover brain hippocampus and prefrontal cortex (PFC) are involved in spatial working memory. Present study was undertaken to investigate the effect of systemic single dose ethanol on working memory in male Wistar rats (250-300 g) using automated Figure-8 maze (The delayed alternation task that investigate working memory processes in rodents). The spatial working memory was investigated 15 minutes after intraperitoneal injection of saline, 20% and 30% ethanol (3 g/kg) using automated Figure-8 maze. Spatial working memory in two 20% and 30% ethanol groups (3 g/kg) have shown a significant decrease in proportion to the control group (P=0.05, P<0.01). Taken together, our results indicate that dose of 20 & 30% ethanol (3 g/kg) impairs spatial working memory performance in rats. Probably a part of working memory impairment is related to increase of GABAergic and decrease of glutamatergic Neurotransmission in Prefrontal Cortex which request more investigations.

Keywords: Ethanol, Spatial Working Memory, Prefrontal Cortex, GABAergic, Maze 8

Roles of 5HT1a on learning and spatial Memory

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The serotonin 1A 5-HT (1A)-receptor is involved in a wide range of physiological functions, but has also been implicated in the pathophysiology of anxiety disorders and depression. Although the 5-HT(1A)-receptor is one of the best described receptor subtypes of the serotonergic system, its complex distribution pattern, pre- and postsynaptic localization, and its impact on various neurotransmitters aggravate the attribution of 5HT(1A)-agonistic effects to behavioral outcomes. The role of 5-HT (1A)-receptors for cognitive processes seems undisputed. However the hippocampus has been implicated in aspects of spatial memory. In a recent study, hippocampal serotonin 5-HT neurotransmission has also been proposed as a candidate to memory processing. Studies have shown that the 5-HT (7) receptor is present in the hippocampus in relatively high abundance. Serotonin’s actions have been linked to alcohol’s effects on the brain and to alcohol abuse. Alcoholics and experimental animals that consume large quantities of alcohol show evidence of differences in brain serotonin levels compared with nonalcoholics. Although serotonin’s effect on individual neurons can be rather modest, its overall effect on the neurons in a given brain area can substantially influence brain functions such as learning and memory, perception of the environment, mood states, and responses to alcohol and other drugs of abuse. The contribution of 5-HT (1A) receptors in cognitive impairments in various psychiatric disorders is still unclear. However, there is evidence that 5-HT (1A) receptors may play differential roles in normal brain function and in psychopathological states. Taken together, the evidence indicates that the 5-HT (1A) receptor is a target for novel therapeutic advances in several neuropsychiatric disorders characterized by cognitive deficits.

Keywords: learning, 5HT receptor, memory.