

2nd International Conference on

Central Nervous System Disorders & Therapeutics

December 05-07, 2016 Dubai, UAE

Effect of repeated methylphenidate administration on serotonin-1A expression and behavior in rat models

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Methylphenidate (MPD) is the most regularly prescribed psychostimulant for patients with attention-deficit hyperactivity disorder (ADHD). It has also been used by general population, especially college students, without ADHD to improve academic and work related performances which later produce addiction. Although dopamine is the main neurotransmitter involved in the pathophysiology of drug abuse, serotonin (5-hydroxytryptamine; 5-HT) can modulate addictive effects of drugs of abuse. The present study was designed to check MPD-induced behavioral sensitization and cognition along with the 5HT-1A receptor expression in the nucleus accumbens and prefrontal cortex of repeated MPD treated rats. Twenty four (24) male albino Wistar rats (180-220 gm) were used to determine dose related effects of MPD (0.5, 2.5 and 5 mg/kg) on cognition in water maze test. Acquisition of memory was assessed after two hours of the three successive training sessions. After 20 hours of drug administration, retention of memory was assessed. In another experiment, 12 male albino Wistar rats were randomly assigned to two equal groups. Water and methylphenidate (2.5 mg/kg) were administered orally to the respective groups. Animals were exposed to 12 (one daily) place conditioning sessions of 30 min each. Motor behavior during this session was also recorded. Reinforcing effects of methylphenidate were monitored during the test session on day 13. On day 14, drug/water was administered and learning acquisition was done after training sessions. Retention of memory was assessed after 24 hours of the drug administration. Decapitation was done on the next day and brains were micro-dissected to collect the nucleus accumbens and prefrontal cortex. 2.5 mg/kg MPD found to enhance cognitive effects in Morris water-maze test. Conditioned place preference test on day 13 revealed that repeated administration of MPD (2.5 mg/Kg) produced reinforcement as well as the behavioral sensitization. While repeated administration of MPD moderately enhanced acquisition of memory while significantly increased memory retention. We also report that 5HT-1A receptor expression was also down regulated in methylphenidate treated rats both in the nucleus accumbens and prefrontal cortex. These findings may help to improve pharmaco-therapeutics in treating ADHD.

Biography

Tabinda Salman has good background knowledge of neuroscience and hand-on experience of working with all type of behavioral models, neurochemical analyses, molecular tools to check gene expression and other related experimental protocols. She is currently working as a PhD Fellow at National Center for Proteomics, University of Karachi, Pakistan. She has done her MPhil in Molecular Medicine (Neuropharmacology). The study which is designed to monitor receptor regulation together with associated changes in serotonin and dopamine metabolism is expected to help identify novel therapeutic targets for improving cognition and to treat addiction in future studies.

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