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Epilepsy and associated behavioural comorbidities: Exploration of serotonergic receptors

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Serotonergic interplay (with different receptor subtypes) in the cortex and hippocampus appears to be one of the important common neurochemical interplay leading to epileptogenesis, depression, learning and memory impairment. Role of different receptor subtypes of serotonin has long been implicated in epileptogenesis, depression, learning and memory impairments, but their role in epilepsy induced comorbidities is still unexplored. Therefore this study was envisaged to evaluate the role of different 5- HT receptors (5-HT 1A/2A/2C/3) in kindling induced depression learning and memory deficit.

In this study male Swiss Albino mice were kindled using subconvulsive dose of PTZ (35 mg/kg). Once the animals were kindled they were treated with vehicle, 8-OH-DPAT (1 mg/kg/day), WAY-100635 (0.3 mg/kg/day), WAY 100635 + 8-OH-DPAT, DOI (1 mg/kg/day), olanzapine (2 mg/kg/day), olanzapine + DOI, ondansetron (1 mg/kg/day; i.p.), m-CPBG (1 mg/kg/day; i.p.) and ondansetron + m- CPBG for 20 days. Seizure severity score, depression like behavior, learning and memory was evaluated on day 5, 10, 15 and 20. After the behavioral evaluations on day 20, animals were sacrificed to estimate different neurotransmitters in discrete brain parts (by HPLC-FD method), nitrite level and AChE activity (microplate reader method).

Ondansetron treatment significantly reduced the seizure severity score and improved the depression like behavior, learning and acquisition performance as compared to vehicle treated kindled animals. The effect of ondansetron was reversed by m-CPBG co-treatment. The neurochemical changes in the cortex and hippocampus also supported the behavioral outcome of the study.

This study substantiates the role of $5HT_3$ receptor in PTZ kindling induced depression like behavior, learning and memory deficit in mice. This study creates a rational to explore the use of more selective $5\text{-}HT_3$ receptor ligands for comprehensive management of depressive behavior and memory impairment in patients with epilepsy.