

## Protective effect of agomelatine on traumatic brain injury induced cognitive deficit in rats: possible role of neurotransmitters

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Traumatic brain injury (TBI) is the leading cause of death and disability among children and young adults worldwide. These patients often have short and long term cognitive, behavioral and emotional impairments. The 5-HT<sub>2C</sub> and melatonin receptors are known to have involvement in memory functions. The aim of the present study is to find the beneficial effect of agomelatine (selective 5HT<sub>2C</sub> antagonist and melatonin receptor agonist) against weight drop induced traumatic brain injury in rats. The weight-drop model closely mimics the real life TBI. Injury was induced by dropping a weight of 450 gm from a height of 1 meter through a hollow metallic tube onto the exposed skull of rats under anesthesia. After 14 days of TBI the agomelatine (10, 20, and 40 mg/kg p.o. daily) treatment was given for next 14 days (i.e. till 28<sup>th</sup> day). The cognitive impairment was observed in Morris water maze (from 24<sup>th</sup> to 28<sup>th</sup> day) and novel object recognition (on 27<sup>th</sup> and 28<sup>th</sup> day) test. Immediately after behavioral parameters animals were sacrificed and hippocampus and cortex were isolated for biochemical (LPO, nitrite, GSH, AChE), neuroinflammatory (TNF- $\alpha$ , IL-1 $\beta$ , IL-6) and neurochemical (serotonin, DA, NA and their metabolites) estimation. The weight drop model significantly induced memory impairment in TBI rats that has been assessed by Morris water maze and object recognition task. A significant rise in acetylcholinesterase activity, neuroinflammatory markers, oxidative stress (lipid peroxidation and nitrite, GSH) was found in both cortex and hippocampal regions of traumatized rat brain. While agomelatine treated rats has been shown to reverse the injury effects and significant increase in serotonin, dopamine and norepinephrine levels in TBI rat brain. Agomelatine has shown to possess memory-enhancing effects, that might be due to involvement of MT1/MT2 and 5-HT<sub>2C</sub> receptors. Hence agomelatine represents a promising new neuroprotective drug for cognitive enhancing effects.