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ORIGINAL ARTICLE

Effect of papaverine on developmental hyperserotonemia induced autism spectrum disorder related behavioural phenotypes by altering markers of neuronal function, inflammation, and oxidative stress in rats

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Abstract

Hyperserotonemia, in the early developmental phase, generates a variety of behavioural and biochemical phenotypes associated with autism spectrum disorder (ASD) in rats. Papaverine is known to provide benefits in various brain conditions. We investigated the role of a selective phosphodiesterase-10A (PDE10A) inhibitor, papaverine on ASD related behavioural phenotypes (social behaviour deficits, repetitive behaviour, anxiety and hyperlocomotion) in developmental hyperserotonemia (DHS) rat model. Also, effects on important biochemical markers related with neuronal function (brain-derived neurotrophic factor (BDNF)-neuronal survival and phosphorylated-cAMP response element binding protein (pCREB)-neuronal transcription factor), brain inflammation (interleukin (IL)-6, IL-10 and tumour necrosis factor (TNF)-α) and brain oxidative stress (TBARS and GSH) were studied in important brain areas (frontal cortex, cerebellum, hippocampus and striatum). Administration of a non-selective serotonin receptor agonist, such as 5-methoxytryptamine (5-MT) to rats prenatally (gestational day 12 – day of parturition) and during early stages (postnatal day (PND) 0 –PND20) of development, resulted in impaired behaviour and brain biochemistry. Administration of papaverine (15/30 mg/kg ip) to 5-MT administered rats from PND21 to PND48, resulted in improvement of behavioural deficits. Also, papaverine administration significantly increased the levels of BDNF, pCREB/CREB, IL-10, GSH and significantly decreased TNF-α, IL-6 and TBARS levels in different brain areas. Papaverine, in both doses rectified important behavioural phenotypes related with ASD, the higher dose

(30 mg/kg ip) showed significantly greater improvement than 15 mg/kg ip, possibly by improving neuronal function, brain inflammation and brain oxidative stress. Thus, PDE10A could be a probable target for pharmacological interventions and furthering our understanding of ASD pathogenesis.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Supporting Information

Filename	Description
cep13459-sup-0001-AppendixS1.pdf PDF document, 145.4 KB	Appendix S1

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