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THE INFLUENCE OF MATERNAL MELATONIN: ASSESSING OXIDATIVE AND MEMBRANE DAMAGE IN NEONATE WISTAR RAT BRAINS USING AN AUTISM SPECTRUM DISORDER MODEL

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Melatonin is a hormone provided by the mother to the fetus during development, acting as an antioxidant in crucial cellular processes of the nervous system. The use of Valproic Acid (VPA) during pregnancy serves as a model for studying Autism Spectrum Disorder (ASD). We assessed whether the absence of maternal melatonin during intrauterine development results in damages similar to autism in offspring, as observed in animals exposed to VPA. Wistar rats were divided into five groups: pinealectomized (PTX) or pinealectomized supplemented with melatonin (MEL), a surgical procedure without pineal gland removal (SHAM), VPA injection on the 13th day of gestation (VPA – ASD positive model), and saline injection as a VPA control (SAL). Two days after birth and at the fourth week of life, the offspring were sacrificed, and their neonatal brain were collected and analyzed for GSH content, H_2O_2 production, lipid peroxidation, and Na,K-ATPase activity and its isoforms. Our model showed that VPA exposure increased oxidative parameters and decreased Na,K-ATPase total activity and isoforms. Experimental results showed differences between groups only after stratifying the data by gender. We observed gender differences in oxidative stress levels, with males exhibiting higher basal levels than females. PTX male groups presented opposite patterns compared to female in GSH, H_2O_2 and lipid peroxidation levels. Na,K-ATPase showed no differences, but stratified data indicated a tendency of activity decrease only in PTX male group, and same pattern only in isoform α1. In summary, this study shows that oxidative stress may play a crucial role in the etiology of ASD and highlight the importance of maternal melatonin in preventing neurodevelopmental disorders in offspring. Additionally, it points to possible gender differences that will be investigated in future studies.

Keywords: Autism, Melatonin, Oxidative Stress, Hippocampus, Cerebellum, VPA, Na+/K+-ATPase Activity.

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