Potential Role of Oxidative Stress in mediating the Effect of Hypergravity on the Developing CNS.

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The present studies will explore the mechanisms through which altered gravity affects the developing CNS. We have previously shown that exposure to hypergravity during the perinatal period adversely impacts cerebellar structure and function. Pregnant rat dams were exposed to 1.65 G on a 24-ft centrifuge at NASA-ARC from gestational day (G) 5 through giving birth. Both dams and their offspring remained at 1.65 G until pups reached postnatal day (P) 21. Control rats were raised under identical conditions in stationary cages. On P21, motor behavior, as determined by performance on a rotorod, was more negatively impacted in hypergravity-exposed (HG) male (39.5%) than in HG female pups (29.1%). The total number of Purkinje cells, determined stereologically in cerebella isolated from a subset of P21 rats, was decreased in both HG males and HG female pups, but the correlation between Purkinje cell number and rotorod performance was more consistent in male pups. The level of 3-nitrosotyrosine (3-NT), an index of oxidative damage to proteins, was determined by ELISA in cerebellar tissue derived from a separate subset of P21 rats. The level of 3-NT was increased by 127% in HG males but only 42% in HG females. These results suggest that the effect of altered gravity on the developing brain may be mediated by oxidative stress. These results also suggest that the developing male CNS may be more sensitive to hypergravity-induced oxidative stress than the developing female CNS.

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