Hyperoxia-induced changes in morphometric parameters of postnatal neurogenic sites in rat

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In literature many works address the effects of hypoxia exposure on postnatal neurogenesis but few data are available about hyperoxia effects, although high oxygen concentrations are frequently used for ventilation of premature newborns. Thus, the aim of the present study was to compare with controls the morphometrical parameters of the main neurogenic sites (subventricular zone and dentate gyrus) in newborn Sprague-Dawley rats exposed to 60% or 95% oxygen for the first 14 postnatal days. Six rats were studied for each of the three groups. The unbiased quantitative method of the optical disector was applied to analyze neuronal densities, nuclear volumes, and total neuron numbers of the subventricular zone and hippocampal dentate gyrus. Apoptosis (terminal deoxynucleotidyl transferase-mediated dUTP nick end-labelling, TUNEL) and proliferation (Ki67) were also studied. The subventricular zone of newborn rats exposed to 95% hyperoxia showed statistically significant higher volume (mean value \pm coefficient of variation: 0.40 \pm 0.20 mm3) than subventricular zone of rats raised in normoxia (0.20 \pm 0.11 mm3) or 60% hyperoxia (0.26 \pm 0.18 mm3). Total neuron number was also significantly higher in 95% hyperoxia while neuronal densities did not reach statistically significant differences. TUNEL showed increased apoptotic indexes in hyperoxic rats. The percentage of proliferating KI67 positive cells was also higher in hyperoxia. The dentate gyrus granular layer of the normoxic rats showed higher volume (0.65 ± 0.11 mm3) than both the hyperoxic groups (60% hyperoxia: 0.39 ± 0.14 mm3; 95% hyperoxia: 0.36 ± 0.16 mm3). Total neuron numbers of hyperoxic dentate gyrus were also significantly reduced; neuronal densities were not modified. Hyperoxia-exposed rats also showed higher apoptotic and proliferating indexes in the dentate gyrus. Hyperoxia exposure in the first postnatal period may affect the main neurogenic areas (subventricular zone and dentate gyrus) increasing apoptosis but also inducing a certain reparative response consisting of increased proliferation. In particular, the increased volume of the subventricular zone may be ascribed to compensatory neurogenic response to the hyperoxic damage. Conversely, the decreased volume of the dentate gyrus granular layer could derive by a non sufficient neurogenic response to counterbalance the hyperoxic neuronal injury.

Keywords: Subventricular zone, dentate gyrus, hyperoxia, TUNEL, rat