

Effects of adverse prenatal conditions on cerebral development: a proton magnetic resonance spectroscopy and quantitative histopathology analysis.

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Introduction:

The fetal brain is susceptible to insults during pregnancy that can adversely impact brain development and function.

Objectives:

Our aim was to compare the effects of adverse prenatal conditions on the developing rat brain, by using quantitative proton magnetic resonance spectroscopy (¹H-MRS) in combination with quantitative histopathology.

Material and Methods:

Caloric restriction (CR: 30%) was induced from gestational days 1 to 20 (term ~22 days), dexamethasone (DEX: 100µg/kg/day) was infused from days 15-22, and nicotine (NIC: 3mg/kg/day) from days 4-22. At postnatal day 7 (P7) and P21, ¹H-MRS was performed under continuous anesthesia with temperature and respiratory monitoring using an actively shielded 9.4T/31cm bore system. Metabolite concentrations in the cortex and hippocampus were analyzed with the LCModel. Brain tissue was collected following spectra acquisitions and assessed histologically for growth and glial development using quantitative measures.

Results:

Significant differences were present in metabolite concentrations in all three groups compared to controls, including but not restricted to: ascorbic acid (Asc), creatine (Cr), N-acetyl aspartate (NAA), phosphorylethanolamine (PE), creatine and phosphocreatine (Cr+PCr), and taurine (Tau). At P21, more metabolites were seen to be altered compared to controls, particularly in the DEX-treated group. Quantitative histological analysis revealed that the area of the hemispheres, cortex and hippocampus were reduced in the DEX and CR cohorts compared to controls. On average, the length of radial glial fibres was longer in the DEX and CR groups in the frontoparietal motor cortex, and in the CR group in the parietal somatosensory area, suggesting a delay in the normal involution of radial glia and maturation into astrocytes. The density of GFAP-positive astrocytes in the cingulum, and the area MBP-positive fibres relative to cortical size, was reduced in all experimental cohorts when compared to controls. The metabolite changes in the cortex and hippocampus suggest a measurable, yet different impact of CR, DEX, and NIC exposure on postnatal neurochemical profile measured with ¹H-MRS.

Conclusions:

Markers of brain structure, energy metabolism and neurotransmitter action appear to be modified in our models. Furthermore, histological analysis revealed a delay cerebral development, and in astrocyte maturation and myelination. Combined, ¹H-MRS and quantitative histopathology provided complementary information about the effect of prenatal insults on cerebral development.