Cerebral Metabolism of Adult Marmoset Monkeys After Intrauterine Hyperexposure to Dexamethasone

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Introduction

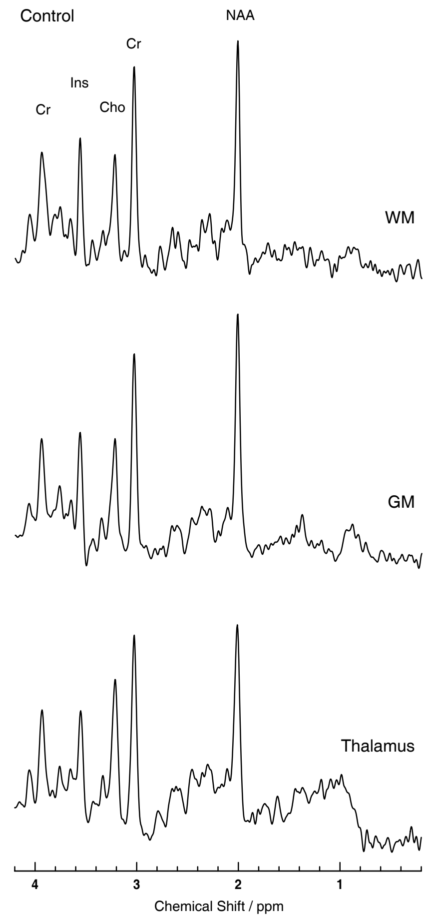
Fetal overexposure to glucocorticoid hormones result in disturbances of the hypothalamic-pituitary-adrenal axis [1]. In rodents, synthetic glucocorticoids such as dexamethasone (DEX) can exert detrimental effects on neuronal tissue including loss of neurons, increased apoptosis, and altered neuronal structure [2]. The purpose of this study was (i) to examine the feasibility of localized proton MRS in the brain of common marmoset monkeys *in vivo*, (ii) to quantify major cerebral metabolites, and (iii) to determine putative metabolite alterations in the adult brain after intrauterine hyperexposure to DEX.

Methods

Pregnant marmoset monkeys received DEX orally (1.0-2.5 mg/kg or 5.0 mg/kg body weight) daily either during early (days 42-48) or late (days 90-96) pregnancy. Control subjects received vehicle only. About two years later, localized proton MRS (STEAM, TR/TE/TM = 6000/20/10 ms, 128 averages) was performed in adult males of the litter (Controls n = 5, DEX n = 8) at 2.35T (Bruker BioSpin, Germany). DEX animals were separated into subgroups with early (n = 4) and late (n = 4) treatment or into subgroups with low (n = 2) and high (n = 6) dose treatment. MRI-guided volumes-of-interest were placed in a mid-sagittal cortical location (i) including parts of the corpus callosum (4.5 × 3.0 × 4.5 mm^3, WM), (ii) excluding parts of the corpus callosum (5.0 × 3.0 × 5.0 mm^3, GM), and in the (iii) thalamus (6.0 × 5.0 × 6.0 mm^3). RF excitation and signal reception were accomplished with use of a 14 cm Helmholtz coil and a 2 cm surface coil, respectively. Metabolite quantification involved spectral evaluation by LCModel and calibration with respect to the brain water concentration [3]. Data expressed as mean ± SD were compared by analysis of variances using the nonparametric Mann-Whitney *U*-test.

Results

In vivo proton MR spectra of different brain regions in the common marmoset monkey exhibit resonances of *N*-acetyl-aspartate (NAA), total creatine (Cr), choline-containing compounds (Cho), and *myo*-inositol (Ins). Line widths of 3.7 ± 0.6 Hz, 4.1 ± 0.3 Hz, and 4.6 ± 0.8 Hz were achieved for WM, GM, and thalamus, respectively. Statistical analysis of subgroups revealed similar metabolite concentrations for early and late treatment as well as for low and high dose exposure (no statistically significant deviations, data not shown). Major metabolite concentrations of control and DEX animals are summarized in the Table.



Discussion

The present results indicate the feasibility of localized proton MRS in the brain of common marmoset monkeys *in vivo*. The achieved spectral quality allows for the quantification of major brain metabolites. In contrast to recent proton MRS studies of tree shrews with disturbances of the hypothalamic-pituitary-adrenal axis due to cortisol treatment [4] or psychosocial stress [5], this study failed to detect statistically significant alterations of the cerebral metabolite concentrations in adult monkeys after intrauterine hyperexposure to DEX. This finding can not exclude acute cerebral metabolite changes, but may indicate that prenatally applied DEX does not lead to permanent concentration changes with corresponding alterations of the adult brain integrity. Furthermore, the previously reported effects of intrauterine hyperexposure to DEX on neuronal tissue might be transient, species dependent, restricted to certain brain regions, and/or beneath the sensitivity of localized proton MRS. However, it may be concluded that localized proton MRS *in vivo* provides new non-invasive insights into the cerebral metabolism in a non-human primate increasingly used to model neurological and psychiatric disorders.

Metabolite (mM/VOI)	Predominantly WM		Predominantly GM		Thalamus	
	Control (n=5)	DEX (n=8)	Control (n=5)	DEX (n=8)	Control (n=5)	DEX (n=8)
NAA	11.7 ± 1.1	11.3 ± 1.5	13.5 ± 1.0	13.2 ± 0.7	12.3 ± 2.4	11.2 ± 1.2
Cr	11.7 ± 0.4	11.0 ± 1.3	12.4 ± 1.1	11.9 ± 0.7	12.5 ± 1.4	11.8 ± 1.2
Cho	2.2 ± 0.3	2.2 ± 0.5	2.1 ± 0.1	1.9 ± 0.2	3.2 ± 0.3	3.1 ± 0.7
Ins	9.6 ± 0.9	9.0 ± 1.5	10.6 ± 1.1	10.0 ± 0.8	11.2 ± 1.8	11.1 ± 2.3

References

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