Effects of Cortisol on Brain Metabolism: a H-1 Magnetic Resonance Spectroscopy Study at 3.0T

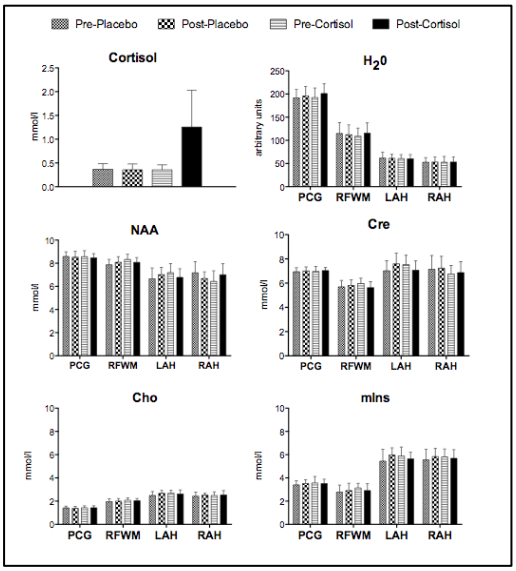
M. Scheel[1], A. Stroehle[1], and H. Bruhn[2]

[1]Clinic for Psychiatry and Psychotherapy, Charite - University Medicine, Berlin, Germany, [2]Department of Radiology, Charité - Humboldt University Medical School, Berlin, Germany

Background: Experimental studies suggest that long-term high-dose glucocorticoids may disturb neuronal integrity and induce dendritic atrophy. In face of controversal and heterogenous H-1 MRS findings (see synopsis in Table 1) we hypothesized that cortisol would cause a reduction of the neuronal N-acetyl aspartate (NAA) concentration, a marker *in vivo* for neuroaxonal integrity. Since decreases of NAA should occur most likely in brain regions with a high expression of corticosteroid receptors, a H-1 MRS study, exploiting the increased SNR at 3-T, was performed with a special focus on the hippocampus.

Study	Subjects	Voxel Placement, MR Hardware and Method (TR/TE/NEX/VOI)	Result
Auer et al, 1997	Single high dose of methylprednisolone in 9 patients (no gender specified)	White matter; 1.5-T, quadrature headcoil; STEAM (3000/30/128/20x20x20mm^3)	*myo*-Inositol reduction of 16%
Brown et al, 2004	17 (16 female) patients with rheumatoid arthritis or asthma and long-term intake of prednisone (7.5 ys)	Left and right hippocampus; 1.5-T, quadrature headcoil; PRESS(1500/144/128/20x20x20mm^3)	NAA reduction of 14%, water peak reduction
Khiat et al, 1999	13 female patients with endogenous M. Cushing	Frontal cortex, hippocampal region, and left thalamus; 1.5-T, quadrature head coil; STEAM (3000/30/192/20x20x20mm^3)	Reduction of cholines in thalamus of 17% and in frontal cortex of 23%
Khiat et al, 2000	Follow-up examination of 10 patients after 6 months from the sample above		Normalization of the reductions reported above
Khiat et al, 2001	Exogenous M. Cushing in 13 (8 female) patients due to long-term intake of prednisone (8.5 ys)		Trends to reduction of cholines, statistically non-significant
Michaelis et al, 2001	Male and female Tupaia belangeri with cortisol intake (28 d)	Forebrain; 2.35-T; STEAM (6000/20/64/7x5x7mm^3)	Reduction of cholines by 29%, NAA by16%, creatines by 13%, and mIns by 20% , only in male animals
Czeh etal, 2001	Only male Tupaia belangeri after 28 d of psychosocial stress	Forebrain; 2.35-T; STEAM (6000/20/64/7x5x7mm^3)	Reduction of cholines by 12%, creatines by15%, and NAA by 13%

Methods: After informed consent and approved of by the institutional ethics board 21 healthy male volunteers underwent a 4-day long cortisol exposure (160 mg/d) employing a double-blind crossover design with placebo and baseline measurements at each condition. H-1 MRS, using a 3-T system with an 8-channel head coil (Signa, GE), was performed in 4 different brain regions including the posterior cingulate gyrus (PCG), right frontal white matter (RFWM), and the left and right anterior hippocampus (LAH and RAH). Measurements were done with PRESS (volume-of-interest of 12x12x12 mm^3 in both hippocampi and of 16x16x16 mm^3 in the PCG and RFWM regions) at minimal T1 and T2-weighting (TR, 6000ms; TE, 30ms; NEX 64). The spectral raw data were analyzed user-independently employing the linear combination method (LCModel, Version 6.01, Provencher) for quantitation.



Results: Cortisol intake led to a nearly threefold increase in serum cortisol levels of the subjects mimicking stress-like effects. In brain, however, for none of the investigated regions a significant corticosteroid-induced variation of the parenchymal metabolite concentrations was observed. Likewise, no cortisol-induced change in water concentration was found.

Conclusion: Our spectroscopic study performed with an improved SNR at 3T in conjunction with a quantitative analysis of metabolite concentrations supports none of the hitherto reported results on the effects of cortisol on neuronal metabolites in humans. While the results mark a baseline, the corticosteroid exposure used could have been too low or too short to induce measurable changes in the cerebral metabolites. The inconsistency of the reported results in the literature demonstrates the necessity of more standardized analysis protocols at enhanced SNR to improve the sensitivity and reliability of MRS measurements.

References:

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