

Decreased energy metabolism in patients with migraine without aura: a ^{31}P MRS study

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Introduction:

Migraine is a primary headache disorder and can be divided into two major subtypes: migraine with aura (MwA) and migraine without aura (MwoA), the latter being the most common form of migraine [1]. There have been described several studies in which ^{31}P MRS was performed in migraine patients, however most of these studies were conducted in MwA patients, patients with migraine with prolonged aura, including familial hemiplegic migraine [2,3]. In most of these studies there was a decreased energy metabolism interictally (= between migraine attacks). Our aim was to re-evaluate the interictal phosphorus energy metabolism, and its possible basal deficiencies, in a homogeneous MwoA patient group.

Materials and Methods:

Subjects: Twenty-two MwoA patients were compared with twenty-five age- but not gender-matched controls. The average age was 33.3 and 27.6 years for MwoA patients and controls, respectively. Patients experienced 2-8 attacks per month, were not using any prophylactic medication and were attack-free for at least 48 hours (verified by e-mail). **Experimental:** ^{31}P MRS measurements were performed on a 3 T whole body MRI scanner (Magnetom Trio Tim, Siemens AG Medical Solutions, Erlangen, Germany) equipped with a double-tuned $^{31}\text{P}/^1\text{H}$ volume coil (Rapid Biomedical, Wurzingen, Germany). Manual shimming of the B_0 magnetic field and manual optimization of the transmitter pulse power were used. Spectra were acquired in the visual cortex using a CSI-FID sequence with TR/TE = 4000/2.3 ms, FOV = 240x240 mm, slice thickness = 30 mm (voxels of 30 ml), NEX = 4, 1024 data points. **Data analysis:** Signal amplitudes of phosphorus metabolites were determined using NUMARIS-software. Absolute quantification was performed using an external reference [4]. As a reference a 500ml spherical phantom containing a 10 mM phosphocreatine (Sigma Aldrich) solution was used. Corrections for coil loading and temperature were applied. A student's t-test was used for comparison. The significance level was defined as $p < 0.05$.

Results:

Table 1 shows the results. There is no significant difference in pH_i . PCr and ATP are significantly decreased in patients while P_i is not significantly increased. The phosphorylation potential (PP), an index of the readily available free energy from the cell and derived from the creatine kinase reaction, is also calculated and shows a significant decrease in MwoA patients. ADP and Mg^{2+} do not show a significant difference between MwoA patients and controls. Finally, the parameter v/v_{max} is derived from the Michaelis-Menten equation and gives an estimation of the velocity of oxidative metabolism. However, it doesn't show a significant difference.

Discussion:

The lack of difference in pH_i confirms results of earlier studies, indicating an absence of acidosis in MwoA patients [3]. The PCr-decrease is not as large as in other studies, however, these mostly evaluated MwA patients [3]. In contrast to our results, ATP has always been assumed constant in the literature [2]. P_i plays an important role in the creatine-kinase reaction and its increase takes place concomitantly with the PCr-decrease. ADP and v/v_{max} do not show an increase in MwoA patients in contrast to earlier studies [2,3], whereas the increase in PP is in good agreement with the literature [2,3]. All these findings point to a basal disturbance of brain energy metabolism. In future work, absolute quantification of phosphorus metabolites will be performed comparing MwoA patients and controls following visual stimulation.

References:

[1] Headache Classification Subcommittee of The International Headache Society, *The International Classification of Headache Disorders* (2nd edition), *Cephalalgia* vol. 24 Suppl 1 (2004), pp. 9–160. [2] Barbiroli et al. *Neurology* 42:1209-1214, 1992. [3] Montagna et al. *Cephalalgia* 14:184-193, 1994. [4] Duc et al. *Magn. Reson. Med.* 39:491-496, 1998.

Table 1

	patients	controls	p
pH_i	7.03 ± 0.09	7.03 ± 0.03	0.702
[PCr] (mM)	4.09 ± 0.58	4.85 ± 0.60	0.001
[P_i] (mM)	1.32 ± 0.50	1.06 ± 0.36	0.129
[ATP] (mM)	2.33 ± 0.63	2.76 ± 0.59	0.023
[ADP] (mM)	0.033 ± 0.018	0.031 ± 0.009	0.735
PP (%)	56.24 ± 21.95	72.87 ± 18.12	0.041
v/v_{max} (%)	53.92 ± 7.48	54.61 ± 6.36	0.752
[Mg^{2+}] (mM)	0.135 ± 0.058	0.156 ± 0.038	0.254