NAA dynamics in normal motor cortex in the period of BOLD response on millisecond stimulus.

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Introduction

The aim of this study was the analysis of dynamics of N-acetylaspartate in motor cortex of normal brain after short single stimulus.

Methods

9 age-matched healthy males comprised test group. Study was performed on clinical Phillips Achieva 3.0 T MRI scanner. Volume of interest in motor cortex was localized on the base of fMRI study (EPI FFE, TR = 3000 ms, TE = 30 ms) as the zone of activation caused by bottom push with the forefinger in response to single auditory stimuli transmitted with the 18 s periodicity (Fig. 1).The BOLD signal was measured each 3 sec. 1H MR spectra (PRESS, TE = 30 ms TR = 3000 ms) were run; FID signals for time points t = 0, 3, 6, 9, 12, 15, 18 s after stimulus were summarized. Thus, the synchronization of BOLD and metabolic responses to single stimulus was achieved. The same method was applied for spectra accumulation in resting state. For FID processing custom made software was used (with apodization filtering (LB = 20, GB = -5), FT and manual phase correction). NAA, Cho, Cr signal intensities for each time point were normalized to their values at t = 0 and to the volume of activated cells containing in the voxel (segmented manually). Intergroup difference and time points differences were estimated using Mann-Whitney criterion with the level of significance $p<0.05$.

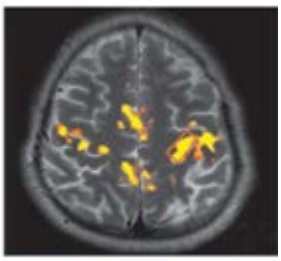

Fig.1. Position of the spectroscopic voxel

Results

Statistical analysis demonstrated that without a load all measured values are constant. The BOLD signal demonstrated maximum at the 6th s after target stimulus. The stable values of [NAA], [Cr] and [Cho] were observed in dynamic of resting state. [NAA] significantly decreased at the 12th s after stimulus and returned to initial value at the 15th s. Thus [NAA] minimum delayed relative to maximum of BOLD by 6 s (Fig.2).

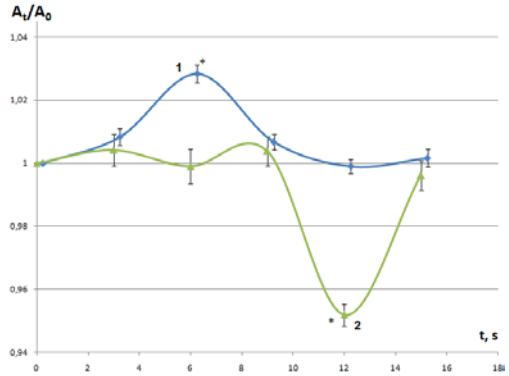

Fig. 2 BOLD signal (1) and dynamics of the averaged NAA signal amplitudes (2) in the ^{1}H NMR spectra of the premotor cortex; * $p < 0,05$

Discussion

BOLD fMRI of brain activity depends crucially on functional hyperemia. Thus BOLD reflects temporal activation of vasodilators synthesis induced with glutamate uptake by neurons and asrtocytes after neuronal activity.

We have observed NAA decrease at the 12th s after stimulus. NAA could compensate increased metabolic demands because its acetyl moiety included in acetyl CoA (Ac CoA) which is a crucial element of Krebs cycle. Substantial number of axons was found to express aspartoacylaze (ASPA) and Ac CoA synthase-1 (AceCS1) [4]. ASPA hydrolyzes NAA into acetate and aspartate. AceCS1 catalyses the reaction between free acetate and coenzyme A to produce Ac CoA. Localization of both enzymes allow one suggestion that NAA-derived acetate can be converted to acetyl CoA for further metabolism in some axons. Incorporation of acetate in Krebs cycle is fast and takes 2 s for astrocytes [5]. Thus fast reversible decrease of NAA observed in the study could provide a short-term activation of neuronal Krebs cycle through a synthesis of Ac CoA using acetate obtained in ASPA reaction.

Conclusion

The oxygen consumption activation processes are kinetically related to the concentration dynamics of the NAA as a neuronal marker. The developed approach reveals the multi-substrate character of the process and makes it possible to formulate hypotheses of the molecular response mechanisms.

References

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