Functional ^{31}P-{^{1}H} EPSI with 6 s temporal resolution of the human brain

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Introduction

In vivo phosphorus-31 (^{31}P) magnetic resonance spectroscopy (MRS) creates a window into brain physiology via non-invasive detection of high-energy phosphates such as adenosine 5'-triphosphate (ATP) and phosphocreatine (PCr). Brain energetics respond to functional activation with an increase in ATP turnover which is buffered by PCr along the creatine kinase reaction. Several ^{31}P functional MRS (fMRS) studies have been performed in humans to determine metabolic changes during visual stimulation (VS) [1-5]. Most of these studies utilized low temporal resolution and hence prolonged VS paradigms of several min were applied. Some [1-3] but not all [4, 5] of these studies indicated a decrease of PCr levels during brain activation. While long VS resulted at best in a moderate PCr change, a considerable PCr signal reduction was observed in one study where very short VS in the order of seconds was performed [3]. In this context we recently demonstrated the feasibility of ^{31}P-{^{1}H} Echo-Planar Spectroscopic Imaging (EPSI) of the human brain [6] with high temporal resolution and improved spatial localization compared to the inhomogeneous excitation profiles of surface coils used in most former ^{31}P fMRS studies. The purpose of the present study was to determine the time course of PCr during short VS of only 6 s with functional ^{31}P-{^{1}H} EPSI which may help to solve the current controversy regarding PCr changes in response to short-term brain activation.

Methods

Eleven healthy volunteers were examined on a clinical 1.5-T MR tomograph (Magnetom Vision Plus; Siemens, Erlangen, Germany) equipped with a second rf channel and a double-tuned (^{1}H/^{31}P) circularly polarized head coil (Rapid Biomedical, Wuerzburg, Germany). The ^{31}P-{^{1}H} EPSI pulse sequence [6] permits acquisition of 64 localized ^{31}P spectra in only 1.5 s. Measurement parameters were: TR = 180 ms, FOV = (400 mm)^2, slice thickness = 40 mm, matrix = 8×8, spectral width $\Delta\nu$ = 1.67 kHz. The block-design paradigm consisted of one period of 6 s visual stimulation (radial black/white checker board flickering at 6.7 Hz) followed by three 6-s periods of resting (fixation cross). For each period four ^{31}P-{^{1}H} EPSI scans were averaged. The paradigm was repeated 125 times, resulting in a total measurement time of 48 min (Fig. 1). Spectra of all paradigm cycles were summed for each individual period to gain sufficient SNR. Spectra were analyzed and fitted using *jMRUI 2.2* software [7]. Results from voxel segmentation were used to correct for cerebral spinal fluid (CSF) contamination. Additionally, quantification of PCr from the time-domain fit was corrected for coil loading. Statistical analysis (paired *t*-test) was done with *SPSS 12.0* (significance was assumed for $p < 0.05$).

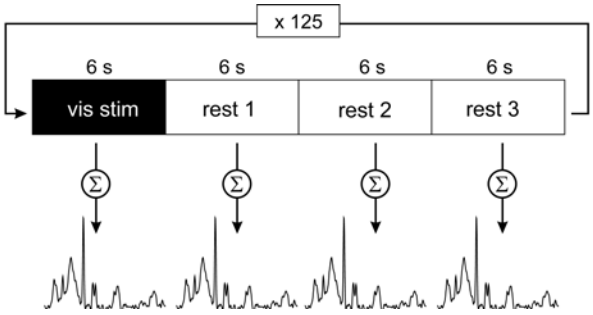

Fig. 1 Block-design paradigm for functional ^{31}P–{^{1}H} EPSI: a period of 6 s visual stimulation is followed by three periods of 6 s of rest. Paradigm was repeated 125 times to gain sufficient SNR. Spectra of all cycles were summed for each period.

Results

For each volunteer one ^{31}P MR spectrum during stimulation and three spectra during resting condition were obtained for altogether 8×8 localized voxels. Fig. 2 shows results from the voxel localized in the visual cortex. Segmentation yielded an average CSF content of 15±3.5 % while grey matter content was 51.6±5.6 % in this voxel for all 11 volunteers. Neither difference spectra of VS *versus* resting condition nor *SPSS* analysis revealed any significant PCr changes between VS and resting periods. Standard deviation (SD) of SD = 7 % of PCr quantification was determined by repeated measurements without VS. Average intracellular pH value was 7.02±0.01 for VS and resting conditions and showed no significant changes upon functional stimulation. The absence of any significant PCr concentration changes during stimulation agrees with previous findings [4, 5]. However, these studies used prolonged VS paradigms and hence steady-state conditions were observed. Otherwise our findings controvert ref. [3] which reports observation of a significant decline of PCr when short stimuli of only a few seconds are presented. Our data suggest that if there are any PCr concentration changes upon short neuronal activity, these changes must be extremely small and may only be detectable with more statistical power. Our observations support recent high-field ^{1}H fMRS findings in humans at 7 T [8] and in animals at 9.4 T [9].

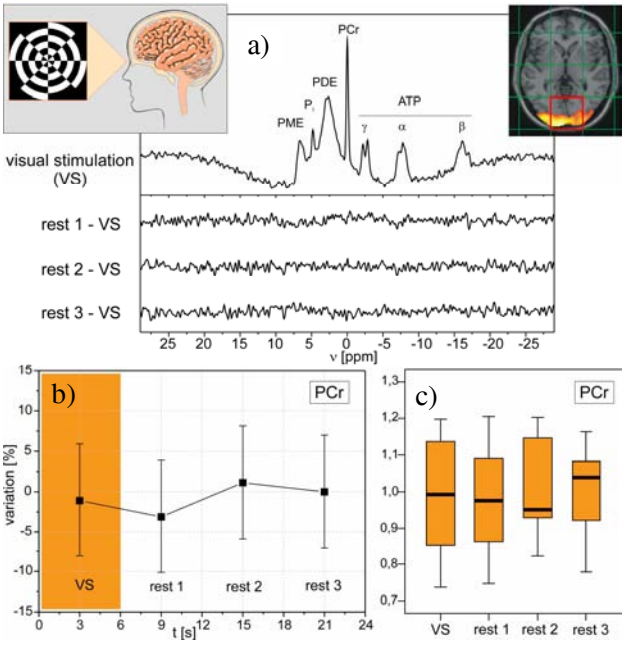

Fig. 2 a) Summed *in vivo* spectrum from 11 subjects acquired during visual stimulation (VS) from the voxel localized in the visual cortex. Below: difference spectra of VS *versus* resting conditions. Insets: illustration of the VS; transverse images with EPSI grid and superimposed BOLD activation map. Voxel localized in the visual cortex is marked in red. b) Time course of PCr signal intensity with 6 s temporal resolution averaged over 11 subjects. Error bars represent SD = 7 %. c) *SPSS* box plots. Statistics shows no significant changes of cerebral PCr concentration upon stimulation.

References:

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