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Research Paper

Dynamic MR Spectroscopy of brain metabolism using a non-conventional spectral averaging scheme

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HIGHLIGHTS

- Standard functional MRS acquisition may be susceptible to movement artefacts.
- Averaging of two spectral lines in steps of 6 s was therefore implemented.
- Higher BOLD changes were observed in single paradigm compared to block paradigm.
- BOLD changes in the block paradigm were generally lower than reported averages.
- Temporal resolution of two averaged lines thus reduces recorded BOLD effects.

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ABSTRACT

Purpose: MRS acquisition based on the blood oxygenation level dependent (BOLD) contrast mechanism was implemented at 3 T to investigate the impact of a non-conventional spectral averaging scheme (determined by the number of RF excitations, NEX) on the dynamics of cerebral metabolism during neuroactivation. Using NEX = 2, water and metabolite BOLD responses were compared to previous results from standard experiments.
Methods: Spectra were recorded from the visual cortex of five healthy volunteers during single and block visual stimulations. The height, width and area of the spectral peaks were calculated (using SAGE v7) in order to estimate their percentage changes from baseline (representing the BOLD change) following visual stimulation. BOLD changes were statistically significant at a significance level of $p < 0.05$ by paired *t*-test.
Results: Significantly greater BOLD changes in all spectra were observed in the single than block stimulation ($p < 0.05$). The water resonance showed significant ($p < 0.01$) BOLD changes in all peak parameters in both paradigms. All metabolites showed significant increase in spectral height ($p < 0.01$) in the single paradigm, but none of them (except the height of Cho) showed significant BOLD response in the block paradigm. BOLD changes observed in the block paradigm were generally lower than reported changes.
Conclusions: The time interval of 6 s offered by NEX = 2 during which each line of spectral data is recorded by the scanner is rather long, leading to some BOLD data loss particularly in a block experimental design.

1. Introduction

Functional magnetic resonance imaging (fMRI) based on the blood oxygenation level dependent (BOLD) contrast mechanism is a common neuroimaging research tool (Ogawa et al., 1990; Frahm et al., 1992; Kwong et al., 1992). Other studies use magnetic res-

Abbreviations: AP, anterior-posterior direction; B_0, field strength; BOLD, blood oxygen level dependent; CHESS, CHEmical Shift Selective preparation; Cho, Choline; Cr, Creatine; FID, free induction decay; fMRI, functional magnetic resonance imaging; fMRS, functional magnetic resonance spectroscopy; FOV, field-of-view; GE, General Electric; Gln, glutamine; Glu, glutamate; mI, myo-inositol; MR, magnetic resonance; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; NAA, *N*-acetyl aspartate; NEX, number of radiofrequency excitations; NSA, number of signal averages; PRESS, Point-RESolved Spectroscopy; RF, radiofrequency; RL, right-left direction; SAGE, spectroscopy analysis by GE; SE, standard error; SI, superior-inferior direction; SNR, signal-to-noise ratio; T_2^*, relaxation time constant due to susceptibility effects; *TE*, echo time; *TR*, repetition time.

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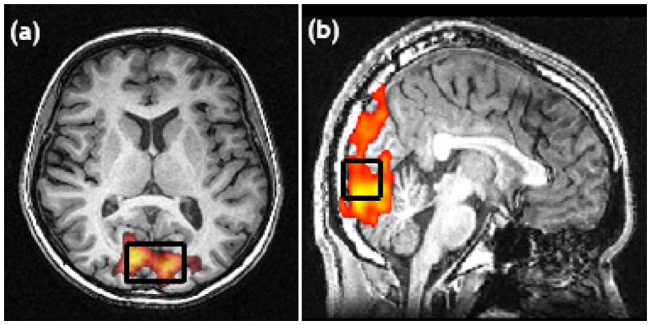

Fig. 1. Axial (a) and sagittal (b) views of the localised fMRS voxel (volume = 20 SI x 20 AP x 30 RL mm^3) within the activation map generated in the V1 brain region during the fMRI examination.

onance spectroscopy (MRS) to probe the dynamics of brain tissue metabolism during neuroactivation, also based on the BOLD effect (Blockley et al., 2013; Malonek and Grinvald, 1996; Zhu and Chen, 2001; Shih et al., 2009; Hennig et al., 1994); this is known as functional MRS (fMRS). The fMRS technique therefore serves as a tool for neurochemistry and neuroscience research (Mangia and Tkac, 2008).

The BOLD effect arises when an external stimulus causes neural activity to increase above baseline physiological state. The new physiological state is associated with changes in cerebral blood flow, cerebral blood volume and the cerebral metabolic rate of oxygen consumption (Blockley et al., 2013). This increases the flow of oxygenated blood to the region of activity, which causes susceptibility gradients to spread around and away from the activation site (Malonek and Grinvald, 1996). This susceptibility gradient, associated with changes in T_2^*, can be detected in vessels (intravascular compartment) and tissue near the vessels (extravascular compartment).

At a lower magnetic field ($B_o \leq 1.5$ T) and in the presence of small bipolar diffusion gradient, the BOLD effect mainly comes from the intravascular compartments in noncapillary vessels and is cancelled out completely through spin dephasing. However, at a higher field ($B_o \geq 3$ T) and in the presence of higher bipolar diffusion gradient (Song et al., 1995; Menon et al., 1995), the BOLD effect mostly comes from the extravascular compartment and does not disappear. This therefore makes the extravascular BOLD effect most desirable for mapping locations of functional activation (Zhu and Chen, 2001). The BOLD signal is also reported to increase with field strength (Wardlaw et al., 2012) due to increased sensitivity of detection at higher fields (Sarchielli et al., 2005).

A localised spin-echo ^{1}H MR Spectroscopy sequence can be used to record the BOLD signal in a functional MRS experiment (Hennig et al., 1994). The spin-echo FID in this case can be defined by three parameters (Zhu and Chen, 2001). The first parameter is the FID amplitude (A_{FID}) of the first sampling point at the centre of the echo. A_{FID} is determined by the transverse relaxation time, T_2 and the initial magnetisation, M_o according to:

$$A_{FID} = M_o.\exp(-TE/T_2), \quad (1)$$

and assuming there is no contribution from spin exchange,

$$1/T_2 = 1/T_{2,int} + 1/T_{2,D} \quad (2)$$

where TE is the echo time, $T_{2,int}$ is the intrinsic T_2, and $T_{2,D}$ is the component of T_2 accounting for the contribution of diffusion. M_o is proportional to the proton density (ρ) and the NMR signal intensity.

The second parameter of the spin-echo FID is the FID decay rate ($1/T_2^*$), defined as:

$$1/T_2* = 1/T_2 + 1/T_{2,SS} \quad (3)$$

where $T_{2,SS}$ is the transverse relaxation time related to local static susceptibility. However, this effect of field inhomogeneity cancels out in the spin-echo experiment.

The third parameter of the spin-echo FID is the FID integral (I_{FID}), which can be determined by both A_{FID} and T_2^*. In the frequency domain, I_{FID}, A_{FID} and T_2^* are quantitatively correlated to three other NMR parameters: peak height (H), linewidth at half peak height ($\Delta\upsilon_{1/2}$), and spectral peak area (A_S). These correlations can be deduced from the following relations:

$$A_S \alpha A_{FID} \quad (4)$$

$$\Delta\upsilon_{1/2} = 1/(\pi T_2*) \quad (5)$$

$$H \alpha I_{FID} \quad (6)$$

Thus, from a typical MR spectrum that is acquired with the spin-echo pulse sequence, information about the following relationships can be deduced: A_S correlates with changes in T_2 and M_o, $\Delta\upsilon_{1/2}$ correlates with changes in T_2 and $T_{2,SS}$, and H correlates with changes in T_2, $T_{2,SS}$, and M_o. With this information, the BOLD contributions from various origins can be studied by fMRS, where M_o increases and manifests as increase in spectral peak height, H and area, As; T_2^* also increases and causes a decrease in $\Delta\upsilon_{1/2}$. The BOLD effect in fMRS is thus associated with increased spectral peak area and height, corresponding with decreased spectral linewidth (Zhu and Chen, 2001; Shih et al., 2009; Hennig et al., 1994).

Cerebral water is present in the intracellular and extracellular spaces, CSF and blood. For this reason, the BOLD effects on both intravascular and extravascular compartments will contribute to the water signal change during the sensory stimulation. On the other hand, the BOLD effects on the cerebral metabolites only manifest the susceptibility changes in the extravascular tissue compartment (Zhu and Chen, 2001).

It has been suggested (Mangia and Tkac, 2008) that studies using similar fMRS paradigms, stimulus type, spectral analysis and quantification schemes, assuming high SNR of spectra, should observe comparable BOLD changes. However, what has not been considered in the literature is whether variations in the number of radiofrequency excitations (NEX) used in a particular fMRS study could impact on the BOLD signal. The NEX value is particularly important because it is the time interval between successive spectral lines in the frequency domain; it thus determines the number of spectral lines that will be averaged and stored (in the data frame) within the total duration of the fMRS data acquisition according to:

$$N_{Total} = 16/NEX + NSA/NEX \quad (7)$$

where N_{Total} is the number of spectral lines stored in the data frame, NSA is the number of signal averages, (16/NEX) is the number of unsuppressed-water spectral lines, and (NSA/NEX) is the number of suppressed-water spectral lines. The standard PRESS sequence on the GE MR scanner acquires 16 averages of unsuppressed-water lines prior to acquisition of the metabolite spectra.

NEX can be varied between only 2 and 8 on the MR scanner used for this study. However, NEX = 8 is commonly used in MRS studies because it allows for the maximum number of spectral lines to be quickly averaged before the FIDs are stored, thus reducing the potential degradation of spectra due to motion effects (Drost et al., 2002). It is however unclear if NEX = 2 would have any significant impact on the signal-to-noise ratio (SNR) of spectra, and consequently on the BOLD effect recorded in the MR spectra.

In this fMRS study, the BOLD effects on brain tissue water and metabolites were recorded during sustained visual stimulation of the primary visual cortex (V1) of the normal human brain. The aim was to investigate MRS BOLD signal changes in the respective MR spectra, using a non-conventional number of RF excitations (i.e. NEX = 2), which determines how the MR spectra are averaged. The