fMRI With Intermolecular Double-Quantum Coherences (iDQC) at 3T

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Introduction

Intermolecular multiple-quantum coherence (iMQC) imaging has attracted a great deal of attention, recently. In a traditional liquid-state experiment, iMQCs are not observed. This is due to the fact that short-range dipolar interactions are averaged to zero in time by rapid molecular motion whereas long-range intermolecular interactions average to zero in space as long as the sample is magnetically isotropic. However, magnetic field gradients can break this isotropy, and long-range intermolecular dipolar couplings can reappear in a mode controlled by the experimenter. Compared to conventional gradient-recalled echo (GE) or spin-echo (SE) techniques, imaging with iDQC contrast is potentially more sensitive to blood-oxygen level dependent (BOLD) magnetic susceptibility variations, which are essential for functional brain studies, than single-quantum coherences (SQC). Previously, three fMRI studies at 7 T and 1.5 T utilizing iMQC effects were published, with visual and auditory stimulation tasks, respectively (1, 2, 3). Despite an improved dynamic range and (potentially) selectivity, a drawback of iMQC experiments is their inherently poor SNR, which makes them extremely susceptible to physiological and instrumental signal instabilities. Consequently, there is a strong demand for sequence optimization to permit reliable evaluation of the potential of this novel type of contrast.

Materials and Methods

As iMQCs benefit from high magnetic fields, all experiments were carried out at 3 T (i.e., the typical field strength of current high-field systems) using two different scanners (Siemens MAGNETOM Trio and Bruker MedSpec 30/100). Two approaches were applied comprising spin-echo iDQC and gradient-recalled echo iDQC sequences. The pulse sequences, which were developed with the ODIN-package (4), are shown in figure 1. This package allowed to play out identical sequence code on both scanners. The data were acquired using standard birdcage coils. A simple 2D EPI readout (matrix 64×64) was used for imaging. Relevant sequence parameters are summarized in table 1. The correlation gradients were applied for 2.5 ms and 5 ms before and after the β pulse, respectively. The gradient amplitude was 22 mT/m, which defines a correlation distance of 218 μm. The evolution time denotes the time between the α and β pulse. To allow refocusing of signal rephrasing, a delay time was inserted after the β pulse, which was either negative or positive for SE-iDQC and GRE-iDQC, respectively.
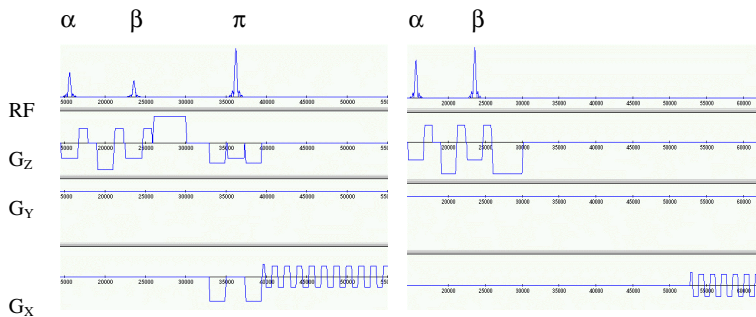

Figure 1. Modified CRAZED sequences for SE-iDQC (left) and GRE- iDQC (right) imaging.

Table 1. Sequence parameters.

	SE-iDQC	GRE-iDQC
Repetition time (TR)	3.5 s	3.5 s
Echo time (TE)	80 ms	35 ms
Transition	$n = -2$	$n = +2$
Evolution time τ	10 ms	10 ms
Delay time	–20 ms	+20 ms
α / β	90°/60°	90°/120°

The signal of iDQC is scaled as $3\cos^2\theta - 1$, where θ is the angle between the interspin vector and the main magnetic field. The direction of the interspin vector is determined by the direction of the correlation gradients. The correlation gradients were applied in z-direction (max. signal intensity). A two phase-cycling scheme (x, -x) was used for the 90° pulse. To verify proper selection of iDQCs, a control experiment was performed prior to each fMRI experiment, in which the correlation gradient was applied at the magic angle ($\theta = 54.7°$). Five healthy volunteers were investigated in the functional study using an established visual paradigm. In a blocked design, rotating red letters "L" were presented for 28 s after 28 s of rest. The total time of the functional scan was 12:08 min.

Results and Discussion

In a series of pilot experiments, the sequence timing (TR, TE, delay time) was systematically varied for optimizing SNR and contrast. Results are given in Table 1. In experiments performed at the magic angle, crusher gradients were optimized in order to eliminate residual signal contributions from unwanted coherences. Reduction of TR below 3.5 s produced increasing signal instability due to additional stimulated echoes between each repetition. Postprocessing of the fMRI data included a correlation analysis with a boxcar design corresponding to stimulus. Figure 3 shows a typical correlation map obtained with GRE-iDQC. Regions of activation were well centered within the primary visual cortex. The data were smoothed with a spatial Gaussian filter of 0.8 pixels. Activated pixels were selected using a threshold of $z > 3.5$. The averaged signal intensity change of activated pixels was approximately 13% whereas typical signal fluctuation were about 9%. The absolute signal intensity of SE-iDQC images was approximately 15% higher than that of GRE-iDQC images. It is currently an open question whether the functional contrast achieved by iDQCs can be tuned to a particular vessel size by proper adjustment of the correlation distance. The optimized sequences provide the basis for future experimental investigation in this direction.
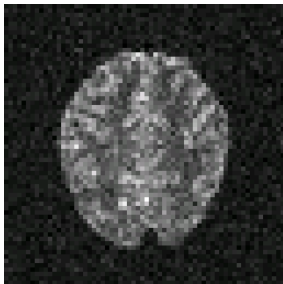

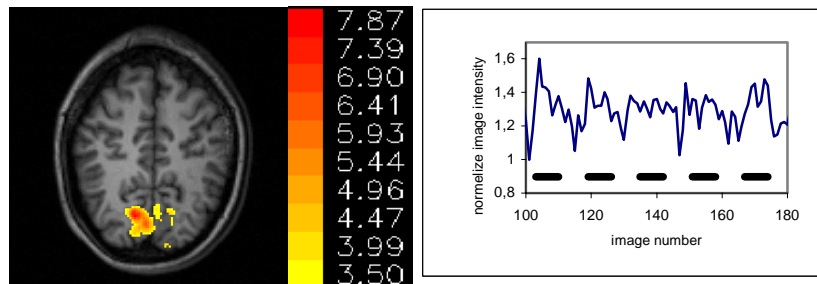**Figure 2.** GRE-iDQC image (5 averages).

Figure 3. GRE-iDQC activation map superimposed on a conventional anatomical T_1-weighted image (left) and time course from all activated pixels (right).

References:

(**1**) W. Richter et. al., *Magn. Reson. Imag.*, **18**, 489, 2000. (**2**) J. Zhong et. al., *Magn. Reson. Med.*, **45**, 356, 2000.(**3**) J.Zhong et. al., *J. of Magn. Reson. Imag.,* **16**, 733, 2002. (**4**) T. H. Jochimsen et. al., *Proc. Intl. Soc. Magn. Reson. Med.*, **10**, 2448, 2002.