Effect of Hypercapnia on the iDQC Response

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Introduction

It is well known that the fMRI baseline signal of gray matter in human brain increases linearly with expired carbon dioxide (CO_2) from hypocapnic to hypercapnic levels (1). It is generally accepted that hypercapnia produces a global increase in cerebral blood volume (CBV) and flow (CBF). By contrast, no changes in the cerebral metabolic rate of oxygen consumption (CMR_{O2}) are expected for moderate hypercapnia, which thus provides a means for manipulating cerebral hemodynamics without affecting oxidative metabolism (2). It has previously been shown that intermolecular double-quantum coherences (iDQC) can be used for susceptibility-sensitive fMRI and it was hypothesized that its contrast is fundamentally different from that detected by the conventional blood-oxygen level dependent (BOLD) effect (3). Currently, the origin of iDQC signal changes is not completely understood. A challenge of multiple quantum imaging is further the intrinsically poor signal-to-noise ratio (SNR) (4). This work investigates the baseline fMRI contrast produced by hypercapnia as detected by iDQC imaging and compares the results to conventional BOLD-based fMRI.

Materials and Methods

All experiments were carried out at 3 T (Siemens MAGNETOM Trio). A modified CRAZED sequence that produces iDQC contrast is shown in Figure 1 (*TR* = 5 s; *TE* = 70 ms; τ = 15 ms; 15 axial slices; voxel size = 4 × 4 × 4 mm³; bandwidth = 65 kHz; β = 120°). The correlation distance in the iDQC sequence was set to 100 µm. The correlation gradient was applied in z-direction to maximize the signal intensity. A two-step phase-cycling scheme (x,–x) was used for the α pulse (90°). In addition to iDQC imaging, a conventional SE-BOLD sequence (*TR* = 5 s; *TE* = 80 ms; voxel size = 4 × 4 × 4 mm³; bandwidth = 100 kHz) was also recorded at the identical slice positions for comparison in all subjetcs. The order of the iDQC and BOLD sequence was randomized across subjects. Four healthy subjects were investigated. Hypercapnia was induced by inhalation of a gas mixture with 5% CO_2. The subjects inhaled the mixture for 1 min. after 1 min. of breathing regular air. The total time of one functional study was 11 min. During the fMRI experiments, the end-tidal CO_2 ($ETco_2$) was recorded. Post-processing of the data included a correlation analysis with a design function corresponding to the recorded $ETco_2$. The data were smoothed with a spatial Gaussian filter of 0.6 pixels.

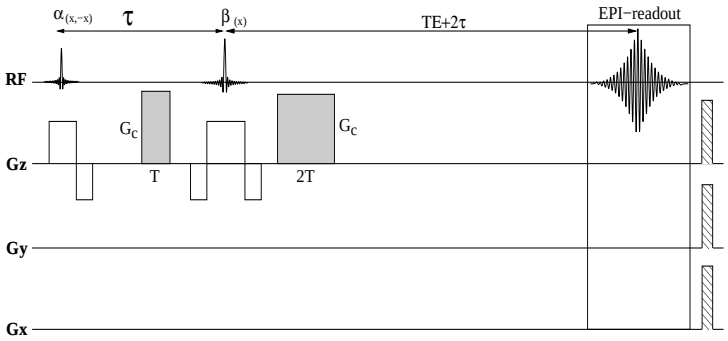

Figure 1. Modified CRAZED sequence for iDQC imaging

Results and Discussion

Figure 2 shows the correlation map of a single subject obtained with SE-BOLD and iDQC ($z > 3.09$). Both methods yield strong positive correlations with $ETco_2$. Activated voxels were well localized in gray matter. The time courses of activated voxels and the general pattern of activation were similar for both methods. The number of activated voxels was less that with SE-BOLD despite quite similar maximum z-scores. Qualitatively, the iDQC images seemed more susceptible to signal loss in areas with strong field variations, which might explain the absence of functional contrast in frontal brain areas. Quantitatively, substantial differences in the signal change were obtained with both methods as shown in Figure 3: The percentage signal change averaged over all subjects was approximately 20% and 3% in case of iDQC and SE-BOLD, respectively. This seems to underline the increased sensitivity of double quantum coherences to local susceptibility changes. In addition, the iDQC contrast recorded at a correlation distance of 100 µm might be more weighted towards veins whereas the SE-BOLD contrast is weighted towards the capillaries.
The results indicate that iDQC-based fMRI is sensitive to pure hemodynamic changes in the absence of changes in CMR_{O2} which is qualitatively similar to conventional BOLD fMRI. Additionally, the high level of signal change during hypercapnia and the global nature of the response should provide good conditions for further optimizing sequence parameters in iDQC imaging.

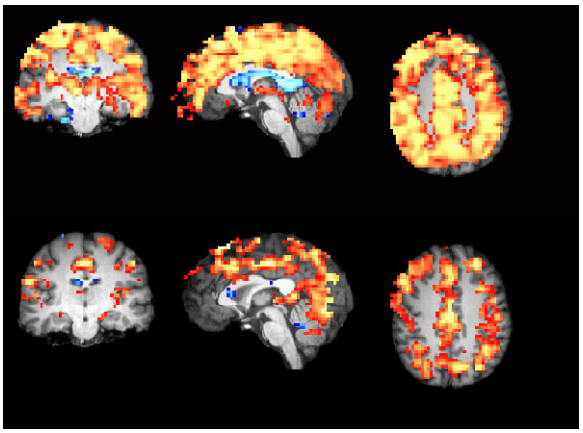

Figure 2. Correlation map correspondending to changes in $ETco_2$ recorded in a single subject (top: SE-BOLD; bottom: iDQC).

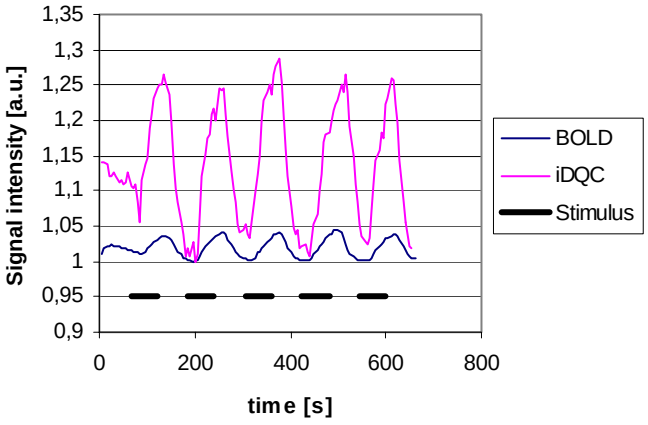

Figure 3. Time courses of activated pixels in the same subject.

References:

(**1**) E.R. Cohen et al., *J. Cereb. Blood Flow Metab.*, **22**, 1042, 2002. (**2**) C. Schwarzbauer, W. Heinke, *Magn. Reson. Med.* **41**, 537, 1999. **(3)** W. Richter et al., *Magn. Reson. Imag.* **18**, 489, 2000. **(4)** W.S. Warren et al., *Science*, **281**, 247, 1998.