Anatomic and Functional MRI with Intermolecular Double-Quantum Coherences at 7 Tesla

W. Richter[1], M. Mescher[2], K. Ugurbil[2], G. Adriany[2], P. Andersen[2], L. Bouchard[3], and W. S. Warren[3]

[1]Institute for Biodiagnostics, National Research Council, Winnipeg MB R3B 1Y6, Canada

[2]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis MN 55455, USA

[3]Department of Chemistry, Princeton University, Princeton NJ 08544, USA

Introduction

While **intra**molecular multiple-quantum coherences have been observed and exploited by NMR spectroscopists for many years, the concept of **inter**molecular multiple-quantum coherences is relatively new.[1,2] Usually, intermolecular correlations are not observed in liquids, because dipolar couplings between nuclei, which are necessary for such correlations to become visible, average out - short range dipolar couplings through molecular diffusion, and long-range dipolar couplings through the magnetic isotropy of the sample. However, magnetic isotropy is broken when magnetic field gradients are applied; in this manner, long-range dipolar couplings can be reintroduced and used to make intermolecular correlations between distant spins visible.

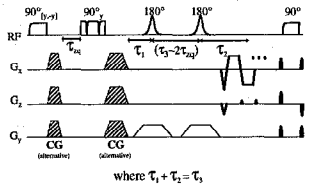
The most remarkable properties of this effect are related to the distance between the spins whose correlation can be made visible. This distance is generally mesoscopic (typically tens to hundreds of micrometers), and it can be tuned through the choice of experimental parameters. This means that we can in principle characterize the sample on a subvoxel scale. A good example is given by the first (one-dimensional) imaging experiment that was carried out several years ago;[3] in that experiment, the thickness of a thin membrane separating two phases could be estimated by this method. To our knowledge, this is the only NMR experiment that can characterize a sample on that distance scale.

While any order of multiple quantum coherences can be excited in principle, the most obvious applications come from signals that evolve at the frequency difference between two spins. These may be zero-quantum coherences, as shown before,[4] or may be derived from double-quantum coherences, as shown here. The signal intensity in those cases is dependent on the distribution of **magnetic field gradients** over the selected distance.

Potential applications of the method to living systems abound. In the context of MRI, two obvious applications are fMRI and enhanced tissue contrast. FMRI is based on gradients induced by local variations in oxygen concentrations; while T2* is a somewhat gross measure for this variation, a distance-selective method is potientially much more sensitive. This prediction is supported by ongoing simulations in one of the authors' lab (W.S.W.). While we previously used intermolecular zero-quantum contrast in our experiments, we sought here to demonstrate contrast based on intermolecular **double**-quantum coherences.

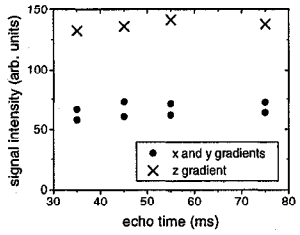
Method

MRI experiments were performed with a 7 Tesla whole body imaging system with a quadrature surface coil. At present, experiments have been carried out with three subjects. After localization of the calcarine sulcus using FLASH, a series of anatomical iDQC images was generated using the pulse sequence shown below. In this pulse sequence, double quantum coherences are created by the first pulse and evolve subsequently. They are then transformed into magnetization and read out through an EPI sequence. The position of the echo and proper timing ensure that the eventually detected signal is actually a function of the frequency *difference* between the two spins. The echo segment is also essential to regain signal strength lost through relaxation. Within this series, several



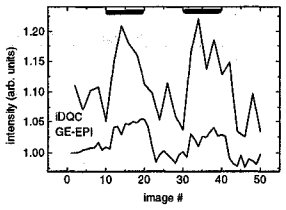
parameters, namely the correlation gradient direction and the echo time, were varied in order to assert some predicted properties of the iDQC signal. Then, conventional BOLD images were acquired using a GE-EPI sequence, followed by a series of iDQC images. The task used in both cases consisted of visual stimulation with flashing LEDs. Data were analyzed by cross-correlation.

Results and Discussion



In all subjects, iDQC contrast images were obtained. This is illustrated in the figure on the left. Shown is the average magnitude of the signal in a ventricle as a function of echo time and correlation gradient direction. Theory predicts that the signal for transverse gradients is half that for longitudinal gradient, and furthermore, that the signal initially rises and then falls with increasing echo time. Both predictions are borne out by this experiment.

Functional iDQC images (correlation distance 250 μm) were obtained in two of three subjects. Shown in the figure below are BOLD signal (bottom) and iDQC signal (top) for our visual stimulation task in the primary visual cortex. The underlying activation map was produced from the iDQC data; both time courses correspond to identical pixels, for comparison purposes. In principle, activation maps may be different for the two methods. The iDQC signal follows the BOLD signal qualitatively. The signal increase in the pixels used is much larger for iDQC, but this may be due to the way we produced the maps. This demonstrates that the iDQC method may become an important method for functional MRI; however, it is too early to interpret the data quantitatively.



Support by the NIH (RR08079) is gratefully acknowledged.

References

1. Warren, W.S., Richter, W., Hamilton Andreotti, A. et al., Science 262, 2005 (1993).

2. Enss, T., Ahn, S. Warren, W.S., Chem. Phys. Lett. 305, 101 (1999).

3. Richter, W., Lee, S., Warren, W.S. et al., Science 267, 654 (1995).

4. Warren, W. S., Ahn, S., Mescher, M., Science 281, 247 (1998).