RELIABILITY OF A BREATH-HOLD PARADIGM TO CHARACTERISE INTER-SUBJECT DIFFERENCES IN COGNITION BASED BOLD CONTRAST

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Background

Breath hold paradigms have recently been proposed to infer regional information about the direct effect of vascular factors on the BOLD response, independent of changes driven by sensory or cognitive processes (1,2). The utility of this approach depends greatly on the reliability and reproducibility of the signals elicited during the breath hold challenge. We have adopted the controlled breath hold protocol proposed by Glover et al (3), which appears to exhibit reduced variance in the BOLD data at the single subject level. A group of eighteen healthy volunteers was scanned twice over two sessions and the voxel-wise reliability of the induced signal changes was determined using the intra-class correlation coefficient (ICC), by means of a methodology tailored to functional imaging applications (4).

Methods

18 healthy participants (9 male, 24-49 yr, mean 31.3, SD 6.7) were scanned twice over two sessions whilst performing a blocked-periodic breath hold challenge. The two sessions were separated by 3 to 60 days (mean 13 days). Each block comprised 36s of normal breathing and 20s of breath hold preceded by a 4 sec preparation time during which participants inhaled whilst expanding their chest to 75-85% of their maximum expansion as shown by an analogue scale projected to a screen at the foot of the scanner bed. The target level was derived from a calibration procedure in which their maximum chest expansion was determined by a pneumatic bellow; and recorded by a computer.

Images were collected using gradient echo EPI. Image volumes of 38 near axial slices were acquired with TE/TR = 25/2000; isotropic resolution of 3.3mm and parallel imaging with acceleration factor = 2. All scans were performed on a General Electric 3 Tesla Excite HDX scanner. This study was approved by the local Research Ethics Committee.

All data was analysed using the SPM-5 software suite and in-house routines for voxel-wise ICC computation written for Matlab (www.brainmap.co.uk). Realignment of the time series was followed by co-registration to a high resolution gradient echo image, normalisation and spatial smoothing (7 FWHM Gaussian Kernel).

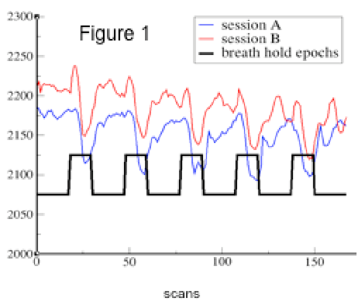


Figure 1

Figure 3

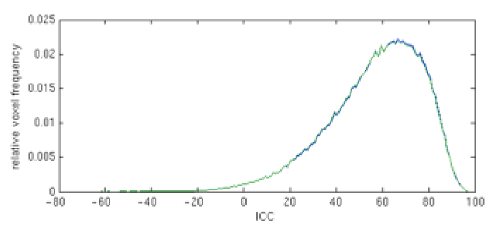
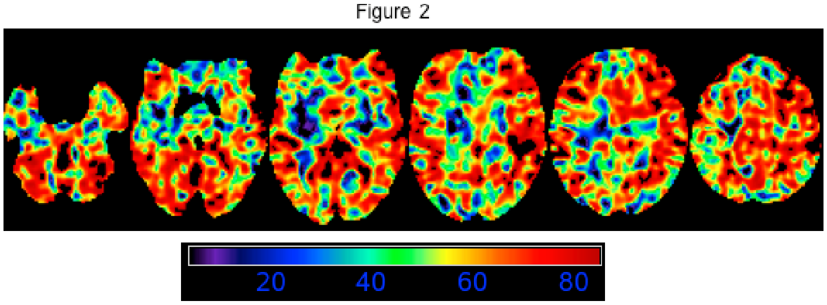


Figure 2



Results

An averaged trace of the whole-brain BOLD signal observed in a typical subject during the breath hold challenge, is shown in figure 1. The figure shows that during breath hold, there is an initial increase in the BOLD signal, followed by a significant reduction below baseline; and a later increase whose peak occurs inside the window of the subsequent period of normal breathing. This average signal was used as a regressor to create maps of breath hold response which were input into a voxel-wise reliability analysis. ICC values were calculated for each voxel (figure 2) and a marginal distribution was plotted for values above T=3.64 (p<0.001); figure 3.

Discussion

In spite of the complex temporal characteristics of the BOLD signal changes induced by this paradigm, the ICC maps computed on these data set exhibit remarkably high reliability over the two scanning sessions. This is evident in figure 2, which shows a marginal distribution that is highly skewed towards the high ICC range, with a coexisting low probability of voxels showing low reliability. In addition, the computed group ICC map (figure 3) exhibits a structure reminiscent of the grey matter distribution, in which the high ICC values (yellow and red), are located almost exclusively in the grey matter tissue. These data suggests that breath hold challenges elicit BOLD signal changes that are ideally suited to explore the vascular origin of grey matter BOLD signals from other sensory or cognitive challenges. The prevalence of high reliability indices also suggests that controlled breath hold paradigms can be confidently applied to group studies based on repeated measures designs.

References

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