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A comprehensive evaluation of increasing temporal resolution with multiband-accelerated protocols and effects on statistical outcome measures in fMRI

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ABSTRACT

Accelerated functional Magnetic Resonance Imaging (fMRI) with ‘multiband’ protocols is now relatively widespread. These protocols can be used to dramatically reduce the repetition time (TR) and produce a time-series sampled at a higher temporal resolution, which may produce benefits in the statistical methods typically used to analyse fMRI data. We tested the effects of higher temporal resolutions for fMRI on statistical outcome measures in a comprehensive manner on two different MRI scanner platforms. Spatial resolution was maintained at a constant of 3 mm isotropic voxels, and an in-plane acceleration factor of 2 was used for all experiments. Experiment 1 tested a range of acceleration factors (1-6) against a standard EPI protocol on a single composite task that mapped a number of basic sensory, motor, and cognitive networks. Experiment 2 compared the standard protocol with acceleration factors of 2 and 3 on both resting-state and two task paradigms (an N-back task, and faces/places task), with a number of different analysis approaches. Results from experiment 1 showed modest but relatively inconsistent effects of the higher sampling rate on statistical outcome measures. Experiment 2 showed strong benefits of the multiband protocols on results derived from resting-state data, but more varied effects on results from the task paradigms. Notably, the multiband protocols were superior when Multi-Voxel Pattern Analysis was used to interrogate the faces/places data, but showed less benefit in conventional General Linear Model analyses of the same data. In general, ROI-derived measures of statistical effects benefitted only modestly from higher sampling resolution, with greater effects seen when using a measure of the top range of statistical values. Across both experiments, results from the two scanner platforms were broadly comparable. The statistical benefits of high temporal resolution fMRI with multiband protocols may therefore depend on a number of factors, including the nature of the investigation (resting-state vs. task-based), the experimental design, the particular statistical outcome measure, and the type of analysis used.

Introduction

Acceleration in scanning speed is a long-standing goal of MRI research, and substantial gains in acquisition speed have been achieved by advances in both hardware and software. One major advance of particular interest to neuroimaging researchers is the development of

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'multiband' or 'Simultaneous Multi-Slice' (SMS) protocols for functional MRI (Feinberg and Yacoub, 2012; Feinberg et al., 2010; Moeller et al., 2010). These use multiband excitation pulses to excite and collect multiple slices simultaneously, and provide increases in temporal resolution in line with the number of slices acquired at once; so a multiband factor of two acquires two slices simultaneously. This allows double the number of slices to be acquired in the same TR, or halves the repetition time (TR) needed for the same number of slices. Acceleration factors up to 16 have been demonstrated at 7T (Moeller et al., 2010) and 8-10 have been tested at 3T (Sahib et al., 2016; Smith et al., 2013); these protocols can substantially reduce the TR required for whole-brain imaging, and produce time-series with very high temporal resolution. However, as an undersampling technique, multiband protocols may produce decreased temporal signal to noise ratio (tSNR; Chen et al., 2015) and increased levels of image artefacts, in particular 'slice-leakage' effects (Barth et al., 2015; Todd et al., 2016). The trade-off between the benefit of higher temporal resolution and the cost of higher levels of noise and/or artefacts is important to characterize as these protocols become widely adopted.

The benefits of higher temporal resolution in fMRI may not be entirely obvious, considering that fMRI samples the BOLD (Blood-Oxygen-Level-Dependent) effect; a relatively low-frequency signal. Sampling this slow signal at a higher rate (beyond that necessary to adequately model it) may therefore seem to provide little benefit. However, BOLD effects are usually quantified using statistical methods, and those statistical tests depend crucially on the number of data points, which (partly) determines the degrees of freedom of the statistical tests. Increasing the sampling rate reduces the influence of noise on statistical measures of the BOLD signal in much the same manner as more averaging of repeated measurements reduces the effect of noise and produces a more robust estimate (Miller et al., 2015; Constable and Spencer, 2001). Higher sampling rates can therefore potentially benefit the statistical outcome measures that researchers are often most interested in.

Previous work has shown that these protocols are indeed useful in this regard, within certain task domains or experimental approaches. Smith et al. (2013) used multiband protocols to increase the image resolution (2 mm isotropic) of the entire brain with the same TR, and with signal-to-noise characteristics equivalent to standard EPI protocols. These protocols were used in the Human Connectome Project to generate high-resolution maps of functional connectivity using resting-state fMRI. Todd et al. (2016) recently evaluated multiband protocols at several acceleration factors (2, 4, and 6) and showed impressive gains on *t*-statistics, which varied depending on anatomical location, and the precise reconstruction algorithm used. Boyacioğlu et al. (2015) also demonstrated benefits of a Multi-Band Multi-Echo (MBME) protocol over a conventional multi-echo protocol at 7T, using both resting-state and task-activation data. Preibisch et al. (2015) found a substantial increase in sensitivity for resting-state analyses with four-fold acceleration, but also noted that higher acceleration levels produced artefacts.

While this previous work is useful, several unanswered questions remain. The majority of previous evaluations of multiband protocols have used resting-state fMRI data, with only a few using basic motor (finger-tapping) or visual (typically, gratings or checkerboards) stimulation paradigms (e.g. Boyacioğlu et al., 2015; Todd et al., 2016). These simple tasks are a classic method for evaluating fMRI protocols, but in many ways are quite dissimilar to the tasks used in modern cognitive neuroscience research, which may be relatively complex, and activate a wider network of brain regions than simple motor or sensory tasks. Secondly, there has been no published evaluation of the interaction between use of multiband-accelerated protocols and factors related to experimental design. Conceivably, higher temporal resolution scanning might be a particular benefit for fast event-related designs, relative to block designs. Thirdly, different analysis approaches have not been compared; the effect of multiband protocols on the signal-detection ability of conventional (i.e. General Linear Model-based) analysis of task data, relative to its effect on Multi-Voxel Pattern Analysis (MVPA) is one example that is currently undocumented. Fourthly, previous studies using multiband protocols have often used them in order to increase temporal *and* spatial resolutions (e.g. Smith et al., 2013), with likely complex effects on signal-to-noise and statistical reliability. Finally, there have been no direct comparisons on the use of multiband protocols on different scanner platforms. Scanner hardware might reasonably be expected to have relatively minor effects, and a number of different scanner platforms have been used in previous evaluation work, but there has never been a direct comparison.

Our aim was therefore to address these questions by performing as comprehensive a test of multiband acquisition protocols as possible using a range of tasks, a number of different analysis approaches, and two different scanner platforms (a long, 60 cm bore system, and a short 70 cm bore system, both 3T). Our broad aim was to evaluate the 'real-world' performance of multiband protocols, using (currently) typical experimental and analysis techniques. A more particular focus was on the effect of reducing repetition time (TR), while holding spatial resolution constant. We conducted two main experiments. The first sought to characterize the effect of a range of multiband acceleration factors (2-6) on a complex task that maps a number of sensory, motor, and cognitive networks, and produces activation in widespread brain areas. This task should therefore provide a more elaborate and comprehensive test case than the typical visual or motor tasks used previously. We then used a narrower range of acceleration factors (2 and 3) to comprehensively evaluate the statistical benefits of multiband protocols in three paradigms (two cognitive tasks, and resting-state data), with a number of different analysis approaches. We completed each experiment on both scanner platforms.

Methods

Experiment 1

Participants

Ten healthy volunteers were recruited for Experiment 1 of the study (5M, 5F, mean age = 24.6, range 20–39). Standard MRI screening procedures were followed for all participants in advance of testing. Informed consent was obtained from all the participants.

Data acquisition

Data were acquired on two scanners of the same field strength, but different RF, gradient, and magnet designs. Scanner 1 was a 3T Siemens Tim Trio (213 cm long, with a 60 cm bore), and Scanner 2 was a 3T Siemens Magnetom Verio (173 cm long, with a 70 cm bore). The in-built body coil was used for RF excitation and the manufacturer's 32 channel phased-array head coil was used for reception in both scanners. Whole-head anatomical images were acquired at the beginning of each scanning session using a Magnetization Prepared Rapid Gradient Echo (MPRAGE) protocol using parameters based on the Alzheimer's Disease Research Network (ADNI-GO; 160 slices x 240 × 256, TR = 2300 ms, TE = 2.98 ms, flip angle = 9°, 1 mm isotropic voxels, bandwidth = 240 Hz/pixel, parallel imaging (PI) factor = 2, Inversion time = 900 ms; Jack et al., 2008).

Six different functional imaging protocols were used: a standard Echo-Planar Imaging (EPI) protocol with in-plane acceleration using a reduction factor of 2 (denoted as R2), and five multiband acquisitions with in-plane acceleration and different levels of simultaneous-slice acceleration: 1, 2, 3, 4 and 6 (hereafter referred to as MB1R2, MB2R2, MB3R2, MB4R2 and MB6R2). These protocols were based on the multiband EPI WIP v012b provided by the University of Minnesota (Cauley et al., 2014; Setsompop et al., 2012; Xu et al., 2013). Detailed characteristics of each protocol are shown in Table 1. While the settings of the standard EPI (R2) and the MB1R2 protocol are identical, the comparison between the two may still be instructive, as the reconstruction algorithm used in the multiband protocol is somewhat different (Moeller et al., 2010), even with no slice acceleration. The protocols were standardized across the two scanners as much as possible, however