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Prospective motion correction with volumetric navigators (vNavs) reduces the bias and variance in brain morphometry induced by subject motion

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ABSTRACT

Recent work has demonstrated that subject motion produces systematic biases in the metrics computed by widely used morphometry software packages, even when the motion is too small to produce noticeable image artifacts. In the common situation where the control population exhibits different behaviors in the scanner when compared to the experimental population, these systematic measurement biases may produce significant confounds for between-group analyses, leading to erroneous conclusions about group differences. While previous work has shown that prospective motion correction can improve perceived image quality, here we demonstrate that, in healthy subjects performing a variety of directed motions, the use of the volumetric navigator (vNav) prospective motion correction system significantly reduces the motion-induced bias and variance in morphometry.

Introduction

The influence of motion on MRI neuroimaging studies, particularly high-resolution, 3D-encoded imaging where scan times can extend to several minutes, has long been recognized in both clinical and research environments (Maclaren et al., 2013; Zaitsev et al., 2015). In both settings, images that are qualitatively considered to be motion-degraded are often discarded and rescanned. In some research studies, subjects are removed from analysis when their scans show unacceptable levels of motion degradation (e.g., Qureshi et al., 2014; Harvard Center for Brain Science, 2015), while in other studies, efforts are made to match controls to experimental subjects with similar amounts of motion (Yendiki et al., 2014; Koldewyn et al., 2014). All of these methods of dealing with motion must be used carefully to avoid introducing biases into group analyses. For example, removing subjects who move during their MRI scans, or selecting control subjects based on how much they move, may result in selection bias.

The importance of accounting for motion has been made clear by recent work showing that differences in motion between groups lead to not just a decrease in statistical power, but can introduce biases in a variety of neuroimaging experiments (Van Dijk et al., 2012; Power et al., 2012, 2014; Satterthwaite et al., 2012, 2013; Yan et al., 2013; Yendiki et al., 2014; Hess et al., 2014; Reuter et al., 2015). Connectivity analyses performed using functional (Van Dijk et al., 2012; Power et al., 2012, 2014; Satterthwaite et al., 2012, 2013; Yan et al., 2013) and diffusion-weighted data (Yendiki et al., 2014) both show significant sensitivity to subject motion. In the case of brain morphometry, (Reuter et al., 2015) demonstrated that the impact of motion is a continuous effect, with even small subject motions biasing the resulting measurements. As a result, only aggressive removal of motion-damaged data, beyond what is normally done in neuroimaging studies, could bring the effect of motion on gray matter volume and thickness estimates below a statistically significant level. This work concluded that even motion

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whose impact on image quality is effectively unnoticeable by visual inspection still biases the morphometric analysis.

The volumetric navigator (vNavs) system allows the scanner to track the subject's head during the scan and prospectively correct for subject motion (Tisdall et al., 2012; Hess et al., 2011). vNavs are inserted into the dead-time in MRI pulse sequences (normally once per TR), with each navigator acquiring a complete, but low-resolution head volume in roughly 300 ms. These navigator volumes are then rapidly registered, and the resulting estimates of subject motion are used to update imaging parameters "on the fly" during scanning, allowing the scanner to image in head-relative coordinates despite subject motion. These motion updates are inherently low-frequency, since they can only occur once per TR (e.g., every 2.53 s during our MEMPRAGE protocol), and subject motion between segments is not fully corrected. To address this, the system can automatically reacquire TRs that it determines to have been motion degraded based on it's estimate of subject motion. Combining the prospective updates with retrospective reacquisition provides a substantial reduction in the impact of head motion on the output images.

In addition to vNavs, other prospective motion correction systems have also demonstrated qualitative improvements in image quality when subjects perform motions that would normally cause substantial artifacts (van der Kouwe et al., 2006; Zaitsev et al., 2006, 2015; Ooi et al., 2009; Brown et al., 2010; Kuperman et al., 2011; Hess et al., 2011; Tisdall et al., 2012; Maclaren et al., 2013). However, given the new awareness that even small amounts of motion may compromise morphometric data, we are interested in evaluating whether vNav-enabled scans can correct the motion-induced bias in morphometry, even when the motions performed are too small to cause obvious image artifacts.

We address this question using a superset of the data that was considered in (Reuter et al., 2015). The previous work considered only scans without prospective motion correction and derived statistical tests to evaluate the effects of motion on uncorrected studies. In the present work we add into our analysis scans where prospective motion correction with vNavs was used, and evaluate whether the corrected scans show a significantly smaller error due to motion than those without correction.

Materials and methods

Scanning

Twelve healthy adult volunteers (5 male and 7 female; ages 21–43, mean age 26.9 years, standard deviation 7.2 years), having given informed consent, were scanned in a 3 T TIM Trio MRI System (Siemens Healthcare, Erlangen, Germany) using the 12-channel head matrix coil supplied by the vendor. For each subject, scans were performed during one visit and the scanning session was divided into two blocks of equal length. Between each of the two blocks, the subject was removed from the scanner and allowed to take as long a break as desired. During each scan block, subjects' heads rested on a pillow, stabilized by foam blocks on both sides. Subjects were located in the bore such that the junction of the top of the nose and the brow was at isocenter.

Each visit included eight repetitions of a 3D multi-echo MPRAGE (MEMPRAGE) (Mugler and Brookeman, 1990, 1991; van der Kouwe et al., 2008): two still scans (both without prospective motion correction), and then two scans in each of three motion conditions, giving a total of six motion scans. Scanning was performed using a research version of the vNavs-enabled MEMPRAGE pulse sequence, which is available as a research sequence for some Siemens scanner platforms. Subjects were asked to perform three qualitatively different motions: nodding (rotation around left–right axis), shaking (rotation around head–foot axis), and moving freely (each subject was directed to make up a short pattern to repeat, with the suggestion "draw a figure-8 with your nose."). These motion types were chosen in order to cover a variety of motion directions. In studies of disease and aging there may be stereotyped patterns and frequencies of motion, but to the best of our knowledge these features of in-scanner behavior have not yet been documented for any specific populations of interest. Our present study was not powered to differentiate effects of different motion types. Instead, our goal in having subjects perform a variety of motion types was to induce within-subject variability in the scans, under the assumption that each motion "type" would also lead to different amounts of motion.

For each type of motion, one repetition was performed with prospective motion correction disabled (but with vNavs measuring subject motion) while the other repetition had prospective motion correction enabled. Each block included scans with one of each motion type (still, nod, shake, and free), but whether the first or second repetition of each motion type had prospective correction enabled was randomized for each subject. Subjects were not informed as to whether or not motion-correction was being applied. Before each scan, an auto-align localizer (van der Kouwe et al., 2005; Benner et al., 2006) was run to ensure each scan began in approximately equivalent alignment with the head. The order of the scans was randomized for each subject in order to reduce potential order-related biases in the results.

Before entering the scanner, subjects rehearsed the motions with the experimenter and were reminded that the motions should remain small (our experience from past studies being that MRI-naive subjects who are asked to move tend to perform very large motions). When inside the scanner, subjects were directed as to which motion to perform and the duration of each motion through written instructions projected on a screen at the head of the scanner bore and visible in a mirror attached to the coil. Subjects were told to begin moving when the screen switched to a move instruction and continue moving until presented with instructions to "remain still". Subjects were instructed to remain still in whatever position they found themselves in when the screen switched back to "remain still" (their pre-scan verbal instructions included the phrase "freeze when the screen asks you to remain still"). Each subject was randomized to be either a "long" or "short" movement subject, with six subjects in each group. "Long" movement subjects were directed to move for a 15-second block during each minute of scanning, while "short" movement subjects were directed to move for a 5-second block during each minute of scanning. Subjects were not informed which group they were in. Similar to our use of multiple motion types, our goal in having long and short motion groups was not to study whether these two amounts of motion produced significantly different effects, but instead to help ensure larger between-subject variability than would occur if all subjects were asked to move for the same duration.

Scans were immediately stopped and repeated if a subject's motion was estimated to have exceeded 8° rotation or 20 mm translation in one TR. This limit is enforced by Siemens' PACE motion-tracking system (Thesen et al., 2000), upon which the vNavs system is based.

All 3D MEMPRAGE scans were acquired with the same protocol: non-selective inversion and excitation, 2530 ms TR, 1220 ms TI, 256 mm × 256 mm × 176 mm FOV with 1 mm isotropic resolution, 4 echoes with a bandwidth of 650 Hz/pixel, and 2× GRAPPA acceleration in the outer-most phase-encode loop. The voxel-wise root-mean-squared combination of the four echoes was used for all subsequent analysis. vNavs (3D-encoded EPI volumes) were acquired once every MEMPRAGE TR as described in (Tisdall et al., 2012); the vNav protocol had a 256 mm × 256 mm × 256 mm FOV with 8 mm isotropic resolution, one excitation per slab and 3/4 partial Fourier in the slice direction, 11 ms TR, 5.3 ms TE, and a bandwidth of 4223 Hz/pixel. Total scan time for the scans without motion correction was 6:12, while the scans with motion correction included 18 extra TRs of reacquisition, and thus their total time was 7:00 (19 extra TRs need to be played for 18 reacquisitions to ensure each imaging TR is sandwiched between vNavs; for more details see (Tisdall et al., 2012)). The choice of 18 extra TRs was made based on the desire to keep a practical scan duration (in this case