Head Motion in RS FMRI: Not the Problem We Think It Is

Hang Joon Jo[1], Richard C Reynolds[1], Stephen J Gotts[2], Alex Martin[2], Robert W Cox[1], and Ziad S Saad[1]
[1]*Scientific and Statistical Computing Core, National Institutes of Mental Health, Bethesda, MD, United States,* [2]*Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institutes of Mental Health, Bethesda, MD, United States*

Purposes

Resting State FMRI (RS FMRI) holds promise for understanding normal brain function and revealing brain regions involved in complex distributed disorders. Part of the appeal of RS FMRI is the relative ease with which the data can be acquired. However, drawing valid inferences, particularly for group comparisons, is fraught with pitfalls, as recently illustrated in two publications that have caused considerable stir in the functional neuroimaging field. The first paper (hereinafter "Study 1") showed that motion differences between subjects might explain perceived differences in the spatial patterns of brain connectivity [1]. In the second paper (hereinafter "Study 2"), the authors showed that differences in the amount of movement - even down to 4 microns on average - could result in measurable group differences in average seed-based correlations [2]. In this work, we show that significant false positives cannot be readily ascribed to motion differences alone, particularly when group differences in motion levels are small.

Motion is Not the Main Source for Distance-Dependent Correlation Bias

In a reproduction of Study 1 (Fig. 1A), we find that censoring differentially affects correlations between ROIs that are close together compared to those that are further apart. This bend in the distribution was considered in Study 1 as evidence that motion was behind this bias, since lessening the effects of motion through censoring in turn differentially affected correlation values between ROIs depending on their distance. However, this is not entirely the case. In Fig. 1B, we recomputed the correlation differences but without including the 6 motion estimates (MO) and their derivatives, thereby amplifying the effect of censoring on the correlations. The scatter plot of the correlation difference increased in variance but the distance-dependent bias remained. In Fig. 1C, we brought back the motion estimates with their derivatives, but omitted any tissue-derived regressors (WM, CSF) and their derivatives, most notable of which is the global signal (GS). With this model, the effect of censoring on the correlations becomes considerably less dependent on the inter-ROI distance. The correlation changes are also more uniformly negative, implying that sharp head motion tends to add more exclusively positive values to the correlations prior to censoring [3]. The average white matter regressor tends to account for the same signal fluctuations as the GS [4]. For Fig. 1D, we repeated the analysis in Fig. 1C except for adding a despiking step at the very beginning of the preprocessing pipeline. The despiking procedure is often used to dampen the effects of extreme signal deviations on motion correction and variance estimates. The addition of despiking further reduced the correlation bias' dependence on inter-ROI distance, as well as reduced the overall values of the correlation changes. In other words, censoring offset the correlation values by the same amount, regardless of the distance between ROIs.

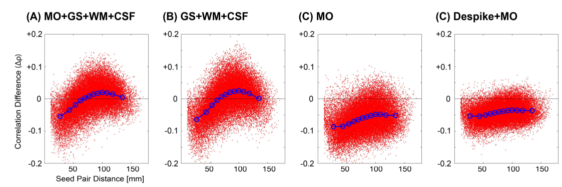

Fig. 1. Distance-dependent correlation bias

Small Motion Difference is Not a Likely Source of Significant False Positives

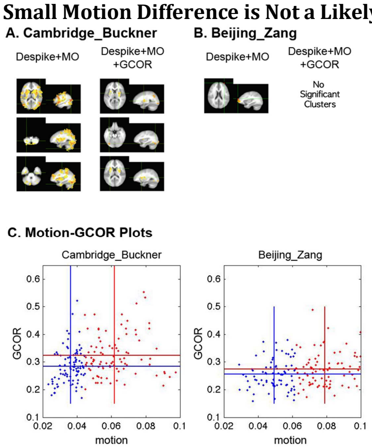

Fig. 2. Group difference between large- and small-motion subgroups

In agreement between Study 2 and our replication (Fig. 2) using Cambridge data from FCON 1000 initiatives, the contrast yielded false positives when none would have been expected from this presumed uniform population of subjects. The t-test result from the data, in our hands, was quite dramatic: four clusters covering a volume of 412,209 mm^3 were observed (see Fig. 2A, left column; uncorrected $p<0.01$, $|t|>2.6$). At first blush this result confirms the conclusions of Study 2, that motion differences are behind such false positives, however, further probing invites more nuanced conclusions. The same contrast between top and bottom movers using the Beijing set, for example, resulted in just one significant cluster that barely met the relatively liberal statistical threshold; that cluster had 92 voxels when the cut off was at 78 voxels (see Fig. 2B, left column). This finding was quite surprising, since in the Beijing set the average difference in motion between top and bottom movers was larger (29 microns) than in the Cambridge set (25 microns). Despite differences in image acquisition that might explain some of this discrepancy, it is difficult to reconcile these two findings if motion were the prominent driver of the spurious results under these groupings. In an effort to understand the factors behind this discrepancy, we examined single-subject correlation results and found some to have markedly increased correlations compared to others. Including global correlation (GCOR) measure as a covariate at the group level greatly reduced the difference between top and bottom movers in the Cambridge set (see Fig. 2A, right column) and eliminated the one cluster in the Beijing set (Fig. 2B, right column). Such global measures (1 value or time-series per subject) are quite unlikely to capture the spatially varying effects of motion any better than the 6 or 12 regressors used to model the motion. On average, the GCOR is greater in subjects with more motion. However, the correlation between GCOR and average motion is relatively weak as shown in Fig. 2C. These global measures are likely capturing a combination of brain-wide fluctuations, both neuronal and physiological in origin [5].

Discussion

In this work, we have sought to add nuance to the conclusions drawn by the two studies suggesting that motion difference between groups can lead to false inferences. While we agree that considerable difference in motion can yield false positives, the empirical evidence suggests that other noise sources may be having more of an effect. To properly ascertain whether or not minute motion differences can lead to false positives would require a dataset acquired with physiological recordings of respiration and heart rate, thus allowing for a more careful parcellations of noise sources. To summarize, motion is a problem but is not insurmountable with proper processing steps, and this mundane issue needs to be revisited more carefully to properly assess the magnitude of its effect.

References

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