Temporal evolution of functional connectivity metrics: Could seven minutes of rest be enough?

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Background: There is emerging evidence that temporal variability in ‘resting-state’ functional magnetic resonance imaging (rfMRI) undermines the reliability of the static rfMRI metrics and challenges their potential as biomarkers for clinical applications in neuroscience. Since various rfMRI metrics are being used to assess brain functional connectivity, it is important to quantify the impact of scan time on the convergence of different metrics. We hypothesized that the rfMRI patterns will reach their asymptotic plateaus at different time scales for metrics obtained from: 1) seed-voxel correlations; 2) spatial independent component analysis (sICA); and 3) graph theory.

Methods: Imaging datasets from 40 healthy subjects (age: 31 ± 3 years; 31 females) were drawn from the publicly available repository of the human connectome project. Four “minimal preprocessing” rfMRI datasets with high spatiotemporal resolution (0.72s TR; 2-mm isotropic resolution; 1200 time points) per subject were included in the analysis (sessions: 1 and 2; phase encoding directions: LR and RL). The temporal evolution of 3 different rfMRI metrics over 864 s was mapped using an expanding-window approach with fixed expanding steps of 36 seconds (50 time points; e.g., a set of time series with increasing scan length was derived from the original fMRI data from each subject). We assessed the effect of scan time on 1) the local functional connectivity density ($lFCD$) computed using in-house software; 2) the sICA default-mode network (DMN) computed with the melodic FSL package; and 3) the FC of an important hub at the occipito-parietal junction, computed with in-house software. For all metrics, we quantified reproducibility, accuracy and reliability as well as gray matter sensitivity and specificity. An exponential saturation model was used to assess the optimal scanning time for $lFCD$, sICA and seed-voxel correlations.

Results: The benchmarks (reproducibility, accuracy and reliability, sensitivity and specificity) of the time-varying connectivity metrics ($lFCD$, sICA and seed-voxel correlations) gradually converged to their maxima with increased window length (goodness of exponential fit: $\chi^2 < 0.0004$). The necessary scan time to significantly attenuate the effects of the temporal dynamics on the five benchmark criteria by 80% or more, varied across connectivity metrics and was shorter for $lFCD$ (6.6 min) than for seed-voxel correlations (11.4 min) or for sICA (10.2 min).

Conclusions: The higher resilience of $lFCD$ to the effects of temporal dynamics compared to standard rfMRI metrics such as seed-voxel correlations and sICA could explain the high sensitivity of $lFCD$ to brain disorders. Thus, the $lFCD$ metric is more suitable for pediatric and patient populations who may not tolerate long scans. Our study suggests that 7-10 minutes scanning could result in stable static rfMRI biomarkers. However, development of dynamics biomarkers such as those reflecting the dynamics of the "state of mind" of each patient may require longer scanning times.