Can Sliding-Window Analysis Map Time-Varying Connectivity? Validation Using Fear Conditioning Data.

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Background: Whether sliding-window analyses are truly able to capture functionally relevant time-varying FC is still a topic of debate. Here, we aimed to test whether fluctuations in amygdala FC during a well-established fear conditioning paradigm, using sliding-window analysis, can be related to changes in physiological arousal and vigilance induced by the task, as assessed by the level of skin conductance.

Methods: Fear conditioning fMRI data (413 volumes; TR=1960ms) from 32 healthy participants were preprocessed and cleaned from noise sources identified with ICA. Time-varying FC was assessed for the amygdala: fMRI data sets and amygdala time series were partitioned into windows with a length of 39.2s (i.e., 20 volumes). Four different overlaps between adjacent windows (98%, 50%, 25%, and 0%) were tested to assess the influence of the amount of window overlap on the results. Next, amygdala FC was determined for each window by regressing (using the GLM) the amygdala time series against the time series of all other voxels. FC maps of all windows were then concatenated to a single 4D connectivity data set. Simultaneously acquired skin conductance level (SCL) time series were resampled to match the TR of the fMRI data, and subsequently averaged over frames that corresponded to the windowed time series of amygdala FC. Next, associations between SCL and amygdala FC changes over time were assessed using the GLM, and tested across the group using non-parametric statistics. Lastly, we performed a PPI, which is the conventional method to study connectivity changes over time when changes in physiology (or task conditions) are known.

Results: Using sliding-window analysis with 98% overlap of the consecutive windows, we identified a set of regions commonly termed the salience network, spanning the bilateral insula and medial prefrontal cortex, which became more strongly coupled with the left amygdala during states of increased SCL. We did not find corresponding results for the right amygdala. Interestingly, analysis of different window overlaps yielded fairly comparable results. Lastly, the PPI analysis demonstrated a connectivity pattern similar to the sliding-window analysis, albeit only at a liberal, uncorrected threshold.

Conclusions: We demonstrate that FC fluctuations of the left amygdala with regions of the salience network are associated with transient changes in physiological arousal and vigilance, the latter likely induced by repetitive exposure to the unconditioned aversive stimuli (shocks). We conclude that sliding-window analysis may be a feasible method to capture transient and functionally relevant changes in FC. This is further corroborated by the results obtained with a standard PPI analysis.