Can sliding-window analysis map time-varying connectivity? Validation using fear conditioning data

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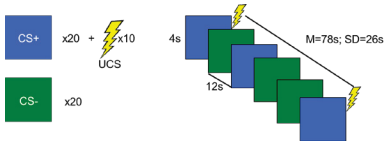
INTRODUCTION

- FMRI functional connectivity (FC) exhibits considerable fluctuations in its strength at the time-scales of seconds to minutes, as can be demonstrated using a sliding-window approach [1].
- Whether sliding-window analyses are truly able to capture functionally relevant time-varying FC is still a topic of debate [2].
- Previous studies evaluated the performance of sliding-window analysis with empirical data acquired under resting conditions, during which specific cognitive processes are hard to infer. To overcome this limitation, we applied the method to a well-described cognitive task.
- Sliding-window analysis was used to test whether fluctuations in amygdala FC during fear conditioning can be related to task-induced changes in physiological arousal, reflected in skin conductance level (SCL).

METHODS

- FMRI and skin conductance data from 32 healthy participants (*M*=26y/o) were acquired during a partial reinforcement learning paradigm [3,4] (Fig. 1).

FIGURE 1 Partial reinforcement learning paradigm.
Participants were exposed to a mildly painful laser shock to the foot, and to colored squares (blue and green), which served as aversive unconditioned stimulus (UCS) or conditioned stimuli (CS), respectively.



- **fMRI data acquisition (Philips 3T)**: 413 volumes, 39 axial slices, 3×3×2.4mm voxels, 0.6mm slice gap, TR=1960ms, TE=30, flip angle=80°
- **fMRI data preprocessing (FSL)**: motion correction, spatial smoothing (6mm FWHM), ICA-based noise removal (FSL MELODIC), high-pass temporal filter (>0.025Hz), normalization to MNI standard space.
- **Sliding-window connectivity**: fMRI datasets and amygdala time series were windowed to 39.2s segments (20 volumes); 98%, 50%, 25%, and 0% overlaps between windows were explored; seed-based whole-brain FC was assessed per window, and for the left and right amygdala separately.
- **Skin conductance level (SCL)**: data were resampled to match the TR of the fMRI scan, averaged within the same windows as the fMRI data, and regressed to the amygdala sliding-window connectivity (Fig. 2).

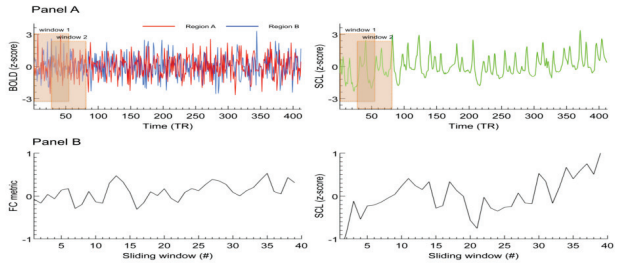


FIGURE 2 Evaluating the temporal association between sliding-window connectivity and SCL fluctuations.

- **Group level analysis**: non-parametric one-sample *t*-test (5000 permutations, *FSL randomise*), *p*<.05, TFCE corrected for multiple comparisons [5] (Fig. 3).
- **Results were validated by**: 1) testing against surrogate data [6] (Fig. 4), 2) assessing different window overlaps (Fig. 5), and 3) comparing them to the results of a physio-physiological interaction (PPI), a more commonly used method to assess task-related connectivity dynamics (Fig. 6).

REFERENCES

[1] Allen, E.A. *et al.* (2014). *Cerebral Cortex*, vol. 24, no. 3, pp. 663-676; [2] Hutchison, R.M. *et al.* (2013). *NeuroImage*, vol. 80, no. 1, pp. 360-378; [3] Bilkei-Gorzo, A. *et al.* (2012). *Journal of Neuroscience*, vol. 32, no. 27, pp. 9335-9343; [4] Phelps, E.A. *et al.* (2004). *Neuron*, vol. 43, no. 6, pp. 897-905; [5] Smith, S.M. & Nichols, T.E. (2009). *NeuroImage*, vol. 44, no. 1, pp. 83-98; [6] Hindriks *et al.* (2016). *Neuroimage*, vol. 127, pp. 242-256.

RESULTS

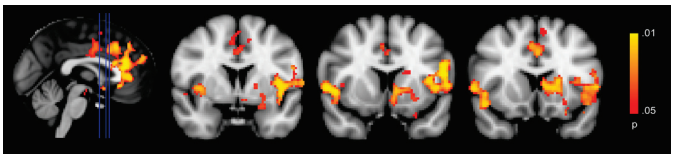


FIGURE 3 Sliding-window connectivity results.
Regions for which temporal fluctuations in FC of the left amygdala obtained with the sliding-window analysis (windows of 98% overlap) showed a positive association with fluctuations in SCL (*p*<.05, TFCE corrected).

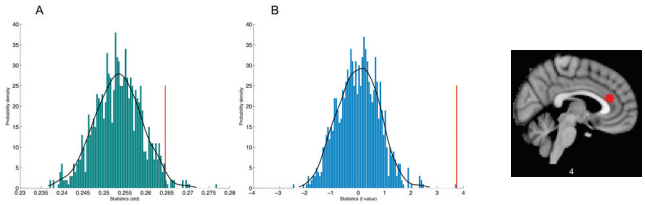


FIGURE 4 Null distributions of surrogate sliding-window functional connectivity.
A) Null distribution of standard deviations (averaged across the group) of surrogate sliding-window FC, computed between 1000 phase-shifted time series of the left amygdala and dorsal ACC, where we found the strongest association with SCL. The observed (true) value was 0.265 (*p*=.024), marked by the vertical red line.
B) Null distribution of surrogate temporal associations (one-sample *t*-test across the group) between SCL and 1000 phase-shifted left amygdala-dorsal ACC sliding-window connectivity time series. The observed (true) value was *t*=3.74 (*p*<.001), marked by the vertical red line.

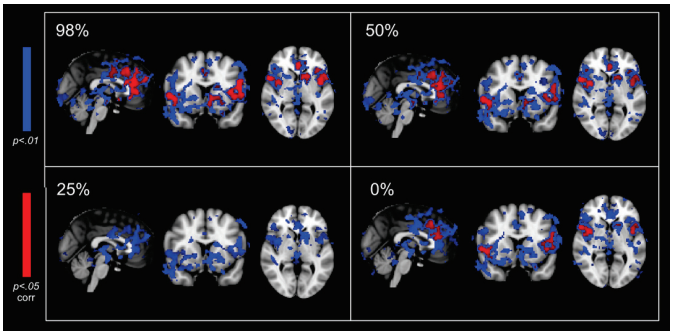


FIGURE 5 Effects of the window overlap in the sliding-window analysis.
Voxelwise TFCE maps are reported for corrected, *p*<.05 (red) and uncorrected, *p*<.01 (blue) thresholds.

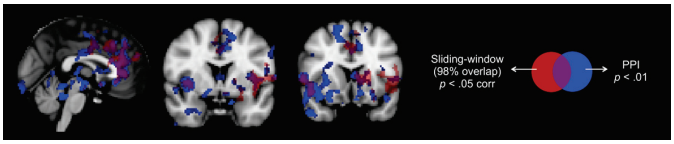


FIGURE 6 Temporal association between fluctuations in FC and SCL using sliding-window and physio-physiological interaction (PPI) analyses.

CONCLUSIONS

- During periods of increased SCL, the left amygdala became more strongly coupled with regions of the salience network, as revealed by the sliding-window analysis.
- The sliding-window analysis yielded a robust connectivity pattern that:
  1. is unlikely to have emerged by chance;
  2. was independent of window overlap;
  3. seemed more robust than PPI analysis.
- Sliding-window analysis may be a feasible method to track cognitively relevant changes in FC over time.

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