Magnitude of Task-induced Deactivation of Insula and Anterior Cingulate Cortex is related to Inter-individual Differences in RMSSD

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**Abstract**—By combining functional Magnetic Resonance Imaging and acquisition of cardiac pulsation during the execution of a cognitive task we identified areas where task-induced changes in brain activity correlated with individuals’ cardiac RMSSD. We show the existence of a relationship between task-induced deactivations and RMSSD.

I. INTRODUCTION

The relation between brain function, as measured by noninvasive functional Magnetic Resonance Imaging (fMRI) and physiological fluctuations is one of the most debated topics in the last decade [1]. We used fMRI and an inter-individual differences analysis to identify brain regions where the magnitude of task-induced changes in brain activity correlated with individuals’ RMSSD during task performance (brain/behavior correlations). We then determined whether these regions showed task-induced activation or deactivation. We found that brain regions demonstrating brain/behavior correlations, notably including the insula and anterior cingulate cortex, tended to be task-deactivated. Thus, the magnitude of deactivation in task-deactive regions partially reflects modulation of autonomic nervous system activity.

II. METHODS

Participants: 11 participants (7 males, mean age = 24.6 yrs, std = 3.5) took part in the study. Brain imaging acquisitions: 1 structural (MPRAGE) image was acquired (spatial resolution = 1 mm isotropic, 176 sagittal slices). One fMRI scan was acquired as well (115 scans / 253 sec, temporal resolution = 2.2 sec, spatial resolution = 3x3x3 mm, 0.45 mm slice spacing, 37 axial, parallel to AC - PC slices). During the fMRI session, participants engaged in a mental arithmetic Continuous Performance Task (CPT), which had a 4-cycle on/off structure (ABABABAB), where A = 10 sec rest period; B = 30 sec task period (B).

Cardiac data were recorded during the CPT using a photoplethysmograph placed on participants’ left forefinger (sampling frequency = 50 Hz). Cardiac data were evaluated manually and annotated to reflect correct R-R intervals. To define an autonomic index we first established the inter-beat interval (IBI) series in the task performance block (initial 30sec task block) and from the IBI series we derived a series reflecting the root mean square of subsequent differences (RMSSD, [2]) of the IBIs. This resulted in a single autonomic activity indicator for each participant. RMSSD indexes beat-to-beat variation and reflects a mainly vagal HRV component.

Neuroimaging analysis consisted of constructing two statistical parametric maps (SPMs) reflecting features of brain activity, and then relating the two maps. One SPM indicated task-related changes in brain activity. The other SPM was based on inter-individual differences, and identified brain regions where the magnitude of task-related activation correlated with participants’ RMSSD values.

1. Modeling: For each voxel (the 3mm³ fMRI spatial sampling unit), activation was defined as the correlation between the timeline of the study (i.e., the 30sec on / 10 seconds off cycle) and the voxel’s time series. This was done via a regression model: Voxel time series = β * study_timeline + ε. Here β is the regression slope.

2. Group level activation SPM: After obtaining the voxel’s β in step #1 for each participant, a voxel-wise one-sample T-test evaluated whether the mean β for the voxel, across participants, departed from chance; i.e., 0 (statistical significance set at p < .005, T(10) > 2.71). Family-Wise Error (FWE) control for multiple comparisons was implemented via cluster-wise thresholding [3], which identifies contiguous clusters of statistically significant voxels (FWE p < .05 using cluster extent). This defined, on a group-level, task-activated or task-deactivated clusters (see Fig. 1A), and constitutes a validity check for the study, as its results should replicate prior paradigms.

3. Group level correlation SPM: For each voxel, we calculated the correlation (Pearson’s R) between participants’ β values and their RMSSD during task performance (β:RMSSD correlation henceforth). FWE was implemented as described above (single voxel p < .005 uncorrected; FWE controlled using cluster extent, p < .05). This identified clusters where all voxels showed a significant β:RMSSD correlation (see Fig. 1B).

4. Finally, we treated each cluster in which the β:RMSSD correlation was significant (step #3) as a functional ‘region of interest’. For each region we determined if it was associated with task-related activation or deactivation, by calculating the mean β in the cluster per participant, and conducting a T-test against 0. This indicated which of the clusters that showed β:RMSSD correlations were also significantly task-activated or deactivated. This analysis returns a matrix that partitions clusters with β:RMSSD correlations into four types depending on whether the correlation was positive/negative and whether voxels in these clusters tended to be task-active or task-deactive (Fig. 1C).

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I. RESULTS AND CONCLUSIONS

Task related effects: task execution resulted in both task-induced activation and task-induced deactivation (Fig. 1A, warm and cool tones respectively). The distribution of reactive regions very well matched a cortical network termed the ‘default mode network’, thought to mediate intrinsic awareness and mind wandering [4]. Active areas matched prior reports of mental arithmetic [5], including areas involved in attention and verbal rehearsal (e.g., left inferior frontal gyrus).

Correlation with RMSSD: areas showing a correlation between task-induced effects and RMSSD included ones with either positive (Fig. 1B, warm tones) or negative (Fig. 1B, cool tones) correlations. Areas showing positive relations included motor cortex, STG, ACC, PCC and the insula (see Fig 1 for acronyms). Areas showing negative correlations included the anterior superior insula and calcarine sulcus. The results corroborate the insula’s involvement in autonomic processes [6], and its functional segregation into 3 areas [7]: posterior, anterior inferior and anterior superior, where the latter show a different relationship between task-related effects and autonomic activity indicative. We note that participants’ RMSSD measures collected during rest did not correlate with RMSSD during task execution, suggesting phasic task effects.

Cross-referencing the task-related and autonomic effects (Fig. 1A, 1B) classified areas as function of the sign of correlation with RMSSD (positive/negative) and whether they were task-active or task-deactive. Of the 38 clusters showing β:RMSSD correlations, 1 was significantly task-active, 11 were significantly task-deactive, and 22 did not fall into either category. Fig. 1C characterizes these clusters via a matrix: each point corresponds to a cluster extracted from the β:RMSSD SPM, which was task-active or task-deactive. The ordinate marks the mean β:RMSSD correlation in the cluster, and the abscissa marks whether the mean β in the cluster indicated task-induced activation or deactivation. The modal pattern in the identified clusters was one associated with positive β:RMSSD correlations, but task related deactivation, which notably held for the posterior and anterior left inferior insula, PCC, ACC and STG. One area, the calcarine sulcus, was an exception to this pattern, showing task-related activation and a negative β:RMSSD correlation.

Our findings show that inter-individual differences in RMSSD are linked to the degree of task-related deactivation of areas frequently associated with the regulation or monitoring of autonomic activity, including insula and ACC. Greater task-related deactivation was associated with lower RMSSD. This suggests that task execution might shape information processing in reactive areas: even if they are not directly involved in accomplishing external requests, they might be in charge of regulating with vagal fluctuations and maintain basic internal autonomic functions.

REFERENCES


Fig. 1. (A) Areas where performance of a mental arithmetic task caused task-related activation (warm tones) or deactivation (blue tones). (B) Areas where inter-individual differences in task-induced activation correlated with differences in RMSSD. (C) Characterization of clusters based on correlation and activation patterns (see text). Most of the areas (top left box) show task related-deactivation, and a positive correlation between activity values and RMSSD. “l” = left; “r” = right; “a” = anterior; “p” = posterior; ACC/PCC = anterior/posterior cingulate cortex; ITG/STG = inferior/superior temporal gyrus; SFG = superior frontal gyrus; CaG = Calcarine gyrus.