Sympathetic effects on the fMRI signal during a mental task

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Introduction

Recent studies have reported initial evidence for a novel source of fMRI signal attributed to systemic CNS vasoconstriction mediated by the sympathetic system. During both light sleep (Özbay et al. 2019b) and wake (Chang et al. 2019), strong correlations were observed between fMRI and peripheral vascular tone measured by photoplethysmography (PPG) from the fingertip. However, because of the close relationship between sympathetic activity and respiratory control, characterizing the unique contribution from sympathetic vasoaction (SV) while accounting for potential confounds from changes in CO[sub]2[/sub] is challenging (Ozbay et al. 2019a). To address this, we designed an fMRI experiment to induce involuntary sympathetic variations, without deep inspirations – to reduce the CO[sub]2[/sub] effect on fMRI signal during wakefulness using cognitive stress. We used both PPG (Özbay et al. 2018) and pupil dilations (Schneider et al. 2016) as indices of sympathetic activity.

Methods

Cognitive stress was elicited by a task requiring numerical summation (Fig. 1A). Two- or three-digit summation problems were periodically displayed against a grey background with fixation dot. This happened at specific times as 10, 50, 130, 170, etc., with successive 80 s and 40 s intervals. FMRI data were obtained at 7 T with gradient-echo-EPI (FA = 70^0, TR = 2 s, TE = 30 ms, isotropic resolution = 2 mm, number of TRs = 375, scan time = 12.5 minutes). Preprocessing of fMRI data followed the suggested 'afni_proc' pipeline (AFNI (Cox 1996)), including removal of signal drifts, slice-timing correction, realignment of consecutive volumes, registration to MNI template, smoothing (3 mm full width at half maximum) and regression of motion parameters while removing outliers (threshold = 0.2). PPG and respiratory signals were collected with a pulse oximeter attached to fingertip and respiratory bellows. PPG amplitude (PPG-AMP), as index of peripheral vascular volume (Özbay et al. 2018), and respiratory volumes per unit time (RVT) (Birn et al. 2006) were calculated. An MRI-compatible camera was used to track a subject's eye movement. Pupil diameters were recorded automatically as secondary measure of sympathetic activity. Data selection was based on high quality pulse oximeter and eye-tracker signals, and 8 subjects were included in the analyses.

As, jointly with SV, deep inspirations may be induced by the task, and both lead to fMRI signal drop, we excluded task segments with increased RVT (> 1 SD from the mean) from the data analysis. Averaged event locked signal analyses and voxel-wise correlations of PPG-AMP and pupil diameter with fMRI were performed across subjects.

Results

Our results demonstrate that SV through mental stress affects fMRI independent of deep inspirations (Fig. 1), as shown by PPG-AMP drops and pupil dilations. Timing and brain distribution of this effect is similar as observed previously (Özbay et al. 2019b). We should note that, variations in RVT in Fig. 1B occur at a later time point (~ 24 s) than observed effects on the

fMRI signals. Voxel wise correlations of fMRI with PPG-AMP and pupil diameter showed widespread patterns with grey matter (except for task related regions, e.g. intraparietal sulcus (IPS (Amalric and Dehaene 2016))) and opposing white matter and CSF-filled/ventricular contrast (Fig. 2), similar to previous work (Birn et al. 2006, Özbay et al. 2018, 2019b).

Conclusions

Our results show evidence of a sympathetic contribution to the fMRI signal during a mental task. The negative fMRI signal changes and their covariance with finger skin vascular tone and pupil diameter are observed regardless of deep inhalations. The delayed negative signal change in cortex is similar to previous observations with deep breathing (Birn et al. 2006, Bright et al. 2014). This suggests that the global signal changes may not be purely caused by respiratory (e.g. CO[sub]2[/sub]) changes. This further supports the notion that measures of PPG-AMP and pupil diameter can be used as regressors to improve the interpretation of fMRI studies.

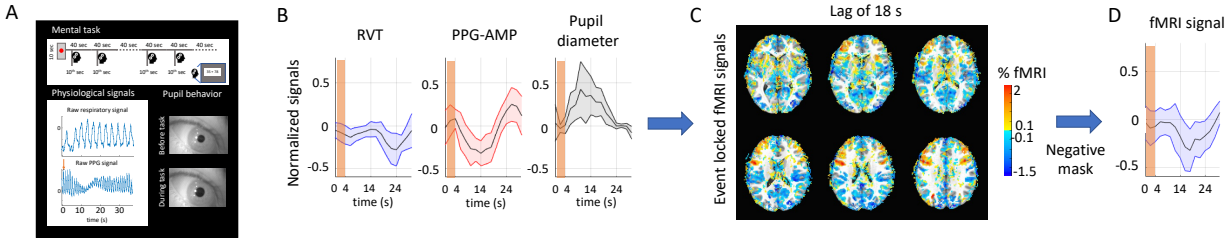

Figure 1: (A) Illustration of mental experiment, with exemplary physiological signals and pupil diameter variations before and during task. Arrow indicates timing of the task. (B) Physiological signals and pupil size changes during events of stable/reduced RVT (events = 40). Shaded orange shapes indicate timing of summation task. (C) Averaged event locked fMRI signals at a lag of 18 s with respect to task presentation. (D) Averaged fMRI signal variations within a grey matter mask based on negative voxels in (C). RVT: respiratory volume per time, PPG-AMP: PPG amplitude.

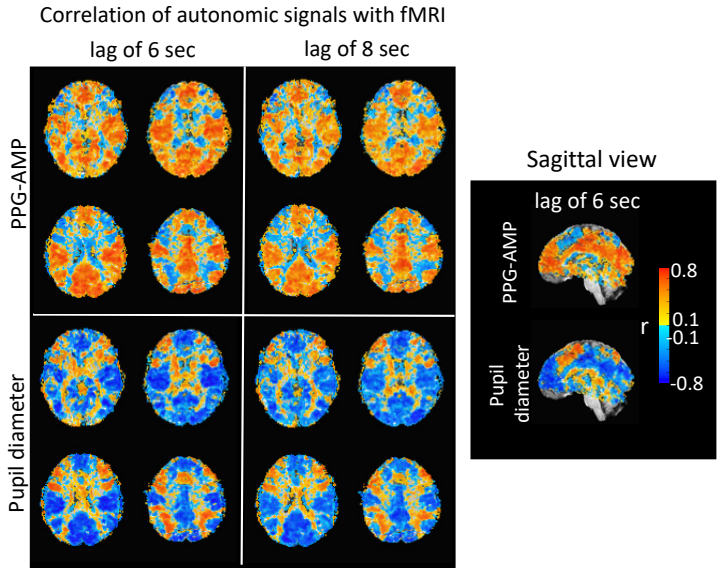

Figure 2: Lagged voxel-wise mean correlations of PPG amplitude (PPG-AMP) and pupil diameter with fMRI during events in Fig. 1B.

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