NeuroImage 171 (2018) 84–98

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Quenching of spontaneous fluctuations by attention in human visual cortex

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ARTICLE INFO

Keywords:
fMRI
Spontaneous fluctuations
Attention
Vision
Human

ABSTRACT

In the absence of a task, the human brain enters a mode of slow spontaneous fluctuations. A fundamental, unresolved question is whether these fluctuations are ongoing and thus persist during task engagement, or alternatively, are quenched and replaced by task-related activations. Here, we examined this issue in the human visual cortex, using fMRI. Participants were asked to either perform a recognition task of randomly appearing face and non-face targets (attended condition) or watch them passively (unattended condition). Importantly, in approximately half of the trials, all sensory stimuli were absent. Our results show that even in the absence of stimuli, spontaneous fluctuations were suppressed by attention. The effect occurred in early visual cortex as well as in fronto-parietal attention network regions. During unattended trials, the activity fluctuations were negatively linked to pupil diameter, arguing against attentional fluctuations as underlying the effect. The results demonstrate that spontaneous fluctuations do not remain unchanged with task performance, but are rather modulated according to behavioral and cognitive demands.

Introduction

In the absence of a sensory stimulus or task, the cerebral cortex exhibits slow fluctuations in activity that are highly consistent and ubiquitous. This activity, termed spontaneous fluctuations (also referred to as "resting state fluctuations") has been observed across all cortical networks (Biswal et al., 1995; Raichle et al., 2001; Greicius et al., 2003; Fransson, 2005; Nir et al., 2006; Fox and Raichle, 2007). These fluctuations have been observed in humans across a wide range of recording methods, from fMRI (Biswal et al., 1995; Fox and Raichle, 2007), EEG (Schurger et al., 2015; Arazi et al., 2017) to intra-cranial and even single unit recordings (He et al., 2008; Nir et al., 2008). The phenomenon has also been observed across different mammalian species, starting with pioneering work in anesthetized cats (Arieli et al., 1996; Kenet et al., 2003), and more recently in primates (Vincent et al., 2007; Shmuel and Leopold, 2008) and rodents (Koukouli et al., 2016). These intrinsic fluctuations are of great interest since spatially coherent patterns of these fluctuations have been linked to task related activity patterns (Smith et al., 2009; Tavor et al., 2016; Arazi et al., 2017) and to clinical conditions (Tian et al., 2006; Wang et al., 2006; Agosta et al., 2012; Hahamy et al., 2015; Drysdale et al., 2017). This led to the suggestion that spontaneous activity patterns may be linked to individual characteristics, habits and personality traits (Gilaie-Dotan et al., 2013; Harmelech and Malach, 2013; Hahamy et al., 2017).

A fundamental question concerns the potential functional role of the spontaneous fluctuations. While a number of studies have uncovered a link between human behavior and spontaneous fluctuations (Hesselmann et al., 2008; Sadaghiani et al., 2009; Ramot et al., 2011; Schurger et al., 2015; Yellin et al., 2015), the precise function of these fluctuations remains enigmatic. We have recently proposed, expanding on Schurger et al. (2012), that these intrinsic fluctuations may play a role in driving spontaneous behaviors (Moutard et al., 2015).

A related question, which is the central aim of the present study, is whether spontaneous fluctuations are ongoing and persist during task modes as well as during rest, or not. One possibility proposes that spontaneous fluctuations continue during task performance, such that task-activations interact with these fluctuations, for example by linearly summating or "riding on top" of them (ongoing model). An alternative model suggests that whenever a cortical network enters into a task mode, spontaneous fluctuations are down-regulated, essentially being replaced by task related activity (a "rheostat" model).

Fig. 1 illustrates these two alternatives in a schematic form. It depicts the slow spontaneous fluctuations with the task responses superimposed on them, as suggested by the ongoing model, as compared to a task-mode and response replacing the slow fluctuations, as proposed by the rheostat model. As shown in the figure, a testable measure that can contribute to

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https://doi.org/10.1016/j.neuroimage.2017.12.089
Received 18 September 2017; Received in revised form 26 November 2017; Accepted 27 December 2017
Available online 30 December 2017

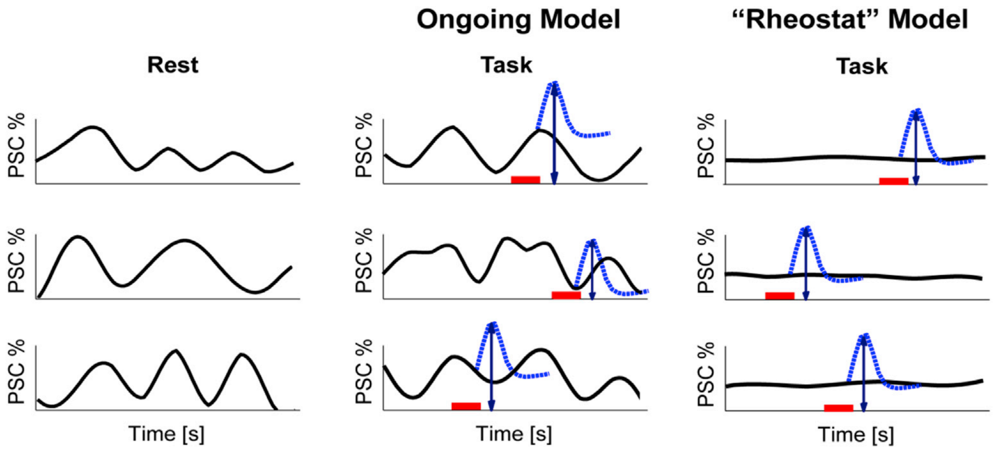

Fig. 1. A schematic illustration of spontaneous fluctuations during rest and during task mode, depicting the two alternative models: The ongoing model, that suggests the intrinsic fluctuations continue during task mode, while task related activations interact with them; and the "rheostat" model, that claims that during task mode the spontaneous fluctuations are down-regulated and replaced by the task related activity. Black lines denote the ongoing or baseline activity. The red line represents the onset of a task related stimulus or other external requirements. The dotted blue line represents the constant task-related response, while the arrow depicts the resulting peak response amplitude. The figure demonstrates that while the mean response amplitude might be equal in both cases, the trial-to-trial response variability is necessarily smaller for the rheostat model, as compared to the ongoing model.

differentiating between these alternatives can be obtained by comparing trial-to-trial response variability between the task and no-task conditions.

Indeed a number of studies have conducted such a comparison. However, the results are so far inconsistent. Examining task related responses in area V1 of anesthetized cats (Arieli et al., 1996) proposed a linear summation of intrinsic activity and task responses, albeit at a short time scale of tens of milliseconds. Yet more recently, Churchland et al. have presented converging evidence from primates showing that response variability is actually quenched upon stimulus onset as compared to pre-stimulus variability, suggesting that the spontaneous fluctuations may be suppressed during sensory processing (Churchland et al., 2010). Moreover, studies using electrophysiological recordings in behaving primates during visual attention tasks have demonstrated that trial-to-trial variability as well as noise correlations are further reduced if the stimuli presented are behaviorally relevant or overtly attended, suggesting that attention down-regulates ongoing fluctuations (Mitchell et al., 2007, 2009; Cohen and Maunsell, 2009; Mitchell et al., 2009; Hussar and Pasternak, 2010). Similarly, human studies have also shown mixed results. In a human fMRI study, Fox et al. argued for summation of spontaneous fluctuations and task activation in motor cortex (Fox et al., 2006, 2007), while EEG studies have shown reduced trial-to-trial variability upon stimulus onset, and further linked this quenching with task performance (Schurger et al., 2015; Arazi et al., 2017). Finally, in an fMRI study, trial-to-trial variability was found to be reduced across extensive brain regions upon stimuli presentation and motor response initiation (He, 2013). He proposed a model in which stimulus activations actively cancel out the ongoing activity.

One complication that may explain this diversity of results is that the stimulus evoked response activations themselves may mask or non-linearly summate with the underlying spontaneous fluctuations. A previous study in primates has taken a step in clarifying this issue, showing that single neurons in the prefrontal cortex maintain the decrease in trial-to-trial variability during 1.5 s delay periods after stimuli presentation in the context of a working memory task, as compared with the same delay periods during a passive viewing mode (Hussar and Pasternak, 2010). However, in order to evaluate whether the relevant cortical networks are modulated upon entering a task-related mode, so as to quench the spontaneous fluctuations, it is necessary to manipulate the task related mode in the absence of the confounding task responses.

Another major methodological difficulty associated with studying spontaneous fluctuations is the inherent difficulty in assessing the cognitive processes during resting state. This is due to the essential inability to obtain on-line behavioral reports from the participants while maintaining the resting condition. However, we have recently proposed an indirect mean to circumvent this difficulty using the pupil diameter as an objective estimator of cognitive load and attentional engagement (Yellin et al., 2015). Here we took advantage of this approach by using an MR-compatible eye-tracker to follow pupil diameter, which allowed assessment of relative attentional engagements and fluctuations during the resting state.

In the present study we examined a pure attentional effect on intrinsic fluctuations in humans during relatively long time periods (12 s), free from possible carryover confounds of task related stimuli processing or working memory computations, by creating an experimental design that manipulated participants' attention per se. The participants were instructed to attend and prepare to respond to visual targets that could appear at any time point during the trial, including very late stages. Therefore, to ensure their optimal task performance, subjects had to maintain sustained attention throughout the entire attended trials. Importantly, we randomly omitted in approximately half of the trials the expected targets. Thus, participants attended a blank field, expecting the appearance of a target to be recognized. By contrasting these blank trials with similar ones in which the participants were instructed to passively watch the screen, we were able to compare the signal variability under task and no task conditions in the absence of a confounding target response.

Our results show a significant suppression of trial-to-trial variability when participants attended the blank fields compared to when they passively observed them, suggesting an inhibition of intrinsic fluctuations. The intrinsic activity fluctuations were negatively coupled to pupil diameter, thus arguing against fluctuations in visual attention as the source of the variability. These results support a model in which the level of spontaneous fluctuations is under cortical control and can be suppressed according to task demands.

Materials and methods

Subjects

20 healthy, right-handed participants (mean age = 28.4, SD = 3.18, 10 females) participated in the experiment. One participant was excluded due to excessive movements. All participants had normal vision, provided written consent, and were paid for their participation in the study. All procedures were approved by the local ethics committee.

MRI setup

The scans were acquired on a 3 T TrioMRI Siemens scanner equipped