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Research report

# Task-positive and task-negative networks and their relation to depression: EEG beamformer analysis

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## HIGHLIGHTS

- Depression is associated with predominance of DMN over task-positive network (TPN).
- This evidence has been obtained using fMRI in patients.
- Here we used seed-based EEG oscillatory-power envelope correlation analysis.
- Depressive symptoms were associated with predominance of DMN over TPN.
- Implicated in depression mechanism may be in action even at preclinical stages.

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## ABSTRACT

Major Depressive Disorder (MDD) has been associated with predominance of the default-mode network (DMN) over the task-positive network (TPN), which is considered a neurobiological base for ruminative responding. It is not known whether this predominance is a signature of the full-blown MDD or it already exists at preclinical stages. Besides, all relevant evidence has been obtained using fMRI, which allows for a precise spatial characterization of resting state networks (RSNs), but their neural correlates remain elusive. Here we show that after leakage correction of beamformer-projected resting EEG time series, seed-based oscillatory-power envelope correlation analysis allows revealing RSNs with significant similarity to respective fMRI RSNs. In a non-clinical sample, depressive symptoms, as measured by the Beck Depression Inventory, are associated with predominance of DMN over TPN connectivity in the right insula and the right temporal lobe in the delta frequency band. These findings imply that in individuals with heightened level of depressive symptoms, emotional circuits are stronger connected with DMN than TPN and should be more easily engaged in self-referential rumination than in responding to environmental challenges. The study's findings are in agreement with fMRI evidence, thus confirming the neural base of the observed in fMRI research effects and showing that implicated in depression neural mechanism may already be in action even at preclinical stages.



## 1. Introduction

Depression is one of the most common psychiatric diseases. According to WHO [1], over 350 million people suffer from depression and it rates the first among all diseases by the number of years lived with disability. Diagnosed depression is just a part of depressive disorders, which exist in the population [2]. Surveys show that considerable number of people with depressive symptoms do not seek professional help [3,4]. However, the first depressive episode significantly increases the likelihood of subsequent clinical depression. Therefore, revealing depressive symptoms-related changes at preclinical stages is a matter of great importance. Many studies investigated depression-related changes in brain activity. Functional magnetic resonance imaging (fMRI) revealed modifications in functioning of frontal and temporal brain areas [5–8].

In recent years, interest has grown in the study of connectivity in the absence of a task. It has been shown that during the 'resting state', blood-oxygenation-level-dependent (BOLD) fMRI signals of spatially separate brain regions are correlated in time, forming the so-called resting state networks (RSNs) [9–12]. Parallel studies, which investigated co-activation patterns in different kinds of

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tasks, have revealed functional networks that are very similar in their spatial distribution to the RSNs derived from connectivity analysis in a resting state. Some of these networks exhibit activity increases during attention tasks (task-positive networks, TPNs), whereas others show activity decreases (task-negative networks) [13]. It is not definitely clear whether and how brain networks measured during the resting-state exhibit comparable properties to brain networks during task performance. Meta-analytic comparison of the co-activation network configurations with those in the resting-state network showed that in spite of some reconfiguration between task and resting-state conditions, the strength of resting-state functional connectivity between two regions is strongly correlated with the co-activation strength, thus giving rise to great similarity between functional networks and the RSNs in their spatial distribution [14]. Similar conclusion was reached by Smith et al. [15] who compared thousands of activation maps derived from the BrainMap database of functional imaging studies with the major co-varying networks in the resting brain.

The TPNs include (among others) the fronto-parietal attention system implicated in directed attention and working memory [16]. The task negative network is referred to as the 'default mode network' (DMN) and has been implicated in self-referential processing and social cognition [17,18]. Altered functional connectivity has been found in MDD patients in both the DMN and the TPNs [19,20]. Increased connectivity within the DMN during rest was interpreted as a sign of increased self-referential thoughts [21–26]. Hamilton and colleagues [23] found that increased dominance of DMN over TPN is associated with the severity of self-focused rumination in depressive patients. In most of these studies, MDD patients were investigated in the course of their treatment and few studies have investigated the DMN in depressed patients before significant use of medications [27]. There are also few studies, which investigated the association between RSNs connectivity and depressive symptoms in the general population [28].

The majority of research in this area has been conducted using fMRI. However, it is not definitely clear how the BOLD signal relates to neuronal events [29]. Therefore, a reproduction of fMRI findings in electrophysiological domain is vitally important. Several magnetoencephalographic (MEG) studies using seed-based oscillatory power envelope correlation or independent component analysis (ICA) in conjunction with beamformer source localization found RSNs similar to that described in fMRI research [30–40]. Some of these studies investigated RSNs in a resting state [31,33,34,36,37,40], while others focused on the effect of tasks [32,38,39]. Some performed sensor-level analysis [37], whereas others used different methods of source imaging, such as the linearly constrained minimum-variance (LCMV) beamformer [31,32,36,38] and minimum norm estimate [33,34,40]. One recent study applied the ICA resting state MEG method to compare RSNs in healthy participants and MDD patients [41]. In the latter study, analysis was limited to the beta frequency band and it showed that MDD patients had decreased connectivity between motor cortex and subgenual cingulate, whereas increased connectivity was seen between temporal regions and amygdala. To our knowledge, there are no published EEG studies, which had successfully applied the same combination of methods to reveal RSNs.

In this study, we had two aims. Firstly, we aimed to test whether application of the seed-based oscillatory-power envelope correlation analysis in conjunction with beamformer spatial filtering to EEG data allows revealing RSNs' topography as it is described in fMRI research. Secondly, we aimed to investigate the relationship between depressive symptoms, as measured in a non-clinical sample by means of self-report questionnaire, and connectivity patterns emerging from seed-based oscillatory-power envelope correlation analysis. Particularly, we sought to test whether depressive symptoms in clinically healthy individuals are associated with increased dominance of DMN over TPN during rest. We expected that DMN spatial pattern could be most convincingly revealed in the alpha frequency band, because association of alpha oscillations with DMN activity has been repeatedly shown using different methods [31,42–46]. On the other hand, we expected to find depressive symptoms-related effects in low (delta and theta) frequency bands, because much evidence points at these oscillations as a correlate of emotion and motivation processes [47,48]. Specifically, existing evidence shows that delta activity, which mostly originates from the medial and orbital frontal cortical regions (the principal cortical sites receiving dopaminergic input) [49], increases when this area receives less dopaminergic firing [47,50]. A striking aspect of depression is a marked diminishment of motivation [51], mostly due to decreased functioning of the dopaminergic reward system [52,53]. Hence, increase of delta power in these individuals is to be expected and is indeed well documented [54–57]. Moreover, delta activity in the rostral anterior cingulate cortex (ACC) correlated negatively with the nucleus accumbens responses to reward and was positively associated with anhedonia scores [57]. Increased theta and delta power have been associated with poor antidepressant treatment response in patients with depression [58]. Pizzagalli et al. [59] have shown that melancholia, a subtype of depression characterized by anhedonia, was associated with increased delta activity in the subgenual prefrontal cortex. Following antidepressant treatment, depressed subjects with the largest reductions in depression severity showed the lowest post-treatment subgenual prefrontal cortex delta activity [59]. One study showed that when subjects expected bad news, delta power and connectivity increased in a network of cortical areas, which included the orbitofrontal cortex and the ACC as its main node [60].

However, we did not a priori exclude a possibility that significant effects will be found in other frequency bands. Thus, the dominant framework in the EEG studies of affective disorders has been the research on hemispheric asymmetry, which suggests that a relative prevalence of left prefrontal activation is associated with positive affect, while prevalence of right prefrontal activation is associated with negative affect, including depression [61–63]. Activation in these studies is usually conceptualized as diminished power in the alpha frequency band. Another line of research on EEG correlates of depression is application of cordance, an index, which combines complementary information from absolute and relative power of EEG spectra [64]. Recent studies have focused on EEG cordance in the theta frequency band at pre-frontal electrodes and have essentially found that a decrease in theta cordance after antidepressant medication predicted longer-term treatment outcome [65–67]. Increased functional connectivity in theta and alpha frequency bands has been observed in MDD patients [68,69]. The only published study, which attempted to reveal depression-related changes in RSNs connectivity in electrophysiological domain, found significant effect in the beta frequency band [41]. Effect of depression on gamma oscillations has also been found in some experimental paradigms [70,71].

## 2. Methods

### 2.1. Participants

The EEG sample included 55 right-handed volunteers (19 men; mean age = 22, $SD$ = 3.5), who were a part of a larger sample (N = 224, 60 men; mean age = 25, $SD$ = 8) of participants who underwent psychometric evaluation. They were graduate and postgraduate students and staff members of Novosibirsk State University and Institute of Physiology and Basic Medicine. Participants were selected for the study based on preliminary interview with a certified clinical psychologist. Exclusion criteria were a history of