Spectral dynamic causal modeling of mindfulness, mind-wandering, and resting-state in the triple network using fMRI

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Objective Functional connectivity in intrinsic brain networks, namely, the triple network, which includes the salience network, default mode network (DMN) and central executive network (CEN), has been suggested as prominent, major networks involved in human cognition and mental state–mindfulness, mind-wandering and resting-state. Despite the established roles of functional connections within and between intrinsic networks, there has been limited research on the effective connectivity of mindfulness, mind-wandering and resting-state using the triple network, as well as on their direct comparisons.

Methods We employed spectral dynamic causal modeling to compare effective connectivity patterns across mindfulness (i.e. attention focused on physical sensations of breathing), mind-wandering (i.e. connecting thoughts) and resting-state (i.e. relaxing while remaining calm and awake) conditions using functional MRI data of healthy subjects who underwent ambulatory training by practicing mindfulness and mind-wandering ($N = 59$).

Results When comparing mindfulness and mindwandering conditions, our analysis results revealed that salience network and CEN interacted depending on mindfulness or mind-wandering. When mindfulness or mind-wandering was compared to resting-state, mindfulness increased the effective connectivity from the left CEN to salience network through DMN, whereas mindwandering increased the effective connectivity from the DMN to right CEN.

Conclusion To the best of our knowledge, this is the first study to examine possible differences in effective connectivity patterns among mindfulness, mind-wandering and resting-state using the triple network. We believe that our findings will provide deeper insights into the neural substrates of mindfulness compared to mind-wandering and resting-state. *NeuroReport* 33: 221–226 Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.

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Keywords: central executive network, default mode network, dynamic causal modeling, effective connectivity, fMRI, mindfulness, mind-wandering, resting-state, salience network, triple network

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Introduction

The triple network, which includes the central executive network (CEN), the default mode network (DMN) and the salience network, have gained attention as prominent, major intrinsic connectivity networks in the human brain [1]. Numerous neuroimaging studies of functional MRI (fMRI) revealed that disrupted interactions within and between three core networks represent significant characteristics of neurologic and neuropsychiatric disorders, such as Alzheimer's disorder and schizophrenia [2,3]. More specifically, the CEN, which includes the dorsolateral frontoparietal cortex, is a critical region in the function of goal-oriented cognition [4,5]. In contrast, the DMN, anchored in the posterior cingulate cortex (PCC), medial prefrontal cortex (MPFC) and the angular gyrus, is involved in self-referential perception [5]. Meanwhile, the salience network, including the dorsal anterior cingulate cortex (dACC) and anterior insula, is known as the hub network of interoceptive perception [6] and for a central, causal role in switching between DMN and CEN [5].

According to recent fMRI studies, changes in functional connectivity between and within the triple network are represented as the underlying functional features of mindfulness, mind-wandering and resting-state [1,7,8]. Mindfulness is frequently described as an awareness of present-moment experience that focuses on sensory input, including interception, and is associated with self-reflective processing and evaluation, which contributes to improved cognitive performance and mental health [9,10]. Mind-wandering is associated with self-referential processing and is frequently defined as shifting attention from the present environment without conscious intention; this contributes to negative effects on primary task performance [8,11]. Unfortunately, such contrastive descriptions do not allow us to determine similarities between the two mental states [12], although subtle reflection on mindfulness, particularly in the aspect of open-mind mediation [7], which has demonstrated its similarities with mind-wandering, involves attentional engagement to mental objects [12]. Resting state has been widely employed as a task contrast and the intrinsic baseline mental state [13]. There is increasing evidence that spontaneous thoughts associated with mind-wandering may influence resting-state fMRI data [14]. Despite the interchangeability among the three mental states, there has been little research on their functional associations with the triple network in the context of effective connectivity.

Therefore, in this study, the effective connectivity of mindfulness (i.e. attention focused on physical sensations of breathing), mind-wandering (i.e. connecting thoughts) and resting state (i.e. relaxing while remaining calm and awake) were investigated using the triple network, and their possible differences were evaluated. To accomplish this, we obtained fMRI data from healthy participants during mindfulness, mind-wandering and resting state. Independent component analysis (ICA) was performed using fMRI data to identify subject-specific triple networks. Furthermore, we conducted spectral dynamic causal modeling (spDCM) to estimate the effective connectivity of the triple network, and statistical analysis was performed to evaluate differences in effective connectivity among mindfulness, mind-wandering and resting state.

Methods

Overall study protocol

Data collection was conducted within a randomized controlled trial registered at ClinicalTrials.gov (NCT03148678; https://clinicaltrials.gov/ct2/show/NCT03148678). The Institutional Review Board of Korea University approved this study. All volunteers for brain imaging acquisition were recruited and screened from Korea University.

Participants

Sixty right-handed, healthy volunteers (all males, no history of neurologic and neuropsychiatric disorders, age = 25.1 ± 2.9 years, mean ± SD) participated in this study and provided written informed consent after undergoing telephone and face-to-face interviews. All participants performed ambulatory training sessions via their smartphones for 10 consecutive days (mindfulness for 5 days and mind-wandering for 5 days in a counter-balanced order; detailed instructions can be found in our earlier report [15]). Sociodemographic information and psychologic traits of the participants are summarized in Table 1.

Table 1 Sociodemographic information and psychologic traits of the participants included in the analyses. All participants were meditation naïve and performed smart-phone ambulatory training by practicing mindfulness and mind-wandering for 5 days each prior to MRI experiments

Categorical variables	Category	Total (*n*)
Marital status	Single/in a relationship	53/7
Highest degree	High school diploma or equivalent degree	48
	Bachelor's degree/master's degree	10/2
Size of household	1/2/3/4/5	6/0/7/38/9
Continuous variables measured on the interview day		Mean ± SD
Age (years)/full time education (years)		25.1 ± 2.9/14.8 ± 1.6
EHI/PHQ-9/PSS		95.0 ± 6.1/2.0 ± 1.5/13.9 ± 4.1
BFI-10	Extraversion/agreeableness/conscientiousness	3.3 ± 1.0/3.3 ± 0.8/3.1 ± 0.8
	Neuroticism/openness to experience	3.1 ± 0.9/3.6 ± 0.8
Continuous variables measured on the first MRI experiment day		Mean ± SD
MAAS/VAS		4.4 ± 0.6/3.7 ± 1.9
Cognitive task performance prior to MRI experiment		Mean ± SD (%)
Emotion recognition/3-back/Wisconsin Card Sorting Test		68.1 ± 2.1/69.9 ± 1.1/93.5 ± 1.1

Relevant references can be found in our earlier report [15].
BFI, big five inventory; EHI, Edinburg handedness inventory; MAAS, Mindful Attention Awareness Scale; PHQ, Patient Health Questionnaire; PSS, Perceived Stress Scale; VAS, Visual Analog Scale for stress perception (0, not stressed at all; 10, extremely stressed).

MRI sessions

After completing the ambulatory training sessions, participants performed an MRI session with a 3-T Siemens Tim-Trio scanner (Erlangen, Germany). In the MRI session, participants conducted three 3-min cognitive tasks – 3-back, facial emotion recognition, and the Wisconsin Card Sorting Test [15]. The first blood-oxygenation-level dependent (BOLD) fMRI run consisted of three 3-min blocks of mindfulness followed by one of the three cognitive tasks. A 3-min resting-state block was also pseudorandomly performed after one of the cognitive tasks was completed. In the next fMRI run, mind-wandering was performed instead of mindfulness, and otherwise was the same as the first run. After completing the mindfulness and mind-wandering blocks, the short version of the state mindfulness scale (SMS) [15] and task-performance feedback (TPF) ratings were collected. Across all subjects, the sequence of the two fMRI runs (i.e. mindfulness or mind-wandering) and three cognitive tasks were randomized and counterbalanced using the MATLAB built-in function 'randperm'. All subjects were asked to conduct each of the three mental states while watching corresponding instructions that were presented on the screen during MRI scanning. The mindfulness instruction was 'Please pay attention to the physical sensation of your breath wherever you feel it most strongly in your body', whereas the mind-wandering instruction was 'Please think about whatever comes to mind and go wherever your mind takes you'. The resting-state instruction was 'Please relax and lie still in the scanner while remaining calm and awake'. Detailed instructions can be found in our earlier report (Table 1 in [15]).

Data preprocessing

Analysis of functional neuroimages software (afni.nimh.nih.gov/afni) was used to preprocess fMRI data obtained during two fMRI runs, including de-spiking, respiration and cardiac-induced noise correction using pulse oximeter signals, realignment, co-registration of fMRI volumes to an individual T1-weighted image, spatial normalization to Montreal Neurological Institute space, spatial smoothing with a full-width half-maximum size of 8 mm, de-trending, nuisance signal regression with 22 regressors (i.e. the first five principal components of the cerebral spinal fluid (CSF) and white matter signals, six motion parameters, and six first-order derivatives of the motion parameters) and scaling to the mean BOLD intensity of 100 in each voxel. A priori maps with a probability greater than 0.7 for the CSF and 0.9 for the white matter were used to extract the principal components of the BOLD signals in the CSF and white matter, respectively. We extracted three mindfulness blocks, three mind-wandering blocks and two resting-state blocks from each subject's two preprocessed fMRI run. Due to severe head motion during the MRI scans, one subject was ruled out for further investigation.

Identification of subject-specific spatial patterns of interest

The triple network was identified by spatial ICA using fMRI data, as implemented in the Group ICA for fMRI Toolbox (https://trendscenter.org/software/gift/). All segmented fMRI data were concatenated across subjects and used for the group-level ICA to estimate 20 independent components (ICs). We selected four spatial ICA maps (Table 2) as the triple network by matching existing templates [16]. For DMN (IC#17), we focused on four regions – the anterior MPFC, PCC, and the left and right angular gyrus. salience network (IC#35) comprised three regions – the dACC and the left and right anterior insula. CEN (IC#24 and #29) comprised four regions – the left/right inferior frontal gyrus and the left/right inferior parietal lobule. Subject-specific peak coordinates were identified as the peaks in subject-specific, back-reconstructed ICA maps within 8-mm radius spheres of the group-level peak coordinates (Fig. 1). Subsequently, the first principal eigenvariate was extracted from all voxels within 8-mm radius spheres of the subject-specific coordinates of each ICA map, and a total of four first principal eigenvariates were used to perform spDCM analysis [17].

Table 2 **Coordinates of the group-level spatial patterns of interest.**

Regions	MNI coordinates X	Y	Z	Network (IC#)
dACC	0	21	39	SN (35)
lAI	−36	15	6	SN (35)
rAI	42	18	3	SN (35)
PCC	0	−54	24	DMN (17)
aMPFC	0	60	18	DMN (17)
lAG	−54	−66	27	DMN (17)
rAG	57	−60	27	DMN (17)
lIFG	−51	18	36	CEN (29)
lIPL	−36	−60	45	CEN (29)
rIFG	51	18	39	CEN (24)
rIPL	48	−60	45	CEN (24)

AI, anterior insula; AG, angular gyrus; aMPFC, anterior medial prefrontal cortex; CEN, central executive network; dACC, dorsal anterior cingulate cortex; DMN, default mode network; IC, independent component analysis; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; l, left; MNI, Montreal Neurological Institute; PCC, posterior cingulate cortex; r, right; SN, salience network.

Spectral dynamic causal modeling

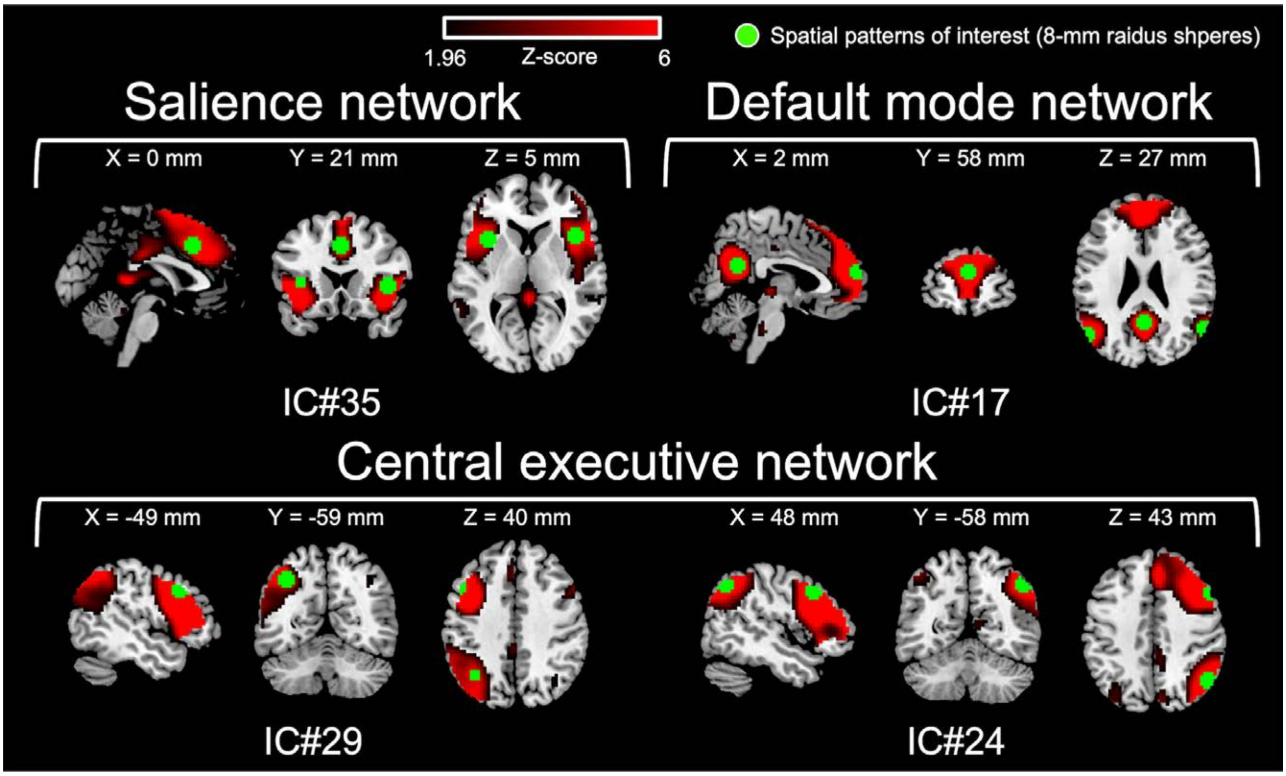
We conducted spDCM analysis using DCM 12.5 implemented in SPM12 (v7771, www.fil.ion.ucl.ac.kr/spm). A fully connected model was created to compare all possible models of the triple network (16 effective connections = 4 IC maps × 4 IC maps) [17]. Then, we estimated the effective connections (or parameters) in the spDCM framework using the complex cross-spectral density of spontaneous neuronal fluctuations in each subject and condition. Bayesian parameter averaging was performed to average the parameters across blocks of each condition. This Bayesian parameter average was used for the group-level analysis using Bayesian Model Reduction (BMR) and Parametric Empirical Bayes (PEB) [17]. To evaluate differences in effective connectivity among the three conditions, we designed parametric regressors (mindfulness vs. mind-wandering, mindfulness vs. resting state, and mind-wandering vs. resting state) in a one-way within-subject analysis-of-variance framework. Subsequently, parameters of each model (i.e. regressor) were estimated based on Bayesian model averaging to estimate connectivity changes. Significant connectivity was defined at a posterior probability of 95% (analogous to a one-tailed frequentist threshold of $P < 0.05$) as DCM analysis tested whether connectivity between two specific brain networks was enhanced based on mental states.

Results

Behavioral SMS scores (from one to nine) obtained in mindfulness were significantly greater than those obtained in mind-wandering (6.0 ± 1.3 in mindfulness; 4.9 ± 1.4 in mind-wandering; $P < 10^{-3}$); however, there was no significant difference in TPF scores between these states (6.3 ± 1.1 in mindfulness; 6.4 ± 1.1 in mind-wandering; $P = 0.44$). Although we did not collect these scores immediately after the resting-state block, in the debriefing session, none of the subjects reported difficulties in switching to resting state from either mindfulness or mind-wandering during experiments. These results may suggest that all subjects were able to switch between these states without any difficulties.

Figure 2 shows effective connectivity patterns across pairwise comparisons and effective connectivity matrices of the triple network after PEB estimation and BMR. As shown in Fig. 2a, connectivity from the left CEN (lCEN) to the right CEN (rCEN) through the salience network

Fig. 1



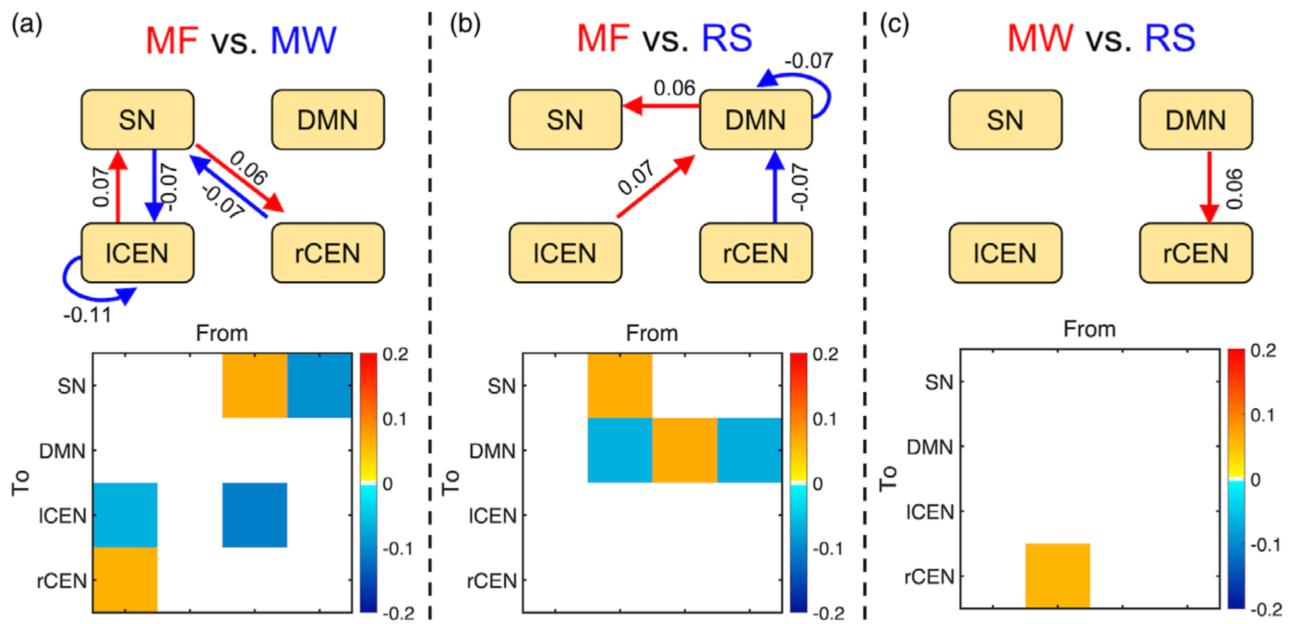
The triple network, including the salience network (SN), the default mode network (DMN) and the central executive network (CEN) is identified using group-level spatial independent component analysis (ICA) maps (z-score>1.96). The spatial patterns of interest are represented as green circles (i.e. 8-mm radius spheres) overlapped with the spatial ICA maps.

was enhanced in mindfulness, whereas connectivity from the rCEN to the lCEN through the salience network, as well as the self-connection of the lCEN, was enhanced in mind-wandering. In the comparison between mindfulness and resting-state, the connectivity from the lCEN to the salience network through the DMN was enhanced in mindfulness, whereas the connectivity from the rCEN to the DMN, as well as the self-connection within the DMN, were enhanced in resting state (Fig. 2b). In the comparison between mind-wandering and resting state, the connectivity from the DMN to the rCEN was enhanced only in mind-wandering (Fig. 2c).

Discussion

This study discovered enhanced effective connectivity from the lCEN to the rCEN through the salience network during mindfulness, whereas the reciprocal direction of this effective connectivity was enhanced in mind-wandering (Fig. 2a). These contrasting results, which had not previously been investigated, may indicate attentional dependence on either connecting thoughts or physical sensations of breathing. The state of focus (CEN-related) is a crucial skill taught in focused attention meditation [18]. Many previous studies have shown a relationship between mindfulness scores and functional connectivity of the lCEN and salience network, but not the rCEN [19,20]. A more recent study demonstrated that the insular region belonging to the salience network received signals from the lateral PFC (part of CEN), which allowed discriminating meditators from controls during mindfulness [21]. The right dorsolateral PFC (dlPFC; part of CEN) has been identified as the primary agent involved in the control of episodic retrieval, whereas the left dlPFC has been discovered as one of its key functions in modifying cognitive control functions [22]. Taken together, these results support our finding (Fig. 2a) that the lCEN implicated in a volitional focus of stable attention may elicit the salience network associated with visceromotor interoceptive perception and the rCEN associated with volitional focus management [4]. In contrast, the enhanced effective connectivity from the rCEN to the lCEN through the salience network in mind-wandering (Fig. 2a) may be due to mind-wandering instruction, which could dominantly exert internally oriented thoughts. A previous study revealed that the salience network automatically influences constrained thoughts by coupling with the CEN, whereas the CEN deliberately exerts constrained thoughts by coupling with the DMN and salience network [23]. In this regard, we propose that the rCEN is a

Fig. 2



The differences in effective connectivity among mindfulness (MF), mind-wandering (MW) and resting-state (RS), which were evaluated in a one-way within-subject analysis-of-variance framework (*N*=59). A schematic that summarizes the effective connectivity between a pair of conditions (top): (a) MF vs. MW, (b) MF vs. RS, (c) MW vs. RS, and effective connectivity matrices of the triple network after Bayesian Model Reduction (bottom). Red and blue arrows indicate connectivity enhancements in the corresponding conditions, respectively. The connections remained after pruning any connections that did not contribute to free energy (i.e. posterior probabilities with vs. without parameter are greater than 95%). CEN, central executive network; DMN, default mode network; lCEN, the left side of the CEN; rCEN, the right side of the CEN; SN, salience network.

core network associated with internally oriented mental processes for mind-wandering.

The connectivity between the salience network and DMN during mindfulness was increased in a group with short-term mindfulness training experience compared to a group without mindfulness training [24]. Furthermore, mindfulness training enhanced functional coupling between the left dlPFC (part of CEN) and DMN compared to that in resting state [25]. Therefore, the enhancement of the effective connectivity from the lCEN to the salience network through the DMN may indicate increased awareness of moment-to-moment input from somatic and sensory systems by conscious executive processing. In contrast, the self-connection in the DMN and connection from the rCEN to the DMN was enhanced in resting state, compared with that in mindfulness (Fig. 2b). Furthermore, the connection from the DMN to the rCEN was enhanced during mind-wandering, compared to that in resting state (Fig. 2c). These results may suggest that constrained thought processing may be involved when the brain is at the mental states of mind-wandering and resting state compared to mindfulness.

Although subjects performed each mental state while watching specific instructions on the screen during MRI scanning, it is inevitable that individuals would experience mind-wandering when attempting to maintain calm (for resting-state) and when focusing on interoception, such as breathing (for mindfulness). Therefore, in future studies, it will be important to obtain temporal information (e.g. a button response) on moments in which subjects become aware of mind-wandering during either mindfulness or resting state. This would help evaluate the presence and frequency of mind-wandering as well as the moment-to-moment mental shifts.

Under task-unconstrained 'rest' conditions, a mind-wandering strategy is commonly used in neuroimaging studies in which subjects are instructed to conduct mind-wandering to bring them into resting-state. Notably, we found that there was a nuanced difference in the effective connectivity between mind-wandering and resting state (Fig. 2c), which suggests that resting-state fMRI data could be affected by mind-wandering. Therefore, in future resting-state studies, more precise instructions must be given to subjects in relation to distinguishing the two mental states.

It is worth noting that only attentional focus on physical sensations of breathing was used as a mindfulness strategy among various alternative mindfulness strategies, and only meditation naïve individuals who experienced short-term mindfulness practices participated in this study. Additionally, we did not consider other networks (e.g. limbic and somatosensory networks) for spDCM analysis. Future studies should use a longitudinal design, an increased number of large-scale functional networks and alternative mindfulness strategies. Furthermore, it would be interesting to explore the relationship between effective connectivity levels, behavioral scores and cognitive task scores.

In conclusion, we discovered distinct causal interactions of mindfulness, mind-wandering and resting-state using the triple network. Our findings may provide new insights into these crucial mental states as well as valuable information for extended effective connectivity analyses.

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Conflicts of interest

There are no conflicts of interest.

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