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Altered Structure of Dynamic Electroencephalogram Oscillatory Pattern in Major Depression

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ABSTRACT

Research on electroencephalogram (EEG) characteristics associated with major depressive disorder (MDD) has accumulated diverse neurophysiologic findings related to the content, topography, neurochemistry, and functions of EEG oscillations. Significant progress has been made since the first landmark EEG study on affective disorders by Davidson 35 years ago. A systematic account of these data is important and necessary for building a consistent neuropsychophysiologic model of MDD and other affective disorders. Given the extensive data on frequency-dependent functional significance of EEG oscillations, a frequency domain approach may reveal the types of brain functions involved and disturbed in MDD. In this review, we systematize and integrate diverse and often unconnected observations on the content, topography, neurochemistry, and functions of EEG oscillations involved in MDD within the general concept of an EEG oscillatory pattern.

Keywords: Anxiety, Brain connectivity, EEG, Electroencephalogram, Interhemisphere asymmetry, Major depression, Oscillatory patterns, Spectral power, Transcranial magnetic stimulation

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The electroencephalogram (EEG) is one of the principal methods for extracting information from the human brain noninvasively. Research shows that neuropsychopathologies such as epilepsy, Alzheimer disease, schizophrenia, depression, obsessive-compulsive disorder, traumatic brain injury, attention-deficit/hyperactivity disorder, and some learning disabilities are associated with specific oscillatory patterns in spontaneous EEG and that these oscillatory patterns provide reliable markers of brain function or dysfunction (1–3). Given that depression is one of the most frequent mental disorder diagnoses in the general population (4) and its considerable economic burden to family members and society (5), the focus of this review is on EEG oscillatory pattern in major depressive disorder (MDD).

Since Davidson's EEG study on affective disorders, research on EEG characteristics associated with MDD has yielded a great deal of data (6). A general framework needs to be developed to allow researchers to understand the enormous amount of diverse observations related to EEG characteristics in MDD. The aim of this review is to organize systematically accumulated observations related to the EEG into a descriptive and comprehensive overview of the structure of the dynamic EEG oscillatory pattern in MDD.

Converging lines of evidence suggest that many EEG characteristics in MDD are altered (7–44). These results have been repeatedly demonstrated and replicated in large samples with 72%–93% sensitivity and 75%–88% specificity (2) for detection of MDD. How are these EEG characteristics expressed in MDD?

We suggest that a general concept of an EEG oscillatory pattern can be useful to systematize diverse observations related to EEG characteristics in MDD. The EEG oscillatory pattern may be considered as a spatiotemporally organized superimposition of multiple EEG oscillations in many frequency bands (45) where different oscillations are mixed in varying proportions, based on the vigilance level; perceptual, cognitive, and mental operations; or extent of pathologic process. The EEG oscillations are rhythmic electrical events in the brain that emerge from the interaction of large populations of neurons and can be observed on several temporal scales (45–49). It is suggested that the oscillatory activity of neuronal pools, which is reflected in characteristic EEG rhythms, constitutes a mechanism by which the brain can regulate changes of a state in selected neuronal networks and cause qualitative transitions between modes of information processing (47).

Capitalizing on these observations, one could combine different EEG descriptors within the EEG oscillatory pattern, which is characterized by 1) frequency content, including composition of delta (.5–3 Hz), theta (3–7 Hz), alpha (7–13 Hz), beta (13–30 Hz), and gamma (>30 Hz) EEG oscillations along with their percent ratio, and 2) spatial heterogeneity (expressed in spatially structured extracellular electrical field), including spatial complexity (amount of brain connectivity), interhemisphere asymmetry, and hubs (cortex areas with highest MDD effect or highest functional connectivity). In the following sections, we describe each attribute of the EEG oscillatory pattern for MDD.

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IMPORTANCE OF RESTING-STATE CONDITION

Studies of the closed-eyes resting state provide an important opportunity to examine EEG oscillatory patterns unbiased by any task. The resting-state condition avoids the confounding effects of visual scenes, instructions, and task execution (i.e., capability to perform a task and strategies employed, motivation or lack of it, fatigue and anxiety associated with task performance). Additionally, resting state seems more self-relevant than standard cognitive tasks, which typically activate numerous cognitive processes and drive subjects to direct their attention away from their personal concerns (50). The resting-state condition permits assessment of "pure" self-relevant brain activity (51). This activity reflects spontaneous processing of an internal mental context (top-down processing), (52) such as random episodic memory (53) and related imagery (54), conceptual processing (55), stimulus-independent thought (56), self-reflection, internal "narrative," and "autobiographical" self (57–59). The frequently expressed concern that unconstrained brain activity varies unpredictably does not apply to the passive resting-state condition of the human brain. Rather, it is intrinsically constrained by the default functionality of the resting-state condition (60). All unstructured features of the resting mental state that do not systematically relate to MDD would cancel out when averaged between different subjects. Features of the resting-state condition associated with MDD would stand out because MDD is the only common feature among all subjects. Abnormalities of resting-state characteristics such as self-referential processing, increased self-focused thinking, and analytical self-focused rumination contribute to the manifestation of MDD (61).

Based on this logic, we consider abnormality in a closed-eyes resting-state EEG in a patient with MDD to be a core feature. In this context, alteration in the closed-eyes resting-state EEG oscillatory pattern in MDD may constitute a tonic component of EEG microstructural organization that can serve as the field of action for abnormalities governed by multiple causes.

FREQUENCY CONTENT OF EEG OSCILLATORY PATTERN IN MDD

Composition of EEG Oscillations

The EEG oscillatory patterns in MDD and healthy condition are predominantly characterized by the same EEG oscillations in multiple frequency bands (delta, theta, and alpha), several of which are superimposed. However, only MDD is characterized by unique EEG oscillations in beta frequencies that are dominant in relation to delta, theta, and alpha (33). Although healthy subjects have beta oscillations, the oscillations are never dominant in relation to delta, theta, and alpha during resting-state condition. In contrast, an EEG from a patient with MDD is characterized by several episodes where coherent beta oscillations are dominant in relation to other oscillations (33). Despite the fact that MDD and healthy condition are mostly characterized by the same dominant EEG oscillations, these conditions differ from one other by the percent ratio of the EEG oscillations.

Percent Ratio of EEG Oscillations

Comparative analysis demonstrated that patients with MDD had more (in amplitude/power) frontal theta, global alpha, and beta oscillations and fewer occipital-parietal theta and global delta oscillations than control subjects without depression (1,7,9,11,12,14,19,20,23,24,30,32,33,38,39,42,62–67). Some studies demonstrated an increase of delta power in MDD (9,38,68,69). Advanced analysis of frequency content of EEG oscillatory patterns revealed that MDD differed from healthy condition not only by amplitude or power of oscillations but also by the probability for the occurrence of particular brain oscillations: Some oscillations were more (alpha, beta, and frontal theta) or less (delta and occipital-parietal theta) probable for MDD than for healthy condition (33).[1] These MDD effects were observed across the whole or major part of the cortex. There was not a single EEG channel without a statistically significant difference in the relative presence of multiple EEG oscillations between patients with MDD and healthy subjects (33).

The importance of theta, alpha, and beta oscillations for MDD is supported by the following facts: 1) Widespread frontal theta excess relates to nonresponsiveness to antidepressant treatments (70–72), whereas frontal-midline theta excess is associated with a favorable treatment outcome (73); 2) alpha excess is associated with a favorable response to antidepressant treatments (74) that decreases alpha power (75); and 3) beta oscillations correlate positively with relapsing depression (76) and number of depressive episodes (77) and have discriminative power to separate patients with MDD from healthy control subjects (78).

Considering that different EEG oscillations reflect functionally different components of information processing acting on various temporal scales (79–81), it is possible to map EEG oscillations onto mental or behavioral states (82). For the functional significance of the altered EEG oscillations in MDD, see section S1 in Supplement 1. Manifestation of particular composition of EEG oscillations within multiple frequencies in MDD may reflect the involvement of particular brain functions in this psychopathologic process (section S1 in Supplement 1). Discrepancies of findings from EEG-based measures may reflect different underlying mechanisms and functions and point to the existence of different subgroups within MDD that are not represented within diagnostic systems such as DSM-IV and ICD-10 (83).[2]

Because EEG oscillations are homeostatically regulated and primarily generated by postsynaptic potentials, they are often sensitive to functioning of particular neural circuits and to alterations in neurotransmission secondary to brain

[1] Although these results are based on one study (33) with relatively small samples, they are consistent with amplitude/power data obtained in other studies (1,7,9,11,12,14,19,20,23,24,30,32,33,38,39,42,62–67). Further study should be directed at replicating findings from this study (33) in larger samples.

[2] Some methodologic aspects (most common is the choice of reference electrode) may also contribute to the diversity of findings. However, close inspection of this issue revealed that it is more a theoretical than practical possibility when it comes to 10–20 EEG montage (section S2 in Supplement 1).