UNDERGRADUATE RESEARCH IN NATURAL AND CLINICAL SCIENCE AND TECHNOLOGY (URNCST) JOURNAL
Read more URNCST Journal articles and submit your own today at: https://www.urncst.com

REVIEW OPEN ACCESS

Electroencephalography and Magnetoencephalography Signatures of Ketamine Treatment in Depression: A Literature Review

Eva M. Geoghegan, BA Student [1]*

[1] Department of Biological Sciences, Columbia University Sherman Fairchild Center, 600, 1212 Amsterdam Avenue, New York, NY, United States 10027

*Corresponding Author: emg2234@columbia.edu

Abstract

Introduction: Ketamine has been shown to have rapid antidepressant effects. In addition, the use of EEG in depression offers a new approach to diagnose patients. It is necessary to understand locational-based EEG and MEG changes following ketamine in patients with depression to establish a potential biomarker panel. This study sought to identify consistent changes in band power as well as to highlight brain regions of interest.

Methods: This review examines studies published in the last 25 years that have trialed ketamine treatment in patients with depression and that utilize EEG or MEG. The studies report on spectral power changes in different bands as well as asymmetry, theta cordance, complexity, event-related potentials, and sleep studies.

Discussion: Resting state was the most reported. An EEG profile was identified of decreased theta, alpha, low beta and increased high beta and gamma following ketamine treatment, primarily in frontal regions. Although the antidepressant effects of ketamine are clear, the EEG research available on ketamine treatment in patients with depression is not comprehensive. Further research in more diverse age groups and larger studies is necessary as well as on the underlying ketamine mechanisms of affecting power bands.

Conclusion: Overall, a largely consistent EEG profile of decreased theta, alpha, low beta and increased high beta and gamma following ketamine treatment was identified primarily in frontal regions. Thus, EEG may be a useful tool for mechanistic treatment monitoring in depression patients subject to ketamine therapy.

Keywords: ketamine; EEG; MEG; depression; NMDA antagonist

Introduction

Depression is a common mental illness with debilitating effects [1]. In 2020 depression affected 18.5% of US adults [2], with the associated economic loss estimated at USD326.2 billion [3]. Low-dose ketamine is a promising novel treatment option for depression [1]. Ketamine induces antidepressant effects as well as other effects, such as dissociative anesthesia, psychodysleptic hallucinations, increased blood pressure and drowsiness [1,4,5]. There are several questions surrounding ketamine's antidepressant mechanisms [6]. By using electroencephalography (EEG) and magnetoencephalography (MEG), we may improve our understanding of ketamine's effect on brain activity for better diagnosis and treatment [7].

Ketamine is an antagonist of glutamate binding sites; the N-methyl-D-aspartate (NMDA) receptor, which plays a role in long-term potentiation and synaptic plasticity [4,5]. Brain activity depends on excitatory and inhibitory balance [8], and ketamine's antidepressant effect is linked to its effect on glutamate, an excitatory neurotransmitter [9]. Ketamine is known to increase extracellular prefrontal glutamate and cause structural changes in the prefrontal cortex (PFC) such as increasing synaptogenesis and spine density [9,10]. Conversely, ketamine decreases activity of inhibitory GABAergic interneurons in the PFC after initial glutamate excitation [10,11]. One of the key attributes of ketamine is its fact-acting antidepressant effects [10], thought to be due to increased glutamate, synaptic plasticity, connectivity [12], as well as increasing synaptogenesis to PFC pyramidal neurons which persist over time [10,13]. Depression is characterized by post-synaptic dendritic spines loss in PFC projection neurons. Ketamine has been shown to rescue spine loss [14], which accompanies symptom improvement and neuronal ensemble changes, indicating that ketamine has longer-lasting effects for people with depression after the initial drug infusion [14]. Ketamine may exert its long-lasting effects through stimulation of mTOR signaling and brain derived neurotropic factor increase (BDNF) [10]. Lower BDNF levels are implicated as a potential biomarker of depression with a proposed genetic link to the single nucleotide polymorphism (SNP) Val66Met [15–20].

The use of EEG in depression offers a new approach to diagnose patients, which will add to current long-standing

standard of clinician-interviewed diagnosis [21]. Possible EEG biomarkers for depression include band power, evoked potential, signal features, functional connectivity, EEG vigilance and alpha asymmetry [7]. The effects of NMDA antagonists on oscillations in transmembrane currents have been studied in model animals and more recently in humans. Delta power seems to increase after administration, with greater increases corresponding with higher doses [22]. Conversely, cortical theta power increases and hippocampal theta power decreases following ketamine administration [22]. Gamma power and high frequency power increases are also widely reported increases in multiple brain regions [22]. The underlying mechanism for these power changes are unclear but are likely a result of ketamine effects on bolstering excitatory unit contribution to rhythmic circuit and network motifs [23]. It is posited that hippocampal gamma power increases during acute ketamine via disinhibition of NMDA receptors of inhibitory interneurons, or direct inhibition of NMDA receptors at glutamatergic neurons [24].

A review is necessary to comprehensively understand ketamine-induced locational spectral band power changes in patients with depression. While it is warranted that studies use different methods to measure and analyze EEG data, it will be useful to identify consistent changes in band power as well as to highlight brain regions of interest to establish potential EEG biomarkers of ketamine treatment in the future. We analyzed band power changes across studies that measure EEG or MEG during resting-state, task-state, or sleep, to investigate the effect of ketamine treatment in depression.

Methods

This review examines studies published in the last 25 years that have trialed ketamine treatment in patients with depression and that utilize EEG or MEG. The studies report on spectral power changes in different bands as well as asymmetry, theta cordance, complexity, event-related potentials, and sleep studies. A search was carried out of PubMed literature in January 2024 using the following combination: "*EEG OR "MEG" OR "ECOG" "depress*" "ketamine"". Studies were excluded if they did not use ketamine treatment, did not have participants with depression, or did not include EEG/MEG analysis. Studies that included a change in minimum one frequency band were included, even if the experimental design focused on other biological changes after ketamine treatment. Studies that included other metrics such as complexity, event-related potentials and sleep studies were included to provide a more comprehensive view of the current available EEG and MEG literature on ketamine treatment for depression.

Data collection was then carried out across all studies. Multiple parameters were collected including demographic of participants, sample size, reference type, recording state, medication status and ketamine dosage. EEG parameters, including reference type, metrics examined, and type of power (relative, absolute or source) were also collected. Depression type, depression scoring system, and changes in depression score post-treatment were also gathered where available.

For applicable studies, significant changes in power bands, asymmetry, and theta cordance were systematized. In instances where bands were split into sub-bands and the significant changes were consistent across the sub-bands, they were collapsed to show general increase or decrease in the overall band. Location was then noted alongside each significant change in power. Waveform shape was collected from studies of event-related potential, entropy was collected from studies of EEG complexity, and changes in slow-wave activity and wakefulness were collected from sleep studies.

Results

Overview of Studies

All studies had a sample size of 55 or less (Table 1). Average age of participants ranged from 30.2 to 62.22. The average sample size was 36. The intervention length in days ranged from 3 to 70. Female participants were slightly more common, with 75% of studies including 50% or more females. MEG was less commonly used than EEG, with 25% of studies using MEG. Across 66.6% of studies participants were medication free. The ketamine dosage remained similar at 0.5 mg/kg in 83% of studies. Controls used included crossover-designs, remifentanil, midazolam and saline.

Reported Metrics

Resting state (eyes-closed) was the most reported metric with five studies, with an additional study that measured both eyes-closed and eyes-open. Three task (event related potential ERP), and three sleep studies were found as well (Table 1). Studies used varied psychiatric scoring systems to determine severity of depression, with the most common being Montgomery-Asberg Depression Rating Scale (MADRS), which was used in 83% of studies. Alpha and theta bands were most reported across studies, excluding sleep and ERP studies. 41% of studies identified responders versus non responders. Studies which measured band power included absolute, relative and source power. The majority of studies (83%) recorded EEG or MEG pretreatment versus post treatment, and all studies provided the effect of ketamine on depression score.

Aggregate Trends Across Frequency Bands

Delta and theta band power showed location-specific increases and decreases in power. Theta cordance decreased across all studies [25,26]. Decrease in power dominated the alpha band, however one study showed increased power (Table 2) [25]. Alpha asymmetry decreased in the one significant result [25]. Low beta band power decreased across studies [26,27]. High beta showed increase and decrease [26,27]. Gamma band power showed an overall increase consistent across all significant results [26–29].

Location-Specific Power Changes

Delta band power decreased globally. Theta band power showed global increase and global decrease. Decrease in theta band power was also seen specifically in the anterior cingulate cortex and frontal midline. Theta cordance decreased in the electrodes Af7, Fp1, Fp2 and Af8, in the prefrontal region and anterior cingulate cortex. Alpha band power decreased globally as well as in the centro-parietal area and the left anterior temporal lobe, striatum, anterior insula, anterior cingulate. An increase in alpha power was shown in the electrodes Af7, Fp1, Fp2 and Af8, which correspond with the frontal area. Alpha asymmetry decreased along the midline. Low-beta band power decrease was reported globally as well as in the left frontal pole, right ACC and PCC, right insula, left precuneus, and right LOC. High-beta band power showed both increase and decrease globally. Gamma power increased in all significant results, in frontal, occipital and temporal cortices and the left frontal pole, ACC, paracingulate gyrus, insula, PCC, and precuneus.

Event-Related Potentials

Two peaks of interest were consistently identified. First, peak ERF time was at 103ms in the calcarine region, corresponding with P100. Second, peak ERF 224ms in the frontal region, corresponding with P250 [30,31].

Sleep Studies

No difference in wakefulness for those with no response to ketamine. In antisuicidal responders to ketamine, wakefulness decreased [32]. Delta sleep ratio (DSR) lowered in responders and correlated with a change in MADRS scores for responders, meaning that lower DSR linked with an improvement with depressive symptoms [33]. Ketamine increased slow wave activity (SWA) [33]. Ketamine infusion increased the mean amplitude and slope of slow waves. Changes in SWA and BDNF plasma levels were proportional to responders [34].

Discussion

To comprehensively understand ketamine's effect on depression patient EEG following treatment, this review collected all reported band power changes after ketamine treatment in patients with depression. Resting state was the most reported. Overall, this study identified an EEG profile of decreased theta, alpha, low beta and increased high beta and gamma following ketamine treatment, primarily in frontal regions. These findings indicate that studies implementing ketamine treatment in depression patients have largely consistent EEG signatures patients, indicating that EEG may be a useful tool for mechanistic treatment monitoring.

Delta Band Power

One resting state study found a global decrease in delta power following treatment [27]. While delta has been primarily focused on as a signature of sleep, increasing evidence suggests a consistent increase in depression patient delta power during resting-state [37], [38]. Recent studies on healthy human subjects under a subanesthetic ketamine dose also showed reduced delta band power [39]. Delta power changes in responders have been seen to predict response in other treatments, such as cognitive behavioral therapy [40]. Mechanistically, NMDA antagonist-induced decreased delta power in rodents is thought to be due to alterations in firing patterns of pyramidal cells and increased excitatory neurotransmission [41–43]. Together, these studies indicate that increased delta power in depression may be affected by increased excitation following ketamine treatment. However, the decrease in power was not correlated with antidepressant response [27], meaning further investigation into resting state delta power changes in ketamine and depression is justified to distinguish between power changes as a biomarker for depression as opposed to a normal response to ketamine in all groups.

Theta Band Power

Theta band power following treatment primarily showed a global increase in power, with a decrease in the anterior cingulate cortex and frontal midline regions. Depression patient EEGs show increased theta band power [38], which likely reflects increased ACC activity [44]. Theta oscillations also reflect hippocampal-frontal communication [22]. In depression, increased theta likely corresponds to alterations in these pathways, reflected by altered emotional processing [45]. NMDA antagonists have several effects on theta power, including reduced hippocampal theta power and increased cortical theta power [22]. Ketamine may decrease theta power by similar means in depression, as supported by other therapies specifically targeting theta activity [46]. Together, these results indicate that decreased theta power may be a signature of ketamine's antidepressant effects.

Table 1. Overview of studies

Study	n	% Female	Mean Age ± SD	Methodology	State	Measurement	Recorded Pre vs Post Treatment	Identified Responders Versus Non-Responders	Intervention Length (days)	Post Treatment Measurement Time	Change in Depression Score
Cao et al., 2019 [25]	55	82	46.5±11.6, 48.1±12.7	EEG	Resting	Band power (relative)	Y	Y	14	240 min	-11.8
McMillan et al., 2020 [27]	30	50	30.2±8.2	EEG	Resting	Band power (source)	Y	N	42	During treatment	-6.38
Anijärv et al., 2023 [35]	25	58	46.41±14.12	EEG	Resting	Band power (absolute)	Y	N	70	42 days, 70 days	*-14.4
de la Salle et al., 2022 [26]	24	58	62.22 ± 5.55	EEG	Resting	Band power (absolute)	Y	Y	49	2 hours	-23.5
Farmer et al., 2020 [28]	57	65	41.7 ± 12.3	MEG	Resting	Band power (source)	N	N	14	6-9 hours	-7.11
Gilbert et al., 2022 [29]	29	66	36.12 ± 10.4	MEG	Task	Band power (source)	Y	N	11	6-9 hours	-8.86
Murphy et al., 2023 [36]	33	30	36.86 ± 10.86	EEG	Resting	Complexity	Y	N	7	During administration - 7 days	n/a
Lundin et al., 2021 [30]	55	61	35.77 ± 9.61	MEG	Task	Event related field	Y	N	17	6-9 hours	-9.39
Sumner et al., 2020 [31]	30	50	30.7 ± 8.85	EEG	Task	Event related potential	N	N	21	3 hours	-7.1
Vande Voort et al., 2017 [32]	34	70	44.97 ± 13.28	EEG	Sleep	Wakefulness	Y	Y	3	1 day	Decrease
Duncan, Sarasso, et al., 2013 [34]	30	33	48.06 ± 2.34	EEG	Sleep	Slow wave activity	Y	Y	4	12 hours	-1.71
Duncan, Selter, et al., 2013 [33]	30	33	47.3 ± 13.3	EEG	Sleep	Slow wave activity	Y	Y	3	1 day	Decrease

Y = yes, N = No.

Table 2. Changes in power across bands and corresponding locations following ketamine treatment

Paper	Delta	Theta	Alpha	Low beta	High beta	Gamma	Theta cordance	Alpha asymmetry
Cao et al., 2019			Af7, Fp1, Fp2, Af8				AF7, Fp1, Fp2, Af8	Fp2-Fp1
Anijarv et al., 2023			Central-parietal					
de la Salle et al., 2022		Global, ACC, FM	Parietal	Central-parietal	Central-parietal	Frontal	PFC, ACC	
McMillan et al., 2020*	Global	Global	Global	left frontal pole, right ACC and PCC, right insula, left precuneus, and right LOC	Global	left frontal pole, ACC, paracingulate gyrus, insula, PCC, and precuneus		
Farmer et al., 2020						Occipital, temporal, frontal		
Gilbert et al.,2022 **		Global	left anterior temporal lobe, striatum, anterior insula, anterior cingulate			Frontal		

Green cells correspond to increased band power following treatment, red cells correspond to decreased band power following treatment. Noted regions in cells correspond to identified regions with the directional change in band power. *EEG-informed Pharmacologic Magnetic Resonance Imaging (phMRI) analysis. Main effect of ketamine on blood-oxygen-level-dependent (BOLD) signal during infusion. **Group-by-SI (suicidal ideation) interactions. No significant group effects across frequency bands. ACC = anterior cingulate cortex, PF = prefrontal, MRF = midline right frontal, FM = frontal midline, PCC = posterior cingulate cortex, LOC = lateral occipital cortex

Theta cordance decreased across all studies in the frontal cortex, PFC and ACC. In one study only responders reported decrease [25] and in the other only the ketamine group experienced decrease [26]. Theta cordance has been studied in predictive value, with changes post-treatment corresponding with response and remission [47,48]. Ketamine is known to decrease frontal theta cordance in healthy controls [49]. In one study, theta cordance predictors did not have high accuracy at predicting anti-depressant response compared to other bands [25], however in the other study cordance was found to be predictive of depressive symptom change [26]. Further study into ketamine's effect on theta cordance in depression is warranted to determine if changes in theta cordance are linked to ketamine's antidepressant effects, or if it is a standard response to ketamine.

Alpha Band Power

Alpha band power primarily increased in frontal and fronto-parietal regions following ketamine treatment. Higher alpha power at baseline has also predicted response to other depression treatments [38]. Reduced alpha power has been shown to increase following other treatments, including electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (rTMS) and selective serotonin reuptake inhibitors (SSRIs) [40]. Similarly, ketamine treatment here appears to cause decrease in power, bar in the frontal region. Alpha asymmetry decreased in one study [25]. Alpha asymmetry represents the relative difference in activity between hemispheres [50]. Higher alpha power in midfrontal region is associated with depression [52] [53]. The authors posit that decreased alpha asymmetry is linked to ketamine's rapid effects [25]. There is much debate on the usefulness of frontal alpha asymmetry in diagnosis of depression and recent studies have concluded that there is a lack of empirical evidence for diagnosis [54] [55]. There is scope to further research alpha asymmetry as a prognostic tool [52]. Thus, more work needs to be done to evaluate its effectiveness in ketamine.

Beta Band Power

Low beta power primarily decreased in the central-parietal region following ketamine treatment. Increased low beta power is consistently shown in depression [38], which is linked to region-specific task performance [54,55]. Thus, altered region activity represented by increased beta activity and associated alterations in cognition and emotionality may be ameliorated by ketamine. Notably, low beta power decreased while high beta power increased following ketamine. This indicates that traditional band power analyses across beta may mask opposing ketamine effects in slow and fast beta oscillations, which also signifies likely unique mechanisms underlying slow versus fast beta oscillations.

Gamma Band Power

Gamma power increased across all studies and in multiple brain regions including frontal, occipital, left frontal pole, ACC, paracingulate gyrus, insula, PCC, precuneus and temporal. In resting-state studies, patients with depression have exhibited lower baseline gamma power, and different classes of antidepressant interact in opposite ways with gamma power, however ketamine is well-characterized to increase gamma power [56]. In rodents, gamma rhythms are correlated with information encoding in the hippocampus and increased neural activity, and changes in power may reflect excitation:inhibition balance in the brain [56]. An increase in gamma power reflects decreased inhibition, and has been documented in non-human primates following propofol administration [8]. Recent studies have also indicated that aperiodic EEG slope strongly reflects excitation:inhibition balance, with decreasing slope (decreased low frequency activity and increased high frequency activity) reflecting increased excitatory activity [8,57]. Thus, increased gamma and altered aperiodic slope may be reliable EEG biomarkers for ketamine treatment.

ERP

The peak ERP time was at 103ms in the calcarine region, corresponding with M100 and 224ms in the frontal region, corresponding with P250 [30,31]. Event-related potentials are averaged responses to stimuli that are captured via EEG [58]. Decreased P300 amplitude and latency are shown in patients with depression, which may reflect decreased excitatory activity [7]. Ketamine may affect the early and late ERP response by increasing excitatory activity. However, no significant relation to antidepressant score decrease and ERF amplitude was found [30], indicating that further work is needed to better understand ketamine's role during task and its associated EEG signatures.

Sleep

Ketamine decreased nocturnal wakefulness in antisuicidal responders [32]. Lowered delta sleep ratio in responders predicted better mood the following week and antidepressant score interactions [33]. Sleep in depression is characterized by shortened early SWA [33]. Shortened early SWA following ketamine may be linked to its action of inhibiting hyperpolarization-activated cyclic nucleotide-gated potassium channel (HCN1) channel conductance, thus reducing hyperpolarization-activated catatonic (I_H) currents, which contribute to SWA and are key for healthy sleep [59,60]. In the long term, the effect of ketamine on BDNF could improve depressive symptoms. SWA biomarkers are related to synaptic strengthening [34]. BNDF is associated with a SNP Val66Met, wherein it blocks activity-dependent synthesis and secretion and is associated with depression symptoms [16]. BNDF plays a role in neuroplasticity, and environmental reductions, such as stress, in BDNF may hinder structural neuroplasticity [61]. Therefore ketamine-dependent increase of BDNF in sleep could reverse depressive symptoms caused by gene-environment (GxE) interactions. Decrease in wakefulness from ketamine is notable in interactions with decreased suicidal ideation (SI), and ketamine appears to regulate circadian processes which are negatively impacted by depression and reduce SI rapidly, potentially due to glutamate-initiated effects of circadian rhythms [62].

Conclusion

This is the most recent study to review ketamine treatments in depression and their associated EEG changes. Previous reviews have focused on long-term potentiation and gamma power [63]. This study identified an EEG profile of decreased theta, alpha, low beta and increased high beta and gamma following ketamine treatment, primarily in frontal regions. The antidepressant effects of ketamine were consistent, and all studies recorded a decrease in antidepressant score. Conflicting results, such as in theta, alpha and high beta band power could be explained by patient-specific factors. Other studies on depression have investigated socio-economic and clinical predictors in the context of SSRI treatment [64], and similar research in ketamine could help discern why band power changes are not consistent, and to create a standard response profile for successful ketamine treatment. The age of average participants across studies was thirty and above, and the average sample size was 36. Due to these demographics, further research in more diverse age groups and larger studies is necessary, although that is challenging due to the nature of treatment resistant depression being diagnosed later in life and ketamine as a second-line treatment. In addition, the mechanisms underlying ketamine's antidepressant effects are not wholly understood, and further research would be beneficial in confirming ketamine's mechanisms affecting band power.

List of Abbreviations

ACC: anterior cingulate cortex
BOLD: blood-oxygen-level-dependent

BDNF: brain derived neurotropic factor
DSR: delta sleep ratio
ECT: electroconvulsive therapy
EEG: electroencephalography
ERP: event related potential
FM: frontal midline
I_H: hyperpolarization-activated catatonic currents
HCN1: hyperpolarization-activated cyclic nucleotide-gated potassium channel
LOC: lateral occipital cortex
MEG: magnetoencephalography
MRF: midline right frontal
MADRS: montgomery-asberg depression rating scale
NMDA: N-methyl-D-aspartate
phMRI: pharmacologic magnetic resonance imaging
PCC: posterior cingulate cortex
PF: prefrontal
PFC: prefrontal cortex
rTMS: repetitive transcranial magnetic stimulation
SSRIs: selective serotonin reuptake inhibitors
SNP: single nucleotide polymorphism
SWA: slow wave activity
SI: suicidal ideation

Conflicts of Interest
The author declares that they have no conflicts of interest.

Approval and/or Participant Consent
This study was a literature review that only assessed pre-existing studies and articles, and therefore did not require ethics approval nor participant consent.

Authors' Contributions
EG: All work contributing to the generation of this manuscript is principally the work of EG. EG collected all studies, analyzed all study data, generated figures, and interpreted all data. Principally drafted and edited the manuscript for final publication.

Acknowledgements
I would like to acknowledge and sincerely thank my URNCST Journal competition mentor, Frank Mazza, for his guidance and support throughout the researching, writing and editing process.

Funding
This study was not funded.

References
[1] Krystal JH, Abdallah CG, Sanacora G, Charney DS, Duman RS. Ketamine: A Paradigm Shift for Depression Research and Treatment. Neuron 2019;101: 774–8. https://doi.org/10.1016/j.neuron.2019.02.005
[2] Lee B, Wang Y, Carlson SA, Greenlund KJ, Lu H, Liu Y, et al. National, State-Level, and County-Level Prevalence Estimates of Adults Aged ≥18 Years Self-Reporting a Lifetime Diagnosis of Depression — United States, 2020. MMWR Morb Mortal Wkly Rep 2023;72:644–50. https://doi.org/10.15585/mmwr.mm7224a1
[3] Greenberg PE, Fournier A-A, Sisitsky T, Simes M, Berman R, Koenigsberg SH, et al. The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018). Pharmaco Economics 2021;39:653–65. https://doi.org/10.1007/s40273-021-01019-4
[4] Mion G, Villevieille T. Ketamine pharmacology: an update (pharmacodynamics and molecular aspects, recent findings). CNS Neurosci Ther 2013;19:370–80. https://doi.org/10.1111/cns.12099
[5] Matveychuk D, Thomas RK, Swainson J, Khullar A, MacKay M-A, Baker GB, et al. Ketamine as an antidepressant: overview of its mechanisms of action and potential predictive biomarkers. Ther Adv Psychopharmacol 2020;10:204512532091665. https://doi.org/10.1177/2045125320916657
[6] Aan Het Rot M, Zarate CA, Charney DS, Mathew SJ. Ketamine for Depression: Where Do We Go from Here? Biol Psychiatry 2012;72:537–47. https://doi.org/10.1016/j.biopsych.2012.05.003
[7] De Aguiar Neto FS, Rosa JLG. Depression biomarkers using non-invasive EEG: A review. Neurosci Biobehav Rev 2019;105:83–93. https://doi.org/10.1016/j.neubiorev.2019.07.021
[8] Gao R, Peterson EJ, Voytek B. Inferring synaptic excitation/inhibition balance from field potentials. NeuroImage 2017;158:70–8. https://doi.org/10.1016/j.neuroimage.2017.06.078
[9] Abdallah CG, De Feyter HM, Averill LA, Jiang L, Averill CL, Chowdhury GMI, et al. The effects of ketamine on prefrontal glutamate neurotransmission in healthy and depressed subjects. Neuropsycho pharmacology 2018;43:2154–60. https://doi.org/10.1038/s41386-018-0136-3
[10] Duman RS, Li N, Liu R-J, Duric V, Aghajanian G. Signaling pathways underlying the rapid antidepressant actions of ketamine. Neuropharmacology 2012;62:35–41. https://doi.org/10.1016/j.neuropharm.2011.08.044
[11] Homayoun H, Moghaddam B. NMDA Receptor Hypofunction Produces Opposite Effects on Prefrontal Cortex Interneurons and Pyramidal Neurons. J Neurosci 2007;27:11496–500. https://doi.org/10.1523/JNEUROSCI.2213-07.2007
[12] Abdallah CG, Sanacora G, Duman RS, Krystal JH. Ketamine and Rapid-Acting Antidepressants: A Window into a New Neurobiology for Mood Disorder Therapeutics. Annu Rev Med 2015;66:509–23. https://doi.org/10.1146/annurev-med-053013-062946

[13] Li N, Liu R-J, Dwyer JM, Banasr M, Lee B, Son H, et al. Glutamate N-methyl-D-aspartate Receptor Antagonists Rapidly Reverse Behavioral and Synaptic Deficits Caused by Chronic Stress Exposure. Biol Psychiatry 2011;69:754–61. https://doi.org/10.1016/j.biopsych.2010.12.015

[14] Moda-Sava RN, Murdock MH, Parekh PK, Fetcho RN, Huang BS, Huynh TN, et al. Sustained rescue of prefrontal circuit dysfunction by antidepressant-induced spine formation. Science 2019;364:eaat8078. https://doi.org/10.1126/science.aat8078

[15] Zorumski CF, Izumi Y, Mennerick S. Ketamine: NMDA Receptors and Beyond. J Neurosci Off J Soc Neurosci 2016;36:11158–64. https://doi.org/10.1523/JNEUROSCI.1547-16.2016

[16] Duncan LE, Hutchison KE, Carey G, Craighead WE. Variation in brain-derived neurotrophic factor (BDNF) gene is associated with symptoms of depression. J Affect Disord 2009;115:215–9. https://doi.org/10.1016/j.jad.2008.08.016

[17] Erickson KI, Miller DL, Roecklein KA. The Aging Hippocampus: Interactions between Exercise, Depression, and BDNF. The Neuroscientist 2012;18:82–97. https://doi.org/10.1177/1073858410397054

[18] Lee B-H, Kim Y-K. The Roles of BDNF in the Pathophysiology of Major Depression and in Antidepressant Treatment. Psychiatry Investig 2010;7:231. https://doi.org/10.4306/pi.2010.7.4.231

[19] Martinowich K, Manji H, Lu B. New insights into BDNF function in depression and anxiety. Nat Neurosci 2007;10:1089–93. https://doi.org/10.1038/nn1971

[20] Casey BJ, Glatt CE, Tottenham N, Soliman F, Bath K, Amso D, et al. Brain-derived neurotrophic factor as a model system for examining gene by environment interactions across development. Neuroscience 2009;164:108–20. https://doi.org/10.1016/j.neuroscience.2009.03.081

[21] Smith KM, Renshaw PF, Bilello J. The diagnosis of depression: current and emerging methods. Compr Psychiatry 2013;54:1–6. https://doi.org/10.1016/j.comppsych.2012.06.006

[22] Hunt MJ, Kasicki S. A systematic review of the effects of NMDA receptor antagonists on oscillatory activity recorded in vivo. J Psychopharmacol (Oxf) 2013;27:972–86. https://doi.org/10.1177/0269881113495117

[23] Womelsdorf T, Valiante TA, Sahin NT, Miller KJ, Tiesinga P. Dynamic circuit motifs underlying rhythmic gain control, gating and integration. Nat Neurosci 2014;17:1031–9. https://doi.org/10.1038/nn.3764

[24] Petzi M, Singh S, Trappenberg T, Nunes A. Mechanisms of Sustained Increases in γ Power Post-Ketamine in a Computational Model of the Hippocampal CA3: Implications for Ketamine's Antidepressant Mechanism of Action. Brain Sci 2023;13:1562. https://doi.org/10.3390/brainsci13111562

[25] Cao Z, Lin C-T, Ding W, Chen M-H, Li C-T, Su T-P. Identifying Ketamine Responses in Treatment-Resistant Depression Using a Wearable Forehead EEG. IEEE Trans Biomed Eng 2019;66:1668–79. https://doi.org/10.1109/TBME.2018.2877651

[26] De La Salle S, Phillips JL, Blier P, Knott V. Electro physiological correlates and predictors of the antide pressant response to repeated ketamine infusions in treatment-resistant depression. Prog Neuropsycho pharmacol Biol Psychiatry 2022;115:110507. https://doi.org/10.1016/j.pnpbp.2021.110507

[27] McMillan R, Sumner R, Forsyth A, Campbell D, Malpas G, Maxwell E, et al. Simultaneous EEG/fMRI recorded during ketamine infusion in patients with major depressive disorder. Prog Neuropsycho pharmacol Biol Psychiatry 2020;99:109838. https://doi.org/10.1016/j.pnpbp.2019.109838

[28] Farmer CA, Gilbert JR, Moaddel R, George J, Adeojo L, Lovett J, et al. Ketamine metabolites, clinical response, and gamma power in a randomized, placebo-controlled, crossover trial for treatment-resistant major depression. Neuropsychopharmacology 2020;45:1398–404. https://doi.org/10.1038/s41386-020-0663-6

[29] Gilbert JR, Gerner JL, Burton CR, Nugent AC, Zarate CA, Ballard ED. Magnetoencephalography biomarkers of suicide attempt history and antidepressant response to ketamine in treatment-resistant major depression. J Affect Disord 2022;312:188–97. https://doi.org/10.1016/j.jad.2022.06.025

[30] Lundin NB, Sepe-Forrest L, Gilbert JR, Carver FW, Furey ML, Zarate CA, et al. Ketamine Alters Electrophysiological Responses to Emotional Faces in Major Depressive Disorder. J Affect Disord 2021;279:239–49. https://doi.org/10.1016/j.jad.2020.10.007

[31] Sumner RL, McMillan R, Spriggs MJ, Campbell D, Malpas G, Maxwell E, et al. Ketamine improves short-term plasticity in depression by enhancing sensitivity to prediction errors. Eur Neuropsychopharmacol 2020;38:73–85. https://doi.org/10.1016/j.euroneuro.2020.07.009

[32] Vande Voort JL, Ballard ED, Luckenbaugh DA, Bernert RA, Richards EM, Niciu MJ, et al. Antisuicidal Respon se Following Ketamine Infusion Is Associated With Decreased Nighttime Wakefulness in Major Depressive Disorder and Bipolar Disorder. J Clin Psychiatry 2017;78:1068–74. https://doi.org/10.4088/JCP.15m10440

[33] Duncan WC, Selter J, Brutsche N, Sarasso S, Zarate CA. Baseline delta sleep ratio predicts acute ketamine mood response in major depressive disorder. J Affect Disord 2013;145:115–9. https://doi.org/10.1016/j.jad.2012.05.042

[34] Duncan WC, Sarasso S, Ferrarelli F, Selter J, Riedner BA, Hejazi NS, et al. Concomitant BDNF and sleep slow wave changes indicate ketamine-induced plasticity in major depressive disorder. Int J Neuro psychopharmacol 2013;16:301–11. https://doi.org/10.1017/S1461145712000545

[35] Anijärv TE, Can AT, Gallay CC, Forsyth GA, Dutton M, Mitchell JS, et al. Spectral Changes of EEG Following a 6-Week Low-Dose Oral Ketamine Treatment in Adults With Major Depressive Disorder and Chronic Suicidality. Int J Neuropsychopharmacol 2023;26:259–67. https://doi.org/10.1093/ijnp/pyad006

[36] Murphy N, Tamman AJF, Lijffijt M, Amarneh D, Iqbal S, Swann A, et al. Neural complexity EEG biomarkers of rapid and post-rapid ketamine effects in late-life treatment-resistant depression: a randomized control trial. Neuropsychopharmacology 2023;48:1586–93. https://doi.org/10.1038/s41386-023-01586-4

[37] Long S, Ding R, Wang J, Yu Y, Lu J, Yao D. Sleep Quality and Electroencephalogram Delta Power. Front Neurosci 2021;15:803507. https://doi.org/10.3389/fnins.2021.803507

[38] Newson JJ, Thiagarajan TC. EEG Frequency Bands in Psychiatric Disorders: A Review of Resting State Studies. Front Hum Neurosci 2019;12:521. https://doi.org/10.3389/fnhum.2018.00521

[39] Hong LE, Summerfelt A, Buchanan RW, O'Donnell P, Thaker GK, Weiler MA, et al. Gamma and Delta Neural Oscillations and Association with Clinical Symptoms under Subanesthetic Ketamine. Neuropsychopharmacology 2010;35:632–40. https://doi.org/10.1038/npp.2009.168

[40] Schwartzmann B, Quilty LC, Dhami P, Uher R, Allen TA, Kloiber S, et al. Resting-state EEG delta and alpha power predict response to cognitive behavioral therapy in depression: a Canadian biomarker integration network for depression study. Sci Rep 2023;13:8418. https://doi.org/10.1038/s41598-023-35179-4

[41] Kargieman L, Santana N, Mengod G, Celada P, Artigas F. NMDA antagonist and antipsychotic actions in cortico-subcortical circuits. Neurotox Res 2008;14:129–40. https://doi.org/10.1007/BF03033805

[42] Kargieman L, Santana N, Mengod G, Celada P, Artigas F. Antipsychotic drugs reverse the disruption in prefrontal cortex function produced by NMDA receptor blockade with phencyclidine. Proc Natl Acad Sci U S A 2007;104:14843–8. https://doi.org/10.1073/pnas.0704848104

[43] Santana N, Troyano-Rodriguez E, Mengod G, Celada P, Artigas F. Activation of thalamocortical networks by the N-methyl-D-aspartate receptor antagonist phencyclidine: reversal by clozapine. Biol Psychiatry 2011;69:918–27. https://doi.org/10.1016/j.biopsych.2010.10.030

[44] Mulert C, Juckel G, Brunnmeier M, Karch S, Leicht G, Mergl R, et al. Rostral anterior cingulate cortex activity in the theta band predicts response to antidepressive medication. Clin EEG Neurosci 2007;38:78–81. https://doi.org/10.1177/155005940703800209

[45] Shim M, Im C-H, Kim Y-W, Lee S-H. Altered cortical functional network in major depressive disorder: A resting-state electroencephalogram study. NeuroImage Clin 2018;19:1000–7. https://doi.org/10.1016/j.nicl.2018.06.012

[46] Mielacher C, Schultz J, Kiebs M, Dellert T, Metzner A, Graute L, et al. Individualized theta-burst stimulation modulates hippocampal activity and connectivity in patients with major depressive disorder. Pers Med Psychiatry 2020;23–24:100066. https://doi.org/10.1016/j.pmip.2020.100066

[47] De La Salle S, Jaworska N, Blier P, Smith D, Knott V. Using prefrontal and midline right frontal EEG-derived theta cordance and depressive symptoms to predict the differential response or remission to antidepressant treatment in major depressive disorder. Psychiatry Res Neuroimaging 2020;302:111109. https://doi.org/10.1016/j.pscychresns.2020.111109

[48] Ward MJ, Karim HT, Jessen ZF, Ghuman AS, Richardson RM, Reynolds CF, et al. Association between increased theta cordance and early response to ECT in late-life depression. Int J Geriatr Psychiatry 2020;35:147–52. https://doi.org/10.1002/gps.5220

[49] Horacek J, Brunovsky M, Novak T, Tislerova B, Palenicek T, Bubenikova-Valesova V, et al. Subanesthetic dose of ketamine decreases prefrontal theta cordance in healthy volunteers: implications for antidepressant effect. Psychol Med 2010;40:1443–51. https://doi.org/10.1017/S0033291709991619

[50] Gotlib IH. EEG Alpha Asymmetry, Depression, and Cognitive Functioning. Cogn Emot 1998;12:449–78. https://doi.org/10.1080/026999398379673

[51] Gollan JK, Hoxha D, Chihade D, Pflieger ME, Rosebrock L, Cacioppo J. Frontal alpha EEG asymmetry before and after behavioral activation treatment for depression. Biol Psychol 2014;99:198–208. https://doi.org/10.1016/j.biopsycho.2014.03.003

[52] Van Der Vinne N, Vollebregt MA, Van Putten MJAM, Arns M. Frontal alpha asymmetry as a diagnostic marker in depression: Fact or fiction? A meta-analysis. NeuroImage Clin 2017;16:79–87. https://doi.org/10.1016/j.nicl.2017.07.006

[53] Kołodziej A, Magnuski M, Ruban A, Brzezicka A. No relationship between frontal alpha asymmetry and depressive disorders in a multiverse analysis of five studies. eLife 2021;10:e60595. https://doi.org/10.7554/eLife.60595

[54] Ray WJ, Cole HW. EEG Alpha Activity Reflects Attentional Demands, and Beta Activity Reflects Emotional and Cognitive Processes. Science 1985;228:750–2. https://doi.org/10.1126/science.3992243

[55] Roh S-C, Park E-J, Shim M, Lee S-H. EEG beta and low gamma power correlates with inattention in patients with major depressive disorder. J Affect Disord 2016;204:124–30. https://doi.org/10.1016/j.jad.2016.06.033

[56] Fitzgerald PJ, Watson BO. Gamma oscillations as a biomarker for major depression: an emerging topic. Transl Psychiatry 2018;8:177. https://doi.org/10.1038/s41398-018-0239-y

[57] Mazza F, Guet-McCreight A, Valiante TA, Griffiths JD, Hay E. In-silico EEG biomarkers of reduced inhibition in human cortical microcircuits in depression. PLOS Comput Biol 2023;19:e1010986. https://doi.org/10.1371/journal.pcbi.1010986

[58] Olbrich S, Arns M. EEG biomarkers in major depressive disorder: Discriminative power and prediction of treatment response. Int Rev Psychiatry 2013;25:604–18. https://doi.org/10.3109/09540261.2013.816269

[59] Buzsáki G, Anastassiou CA, Koch C. The origin of extracellular fields and currents — EEG, ECoG, LFP and spikes. Nat Rev Neurosci 2012;13:407–20. https://doi.org/10.1038/nrn3241

[60] Tian F, Lewis LD, Zhou DW, Balanza GA, Paulk AC, Zelmann R, et al. Characterizing brain dynamics during ketamine-induced dissociation and subsequent interactions with propofol using human intracranial neurophysiology. Nat Commun 2023;14:1748. https://doi.org/10.1038/s41467-023-37463-3

[61] Yang T, Nie Z, Shu H, Kuang Y, Chen X, Cheng J, et al. The Role of BDNF on Neural Plasticity in Depression. Front Cell Neurosci 2020;14:82. https://doi.org/10.3389/fncel.2020.00082

[62] Duncan WC, Ballard ED, Zarate CA. Ketamine-Induced Glutamatergic Mechanisms of Sleep and Wakefulness: Insights for Developing Novel Treatments for Disturbed Sleep and Mood. Handb Exp Pharmacol 2019;253:337–58. https://doi.org/10.1007/164_2017_51

[63] Gilbert JR, Zarate CA. Electrophysiological biomarkers of antidepressant response to ketamine in treatment-resistant depression: Gamma power and long-term potentiation. Pharmacol Biochem Behav 2020;189:172856. https://doi.org/10.1016/j.pbb.2020.172856

[64] Balestri M, Calati R, Souery D, Kautzky A, Kasper S, Montgomery S, et al. Socio-demographic and clinical predictors of treatment resistant depression: A prospective European multicenter study. J Affect Disord 2016;189:224–32. https://doi.org/10.1016/j.jad.2015.09.033

Article Information
Managing Editor: Jeremy Y. Ng
Peer Reviewers: Frank Mazza, Arthur Tung
Article Dates: Received Apr 07 24; Accepted May 30 24; Published Jul 11 24

Citation
Please cite this article as follows:
Geoghegan EM. Electroencephalography and magnetoencephalography signatures of ketamine treatment in depression: A literature review. URNCST Journal. 2024 Jul 11: 8(7). https://urncst.com/index.php/urncst/article/view/610
DOI Link: https://doi.org/10.26685/urncst.610