Acta Neuropsychiatrica 2009: 21: 58–66

DOI: 10.1111/j.1601-5215.2009.00359.x

ACTA NEUROPSYCHIATRICA

Review article

A review of EEG and ERP studies in bipolar disorder

Degabriele R, Lagopoulos J. A review of EEG and ERP studies in bipolar disorder.

Objective: The electroencephalogram (EEG) can be a useful tool in determining differences in general neural activity and specific waveforms in individuals with a number of psychiatric disorders. This paper aims to outline and discuss significant findings in EEG and event-related potential (ERP) research into bipolar disorder (BD).
Methods: A literature review was performed through searches of MedLine, EMBASE, CINAHL and PsycInfo medical research databases for papers published from 1985 onwards. References of selected articles were also examined for other relevant studies.
Results: Differences in general EEG data were found in subjects with BD, namely increased theta and delta and decreased alpha wave bands. Changes in EEG were also found in euthymic BD subjects and those undergoing medication programmes. ERP studies commonly report prolonged latencies and reduced amplitudes in the P300 component. Hyperfunctioning of the right hemisphere in BD was also reported in some studies, although further confirmation of this finding is required. Finally, the effects of medication and the role that genetics plays in EEG still remain unclear.
Conclusions: The literature reviewed demonstrates supporting evidence for the presence of significant differences in EEG and ERP data in subjects with BD. However, methodological considerations such as varying mood states and medication status of the patients need to be followed more stringently for future research to bring about a robust model of the cognitive deficits of BD.

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Keywords: bipolar disorder; EEG; electrophysiology; ERP; P300

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Introduction

Historically, investigations into mood disorders have targeted the symptoms associated with the disorder, and many studies have concentrated entirely on behavioural aspects. However, less research has been undertaken examining the underlying cognitive impairments that manifest in these patients or the neurobiological substrates that underpin these deficits. While cognitive impairments are well recognised in idiopathic depression, fewer studies have investigated bipolar disorder (BD). The studies have reported subtle cognitive deficits that persist even while the patient is considered 'well' during the euthymic phase (1).

Recent pathological findings in structures such as the subgenual prefrontal cortex (2) in patients with mood disorders have precipitated the exploration of possible disturbances in *information processing*. The cognitive deficits explored have in many instances been likened to deficits commonly reported in patients with frontal lobe damage, such as impairments in executive functioning (3). As a result of these findings, there has been a significant impetus to better understand the underlying neurobiology of BD, and hence, there have been a growing number of studies that are utilising modalities such as electroencephalogram (EEG) and event-related potentials (ERPs) to study these networks.

The EEG

The electrical activity of the brain can be measured directly off the scalp in the form of EEG, while the subject is resting or performing an experimental

task. From the raw EEG, it is possible to extract brain potentials otherwise known as ERPs that are time-locked electrophysiological processes that occur in response to discrete stimuli. In unison, EEG/ERP measures provide a robust method for studying sensory pathways and cognitive processing in patients with BD.

EEG studies of BD have typically recorded neural responses from subjects in both eyes open and closed (4–7) modalities, and some studies even utilised hyperventilation (8), drowsiness (9) and sleep (10). Advances in computer technology have provided unlimited potential with respect to the presentation of visual stimuli, including affective images, through the use of video monitors (11) as well as a large range of auditory stimuli. However, the most common stimuli uncovered in this review were that of auditory tone stimuli used in the context of an auditory oddball paradigm to evoke an ERP waveform known as the P300.

Acquiring the EEG requires the subject to be fitted with a specialised cap that has electrodes incorporated into it that sit on the surface of the scalp. The electrodes have predefined spatial locations on the cap based on the international 10–20 system. The electrode cap along with additional reference electrodes (that may be located on the earlobe, nose or other mastoid areas) is connected to a biological amplifier for amplification, and the resultant signals are then transferred to a computer for acquisition and *post hoc* analysis.

The EEG is often acquired during resting 'eyes closed' and 'eyes open' conditions. Following this, there is often an activation-type condition where EEG is recorded while the subject is completing an experimental task, which may include the presentation of auditory and/or visual stimuli. This section of the experiment evokes specific waveforms known as ERPs. Visual-based experimental paradigms, such as facial affect recognition tasks, are presented through a high-resolution monitor synchronised to a stimulus presentation computer. Auditory stimuli because of the precise nature of the tone characteristics are produced through dedicated sound generation hardware and are often presented through earphones.

ERP data are viewed and analysed according to time-locked segments known as epochs that represent a snippet of neural activity of interest. The length of the epoch is chosen according to the difference in time between the stimulus and the neural response. As an example, if a stimulus usually results in certain EEG 'spikes', 'peaks' or a modified waveform at 200 and 550 ms, an epoch incorporating an 800-ms poststimulus window may be chosen to view the desired events. Repeated presentations of the stimulus result in ERPs being obtained from the subject over many epochs of time. Averaging epochs result in a 'typical' evoked response that allows for further analysis across the paradigm as well as across subjects and ultimately a comparison between groups of subjects.

Aim of the study

The aims of this review were to summarise the findings from EEG and ERP studies in BD and to communicate some future directions for this field of research.

Materials and methods

A literature search was performed using MedLine, EMBASE, CINAHL and PsycInfo medical research databases for papers published from 1985 onwards. The terms 'bipolar disorder', 'affective disorder', 'mood disorder' and 'mania' were searched in conjunction with EEG, ERP and electroencephalography. Other relevant articles were found through citations from papers in this search. A total of 32 articles were included for review. Papers exploring other technologies in regard to BD research were excluded as they fell outside the scope of this work. It should be noted that because of the variable use of keywords in different articles, some relevant papers may have inadvertently been overlooked.

EEG studies in BD

The purpose of this review was to outline the various EEG and ERP studies that have been conducted into BD. As is evident from Table 1, while there have been several studies produced, it is apparent from these that there has been a lack of systematic approach towards experimental design and medication status. This in part has hindered the formulation of a robust model of information processing in BD. However, these studies do offer promising insights, such as impairments in information processing, as reflected by changes in P300 amplitude and latency, evidence for right hemisphere dominance as well as shedding some light on the role that genetics assumes in the aetiology of BD.

Resting EEG

A large study by Clementz et al. that investigated resting EEG for 50 first-episode schizophrenia patients and 31 first-episode BD patients, together with their relatives, reported increased delta and

https://doi.org/10.1111/j.1601-5215.2009.00359.x Published online by Cambridge University Press

Table 1. Literature review findings of EEG and ERP studies into BD

Study	Medication	Number of subjects	Electrodes (recording and scalp)	Paradigm used	Principal findings	Interpretation
Cook et al. (28)	Unmedicated. 48-h drug wash-out period before EEG	Patients with BD and with 'abnormal' EEGs ($n = 23$) (12 male) (mean age: 32.43 years) and 23 patients with 'normal' EEGs (12 male) (mean age: 32.8 years)	16	None	EEG abnormalities included generalised slowing, L temporal-parietal slowing, L and R temporal spike waves. The abnormal EEG group was significantly related to absence of family history for the disorder	BD may be more heterogeneous in aetiology than is widely believed
Dewan et al. (8)	Yes	Patients with BD, euthymic ($n = 26$) (19 male) (mean age: 32.7 years) with ($n = 9$) and without ($n = 17$) specific CT abnormalities: third ventricle enlargement, and hyperdensity of the caudate, thalamus, anterior frontal white matter, and right temporal lobe	Undisclosed	Eyes opening and closing and hyperventilation	The EEG, the Halstead-Reitan neuropsychological battery, premorbid personality adjustment, family history of affective disorder, positive and negative symptoms, employment history and response to Li carbonate treatment could not differentiate between CT abnormal and CT normal subgroups	Study reports no lateralisation of EEG abnormalities or negative correlation between abnormalities and family history of affective disorder. Abnormal EEG results were not related to lateral ventricular enlargement
Small et al. (9)	Yes	Total of 16 patients with schizophrenia, 14 patients with mania, 15 patients with depression and 6 with OCD; all with equal numbers of age-matched and sex-matched controls	22	Waking, hyperventilation, photic stimulation and, in some cases, drowsiness and sleep	Significant EEG changes detected during treatment with Car and Li in patients with affective disorders. EEG did not differentiate between mania, depression, OCD and controls	During drug treatment, EEG amplitudes were negatively associated with cases of withdrawal retardation and positively correlated with anxiety and depression ratings. Thus, EEG topography may be useful in treatment monitoring
Muir et al. (16)	In most subjects	Patients with schizophrenia ($n = 96$) (67 male) (mean age 31.5 years), 88 with BD (54 male) (mean age: 35.2 years), 46 with major depression (21 male) (mean age: 38.2 years), 32 in-patients with non-psychotic psychiatric disorders (11 male) (mean age: 30.6 years) and 213 healthy volunteers (123 male) (mean age: 30.5 years)	1	P300 with subjects silently counting infrequent tones	The latency of the P300 component was significantly increased in the schizophrenic and bipolar subjects compared with other groups. This difference was stable in relation to clinical state and was not because of medication effects	The results show a distinction between bipolar and unipolar affective disorders and provides evidence for P300 abnormalities in BD as well as schizophrenia
Gerez et al. (14)	Yes	Total of 90 psychiatric, including bipolar, patients (39 male) (mean age: 31.9 years), grouped into conventionally treated (neuroleptics, antidepressants and benzodiazepines) and anticonvulsant groups	19	Resting EEG. Visual evoked potentials paradigm with responses to 100 flashes at a 2.1/s rate. A P300 oddball paradigm, responding to frequent and infrequent target tones	Focal EEG and evoked potential changes predicted good response to anticonvulsants. The presence of epileptiform activity did not. Structural abnormalities and some neuropsychological deficits were only seen in the focal group	Subtle topographical changes not easily observed reflect disordered neuronal activity. Psychiatric patients with disordered activity respond better to anticonvulsant medication than to conventional treatments
Kano et al. (4)	Yes	Total of 21 patients with major depression and melancholia (mean age: 41.4 years) and 16 without melancholia (mean age: 41.3 years), 7 patients with BD, manic (mean age: 45 years) and 44 age-matched and sex-matched healthy controls (mean age: 41.5 years)	16	Eyes closed	Alpha activity predominated in the right occipital hemisphere in controls but was significantly increased in the left posterior areas and decreased in central regions in patients with BD	Interhemispheric relationships between central and parietooccipital areas are disturbed in bipolar patients. Intrahemispheric relationships may also be disturbed in major affective disorder

Table 1. Continued

Study	Medication	Number of subjects	Electrodes (recording and scalp)	Paradigm used	Principal findings	Interpretation
Clementz et al. (12)	Yes	First-episode schizophrenia patients ($n = 50$) (39 male) (mean age: 22.5 years) and 55 of their relatives (25 male) (mean age: 42.2 years), 31 first-episode bipolar patients (19 male) (mean age: 26.2 years) and 35 of their relatives (18 male) (mean age: 36.8 years), 113 healthy volunteers (63 male) (mean age: 31.0 years) and their relatives	3	Resting EEG while listening to audiotaped white noise. Some subjects were retested after 9 months	Schizophrenia and bipolar patients showed increased delta and theta and decreased alpha activity compared with controls. Bipolar patients had additional right hemisphere activity. Bipolar patients and their relatives plus schizophrenia relatives displayed significantly reduced peak alpha frequencies	Bipolar finding supports argument of non-dominant hemisphere involvement in the regulation of elated mood. Differences seen in both schizophrenia and BD may reflect an abnormal subcortical discharge substrate (hippocampal theta spiking) found in all psychoses
Koles et al. (5)	Unmedicated. Drug wash-outs for those medicated	Patients with schizophrenia ($n = 31$) (20 male) (mean age: 34 years), 22 manic (9 males) (mean age: 34 years), 33 depressed (16 male) (mean age: 36 years) and 113 normal controls (57 male) (mean age: 33 years)	8	Eyes closed and open and three cognitive tasks: Vocabulary and Oral Word Fluency subtests (both verbal recognition) and a Block Design subtest (spatial cognition) of the Wechsler Adult Intelligence Scale	All groups were distinguishable in a pairwise comparison based on common EEG patterns. The manic and control groups were significantly different in the verbal tasks and the schizophrenic and normal groups during the spatial task. The depressed and control groups were significantly different during the word fluency verbal task and the spatial task	Significant differences in EEG results between groups, the strongest being in the resting condition. Left-sided hyperactivity reported in the schizophrenia group during the resting conditions persisted in the spatial cognitive task but not in the verbal tasks.
Souza et al. (15)	Yes	Total of 26 patients with schizophrenia (20 male) (mean age: 35 years), 19 patients with BD (5 male) (mean age: 39 years) and 27 healthy volunteers (16 male) (mean age: 29 years)	5	P300 task where subjects silently counted the number of infrequent, target tones	Prolonged P300 latency in schizophrenia and BD from central and temporal electrodes. Significantly reduced amplitude of P300 in schizophrenia only at midline and left temporal electrodes	The functional impairments underlying P300 abnormality may be different in schizophrenia and BD
Small et al. (6)	Li or Car alone or Li combined with Car, haloperidol or risperidone	Hospitalised manic patients newly medicated after a drug wash-out ($n = 37$)	28	Eyes closed	Increased delta amplitudes and total power with Li compared with Car. Increased fast delta frequencies in Li and Car plus Li groups compared with Car alone. After treatment, non-responders had higher amplitudes in left temporal areas	Level of psychopathology was negatively related to EEG amplitudes. qEEG findings implicate temporal lobe dysfunctions in mania
Small et al. (24)	No. 10- to 14-day wash-out	202 patients with BD hospitalised for acute mania (108 male) (mean age: 38 years)	22	EEG recorded during waking, photic stimulation, hyperventilation, natural-induced or sedative-induced drowsiness and light sleep. EEGs repeated in 75 patients rehospitalised for subsequent manic attacks and in 37 patients who cooperated after drug wash-out and again on completion of randomly assigned pharmcotherapy	Normal EEGs were found in most patients. Moderately abnormal EEGs found in 16% significantly correlated with absent family histories of affective disorder. Left-sided abnormalities were more common than right. EEG findings during subsequent manic episodes did not suggest greater CNS vulnerability. 'Small sharp spikes' and 'microsleep' were found in 17 and 10%, respectively, of patients who drowsed. EEGs showed significant differences between pharmacotherapies	Results could be more informative if a larger sample was taken, although evidence suggests dominant hemispheric dysfunctions in mania

Table 1. Continued

Study	Medication	Number of subjects	Electrodes (recording and scalp)	Paradigm used	Principal findings	Interpretation
Schulz et al. (32)	Yes	12 patients with affective disorders (7 male) (mean age: 59 years)	8	Eyes closed EEG before Li treatment and 4.4 months after. Patients were on varying types of medication before Li treatment	An increase in relative power in both delta and theta bands, the latter that was related to the Li plasma level. A decrease in relative alpha power, especially at occipital leads. A reduction of the dominant alpha frequency	The changes in relative power were greater in the right hemisphere
El-Badri et al. (13)	Yes	29 euthymic bipolar patients (10 male) (mean age: 30.7 years) and 26 healthy volunteers (14 male) (mean age: 27.7 years)	9	Eyes open and closed plus neurocognitive tasks	Greater power in all wave bands (beta, alpha, theta and delta) in patients compared with controls, especially in right temporal (theta) and left occipital (beta) – i.e. areas concerning visuospatial processing	Neurocognitive performance significantly impaired in patients compared with controls in visuospatial tasks. Thus, despite euthymia, underlying brain abnormalities in spectral power result in neurocognitive deficits in BD
Ikeda et al. (7)	Yes	58 patients with BD (22 male) (mean age: not reported) classified into groups of responder and non-responder to Li and into three groups of EEG finding: normal, borderline and abnormal. Age at onset was controlled for and found not to impact on Li response	20	Waking with eyes closed and open, photic stimulation, hyperventilation, and natural drowsiness and sleep if possible	Five cases were classified as Li responders and none of these subjects had abnormal EEG, and all the five patients with abnormal EEG were non-responders, but no significant relationship was found between EEG finding and Li response	Epileptiform EEG abnormality may be a predictor of Li resistance in BD
Rao et al. (10)	No medication 2 weeks prior to initial study	Adolescent patients with depression ($n = 28$) (10 male) (mean age: 15.4 years) and 35 healthy volunteers (14 male) (mean age: 15 years)	Unknown (standard polysomnography amount)	Sleep polysomnography study. Re-analysis of sleep data was performed and compared with change of clinical course 7 years later	Depressed subjects with unipolar course showed reduced REM latency, higher REM density and more REM sleep compared with depressed adolescents whose diagnosis converted to BD and still-healthy controls. Depressed subjects who became bipolar had more stage 1 sleep and less stage 4 sleep compared with unipolar subjects	Some of the variability observed in EEG sleep measures in adolescent depression may be confounded by a later bipolar course. Sleep regulatory changes associated with unipolar vs. bipolar may vary
O'Donnell et al. (18)	In most subjects	13 patients with manic or mixed BD (BP type I) (4 male) (mean age: 39.6 years), 12 patients with schizophrenia (8 male) (mean age: 40.8 years) and 24 healthy volunteers (14 male) (mean age: 37.8 years)	32	Auditory P300 task where subjects pressed a key in response to an infrequent tone	N100, P200 and N200 amplitudes were reduced in schizophrenia but not bipolar patients. Both patient groups showed reduced P300 amplitude and prolonged latency	Amplitude reduction in the early ERP components suggests auditory processing deficits in schizophrenia. Reduced amplitude of P300 in both groups implies disturbance of the temporal-parietal generators of this component. Prolonged P300 latency implies impaired attentional processing

Table 1. Continued

Study	Medication	Number of subjects	Electrodes (recording and scalp)	Paradigm used	Principal findings	Interpretation
Hall et al. (19)	In most subjects	10 MZ twin pairs discordant for BD (2 male) (mean age: 41.8 years), 12 MZ twin pairs concordant for BD (6 male) (mean age: 40.3 years), 10 MZ twin pairs discordant for but unaffected by BD (2 male) (mean age: 41.8 years) and 154 control twin pairs (34 male) (mean age: 36.03 years)	17	P300 task where subjects responded to an infrequent tone by pressing a button. P50 suppression task with blocks of conditioning and test click pairs. Mismatch negativity elicited by a duration auditory oddball task	Smaller amplitude in P300 task and decreased P50 suppression in BD. Genetic correlations were the main source of correlation: −0.33 for P300 amplitude and 0.46 for P50 ratio	P300 amplitude and P50 suppression ratio may be endophenotypes for BD
Flaisch et al. (11)	No	24 healthy volunteers (11 male) (mean age: 19 years)	256	Viewed 300 pictures from the International Affective Picture System in a rapid stream of 335 ms each	Emotional pictures were associated with a larger amount of posterior negativity compared with neutral pictures. The emotional content of previous pictures affected following pictures; pleasant or unpleasant primes resulted in reduced negativity of the following picture	The findings of this study may be because of resource competition among successively presented pictures

Car, carbamazepine; CNS, central nervous system; CT, computed tomography; Li, lithium; MZ, monozygotic; OCD, obsessive-compulsive disorder; REM, rapid eye movement.

theta and decreased alpha activity in both patient groups when compared with controls (12). Although this study lacked specificity when it came to distinguishing between the two patient groups, the findings robustly differentiated individuals with and without psychiatric illnesses.

Patients with BD in a state of euthymia differ to manic or depressed patients in that their mood is stable, with no obvious highs or lows. However, differences in neural frequencies between euthymic bipolar patients and healthy volunteers persist (13), indicating that phenotypical traits such as resting EEG frequencies may be central to BD and not state dependent. In this study, greater power in all bands, i.e. beta, alpha, theta and delta, was found, especially in areas involved in visuospatial processing (13). There were no significant differences between medicated and unmedicated groups of BD subjects with euthymia, suggesting that the effects of medication did not impact on the EEG. In addition, results from neurocognitive tasks given to both patient and control groups yielded further cognitive deficits in the processing of visuospatial tasks in patients. The results suggest that despite patients being euthymic, there remain residual cognitive deficits in the visuospatial domain as revealed by EEG and neurocognitive data. Cognitive deficits in the euthymia state of BD have since been corroborated (1).

The P300 ERP

When investigating specific waveforms that differ in BD, the P300 is one that has been widely studied (14–16). It has been associated with the orienting response and occurs as a result of the presentation of an infrequent or 'target' stimulus embedded among a series of frequently occurring background stimuli. It is often suggested that the P300 reflects a comparator process in the brain whereby an existing neuronal template is compared with incoming stimuli (17). A large study of the P300 was conducted by Muir et al. that examined 96 patients with schizophrenia, 88 with BD, 46 with major depression and 213 healthy controls. The study employed an auditory oddball paradigm, which involved subjects silently counting the randomly presented, infrequently occurring, higher pitched tones among the more frequent lower pitched tones. It was found that a significantly increased latency for the P300 component existed in patients with schizophrenia and BD when compared with depressed patients and healthy controls. From this study, it was reported that the prolongation of the P300 latency could not be attributed to medication effects as it was also

https://doi.org/10.1111/j.1601-5215.2009.00359.x Published online by Cambridge University Press

present in unmedicated patients. This increase in P300 latency in BD has been consistently reported in subsequent studies (15,18). Moreover, reduced amplitude of the P300 component has also been reported (18,19).

It has been suggested that the amplitude of the P300 reflects resource allocation (17,20) and that the latency of the P300 is an indicator of the speed of information processing or the time taken to categorise the infrequent stimulus (21). Both these characteristics of the ERP have been shown to be abnormal in BD. Such impairments go beyond the typical mood-related symptoms and exist as secondary deficits in information processing.

It is possible that the P300 changes seen in BD are related to structural brain changes. Few studies have demonstrated these functional-structural relationships in BD, yet it has been argued that temporal-parietal abnormalities affecting regions involved in language and audition are responsible for the reductions in amplitude (18). There is some evidence that the reduced amplitude, which is also seen in schizophrenia, may be related to structural abnormalities in temporal areas (22). However, further imaging studies of BD and other mood disorders are required to explicate a structural cause for the changes seen in the P300.

Laterality

Another interesting finding from the Clementz et al.'s study of resting EEG was that those patients with BD had additional right hemisphere activity, suggesting non-dominant hemisphere involvement in regulation of elevated mood (12). This is consistent with another study that revealed right hemisphere hyperfunctioning in mania as well as moderate hypofunctioning in depressed subjects and severe hypofunctioning in those with schizophrenia (23). Koles et al., however, demonstrated left-sided hyperactivity in schizophrenia, right-sided hyperactivity in the depressed group and bilateral hyperactivity in those with BD (5); with the author arguing that right-sided hyperactivity in BD was a consequence of verbal cognitive activation. However, a study by Small et al. found that EEG abnormalities were less common in the right hemisphere than in the left (24).

These results reveal the possibility of laterality in BD because of the persistent finding that the right side of the brain displays hyperactivity in patients with the disorder and may thus implicate this hemisphere in the regulation of mood. It has been suggested that the propensity for abnormally elevated mood during the manic phase of BD relates to increased noradrenergic arousal in the right hemisphere and hence the increased activity reported therein (12). Another explanation that has been posited is that patients with BD have 'sticky' right hemisphere neural circuitry (25). No matter what the root cause for right-sided hyperactivity in patients with BD, these findings provide supporting evidence for the hemispheric theory of duality that differentiates left (logical) vs. right (creative) hemispheres (26). Moreover, an overactive non-dominant hemisphere may explain patient traits such as the intense artistic creativity, which has been demonstrated in some cases (27). However, further studies are required to reinforce hemispheric dominance in BD.

Genetics

One of the earliest studies to investigate BD using EEG technology found a correlation between 'abnormal' EEG results and no familial history of the illness (28), a finding corroborated by a subsequent study (24). Cook et al. defined an abnormal EEG as one involving generalised slowing, left temporal-parietal and occipital slowing, as well as presence of spike and slow waves (28). Further support for lack of genetic involvement in the aetiology of BD is demonstrated in another study (12). EEG data obtained from patients and their first-degree relatives showed that patients with schizophrenia and BD had reduced alpha activity when compared with controls; a trait that was also found in the first-degree relatives of patients with schizophrenia but not in those of BD (12). However, one study uncovered in the literature does suggest genetic causative factors for incidence of BD (29). A large phenome database of BD uncovered strong familial traits such as history of psychiatric hospitalisation (odds ratio = 3.94), psychotic features (odds ratio = 2.01), co-morbid obsessive-compulsive disorder (odds ratio = 3.53) and absences from work because of mood disorder (odds ratio = 3.07) ($p < 0.0001$ for all).

The BD EEG literature would suggest that genetic factors do not appear to underpin the changes observed in electrical brain activity. This lack of association highlights the importance of environmental and stress-related factors in the development of BD. However, it should be noted that genetic heritability may still exist in non-familial cases of BD and that cases with a positive family history of BD may be illnesses otherwise acquired (30). In addition, a large study of phenotypic variables for BD does indicate familial traits of the disorder (29). This particular study, arising from a significant cohort of 5721 subjects, suggests that genetics do play a role in the

https://doi.org/10.1111/j.1601-5215.2009.00359.x Published online by Cambridge University Press

aetiology of BD. Therefore, the evidence outlined above, while principally one sided, suggests a variable aetiology of BD that could differ between patients, i.e. that some cases have a strong genetic component, but others are independent of genetic make-up as a causal factor. It is clear that further verification is required to confirm genetic involvement, and large samples of bipolar patients are needed to detect any environmental effects that may be the causal factors of the illness (31).

Summary

The most common EEG findings in BD as uncovered in this review can be summarised as follows. Resting EEG data demonstrated increased theta and delta but decreased alpha band power in patients with the disorder (12). Studies that investigated euthymic BD patients compared with healthy controls demonstrated differences in EEG results in areas associated with visuospatial processing (13), which the authors attribute to underlying disruptions in beta, alpha, theta and delta waves. In regard to ERPs, longer latency of the P300 has been demonstrated in several studies (15,16,18), and evidence of reduced amplitude has also been observed in patients with the illness (18,19). Lastly, hyperactivation of the right hemisphere has been reported by some studies in subjects with BD (12,23). The role of genetics in the aetiology of BD, however, still remains unclear (12,24,28,29).

Methodological limitations in EEG studies of BD

The issue of how medication impacts on the EEG remains unresolved. Some studies have demonstrated effects on the EEG in response to neuroleptic therapy (9,32), with other studies reporting increased delta amplitudes as well as overall total power in patients taking lithium compared with carbamazepine (6). A common dilemma in EEG research into BD is that patients with BD are dependent on medication as they need to remain stable, making it very difficult to recruit non-medicated or even *de novo* patients for EEG testing. Therefore, the possibility that lithium or other neuroleptic treatment may be responsible for the differing neural activity seen in patients cannot be excluded at this stage.

To be able to discriminate whether findings are a 'trait' (i.e. specifically BD) or 'state' feature of BD (i.e. mania or depression), a cross-section of many subjects in different phases of the illness need to be tested or longitudinal studies involving testing and retesting subjects over their own mood fluctuations would be required.

Another consideration that needs to be taken into account when examining EEG data are the number of electrodes used to record neural activity. A large study conducted by Muir et al. used only one recording electrode for simplicity (16). The authors discussed that because of this methodological restriction, the two components of the P300 waveform, namely the P3a (which occurs frontally) and the P3b (which occurs centroparietally), could not be differentiated because of their regional specificity and that the longer latency (P3b) witnessed in psychiatric subjects may actually have been caused by the absence of the earlier (P3a) element. In comparison, evidence of a longer P300 latency in BD may be clearer in another study that employed a 32-channel EEG (18). Furthermore, because of this more global measurement of neural activity, the authors were able to observe that the P300 component was largest at parietal sites and smallest at frontal lobe sites. They were therefore able to deduce that the temporal and parietal regions are likely to contribute to the generation of the two subtypes of the P300 ERP component.

Directions for future research

This review summarises studies that have investigated EEG activity in patients with BD, comparing them with healthy controls, unipolar depressed patients as well as with patients with schizophrenia. Although EEG studies of BD have demonstrated many confounds and features that need to be controlled for, they are still of significant importance and meaningful in developing a pattern of brain function in BD. Future studies need to consider the different phases of the illness (i.e. depression, mania and euthymia) separately as well as aim to control for medication and technical considerations, such as numbers of electrode channels. Finally, future studies need to have greater control of variables such as co-morbidity with other illnesses more stringently if the results are to be of clinical salience.

Acknowledgements

This research was supported by NHMRC Program Grant 510135.

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https://doi.org/10.1111/j.1601-5215.2009.00359.x Published online by Cambridge University Press