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Impaired frontal synchronization of spontaneous magnetoencephalographic activity in patients with bipolar disorder

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ABSTRACT

Recent functional imaging studies demonstrated that brain exhibit coherent, synchronized activities during resting state and the dynamics may be impaired in various psychiatric illnesses. In order to investigate the change of neural dynamics in bipolar disorder, we used a new nonlinear measurement "similarity index" to analyze the magnetoencephalography (MEG) recordings and test the hypothesis that there are synchronization changes within different frequency bands in the frontal cortex of patients with bipolar disorder. Ten patients with bipolar I disorder during euthymic phase and ten normal controls underwent 2 min eye-closed resting recording with a whole-head 306-channel MEG system. Eleven channels of MEG data from frontal area were selected for analysis. Synchronization level in the delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz) and beta (12–24 Hz) bands was calculated for each subject and compared across group. The results showed that significant dynamic changes in bipolar patients can be characterized by increased synchronization of slow frequency oscillations (delta) and decreased synchronization of fast frequency oscillations (beta). Furthermore, the positive correlation between beta synchronization level and preservative errors in Wisconcin card sorting task was found which would implicate the deficit of executive function in bipolar patients. Our findings indicate that analysis of spontaneous MEG recordings at resting state using nonlinear dynamic approaches may disclose the subtle regional changes of neural dynamics in BD.

Bipolar disorder (BD) is a chronic psychiatric illness characterized by recurrent manic and depressive episodes that are polar opposite on a continuum between elevated mood, grandiose, self importance on one side and depressed mood, feelings of self-loathing, incompetence on the other. Despite lots of molecular, neurobiological and neuroimaging studies, the cause of this pathological mood fluctuation remains unclear. Synchronization among oscillatory networks can be viewed as a mechanism of integration for specific frequency band-associated functions [28]. Investigation of synchronization in spontaneous brain activity at resting state would help to understand impairment of cognitive default network in BD patients.

Recently, chaos theory or nonlinear dynamics has become a potential tool to explain the mechanisms of psychiatric illness [6,19]. The method of nonlinear dynamics is especially attractive to the researchers on BD because the symptoms of each patient oscillate between different mood states such as mania, hypomania, euthymia, dysthymia, and depression. There are two kinds of analytic strategies while applying nonlinear dynamics to the research of bipolar disorder. One is to analyze the time course of self-report mood data. For instance, Glen et al. calculated the approximate entropy of self-reported mood in bipolar patients and found that approximate entropy was significantly greater in the 60 days prior to a manic or depressive episode than the 60 days prior to a month of euthymia [8]. This result implicated that irregularity in mood could be viewed as an indicator of onset of an episode. The other application of nonlinear dynamics is to analyze the biological signals recorded from the BD patients, such as. Electroencenphalographic (EEG) and magnetoencephalographic (MEG), since the signals directly obtained from brains were proposed to be more related to the psychopathology. Bahrami et al. analyzed the EEG recordings of bipolar patients and found that the fractal dimension was significantly augmented in patients during

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manic phase compared with normal controls [5]. They concluded that the measurement of brain complexity was able to differentiate the EEG data of normal and abnormal mood states. However, their study dealt with the time series recorded at each channel separately. Recent studies suggested that brain function could be characterized by synchronized activities between neural assemblies which motivate us to investigate if synchronized index can be used to detect the neural abnormally in bipolar patients.

In this study, we modified similarity index (SI) proposed by Arnhold et al. [4] as synchronization level to evaluate and detect the impairments of underlying neural dynamics in euthymic bipolar patients. Based on previous functional studies which showed frontal cortical dysfunction in bipolar patients [3,10,12], we hypothesized that in the frontal region of bipolar patients there is a change in the dynamics of neural oscillations during resting state. Since various cognitive and emotional functions are associated with neural oscillations of different frequency bands, similarity indices in different bands were calculated, respectively, and statistically compared between normal subjects and bipolar patients and to reveal the correlation between cognitive dysfunction and brain dynamics.

Ten patients with bipolar I disorder during euthymic phase (five males, mean age = 32.5 ± 10.3 y/o, range = 21:53) were selected from the outpatients of psychiatric department of Taipei Veterans General Hospital. The clinical diagnosis was made by two independent psychiatrists using DSM-IV-TR. The mean illness duration was 9.0 ± 5.2 years. All patients were taking a range of medications, including lithium ($n = 1$), anticonvulsants ($n = 10$), antidepressant ($n = 4$), and antipsychotics ($n = 1$). Ten gender- and age-matched normal controls (five males, mean age = 32.2 ± 11.6 y/o) were recruited through advertisement from the community. All the normal controls underwent Mini International Neuropsychiatric Interview (M.I.N.I.) before the experiments to exclude the possible morbidity of major psychiatric illness. All subjects were without a history of substance misuse or abuse and provided written informed consent to participate in the study according to the guidelines approved by the Institutional Committees of Medical Ethics and Radiation Safety.

At the day before image acquisition, the mood symptoms were rated using Young Mania Rating Scales (YMRS) and 17-item Hamilton Rating Scale for Depression (HAMD17) and the scores were 1.6 ± 2.27 and 4.7 ± 3.9, respectively. The scores posited that our BD patients were not of overt depressive or manic phase. Three kinds of cognitive test batteries, including Wisconcin card sorting test (WCST), wordlist recall, and attention test, were used to test the cognitive impairments of the BD patients. At the time of imaging procedure, the BD patients were all clinically stable and cooperative to follow the requirements of experimental tasks.

For each subject, 2 min eye-closed resting MEG data with 1000 Hz sampling rate and bandpass filtered at 0.03–330 Hz was recorded with a whole-head 306-channel MEG system (Vectorview; Elekta-Neuromag, Helsinki, Finland). Four head-position-indicator (HPI) coils attached on subject's head and three defined anatomical landmarks (nasion and bilateral preauricular points) were used to ensure coverage of the same cortical regions under the selected sensors among all the subjects. The mean translation of all the subjects' heads located within scanner in this study was around 2.2 mm, which were much smaller than the distance between sensor pair (34 mm). After offline artifact rejection, the noise-free MEG data from 11 pairs of planar gradiometers covering frontal regions of individual brains were selected for the calculation of SI. Based on our previous findings from the average power spectrum analysis [27], we specified four frequency bands, delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz) and beta (12–24 Hz). For each subject, the similarity index of each pre-specified frequency band was calculated for each combination of 2 channels among 11 frontal channels (i.e. 110 values in total).

We in this work modified the SI method proposed by Arnhold et al. [4], which is described as follows. Let x_n be a scalar filtered time series with delta (theta, alpha or beta) band at time point n. By the time-delay procedure [25], we can construct a d_x-dimensional vector $\mathbf{x}_n$ with the coordinate $(x_n, \ldots, x_{n+(d_x-1)\tau})$, where τ_x is the delay time and d_x is the embedding dimension. A reconstructed trajectory $\mathbf{X}$ denotes the collection of the points, $\mathbf{x}_1^{\mathrm{T}}, \mathbf{x}_2^{\mathrm{T}}, \ldots$, where T denotes transpose. For each $x_n \in R^{d_X}$, the mean Euclidean distance for the set of $\mathbf{x}_n$ and its k nearest neighbors (KNN), $\Gamma_n^k = \{\gamma_{n,j} | j = 1, \ldots, k\}$, is defined as $V_n^{(k)}(\mathbf{X}) = (1/k)\sum_{i=1}^{k} ||\mathbf{x}_{\gamma_n} - \mathbf{x}_{\gamma_{n,i}}||^2$. The conditional mean Euclidean distance is defined by $V_n^{(k)}(\mathbf{X}|\mathbf{Y}) = (1/k)\sum_{j=1}^{k} ||\mathbf{x}_{\omega_n} - \mathbf{x}_{\omega_{n,j}}||^2$, where $\Omega_n^k = \{\omega_{n,j} | j = 1, \ldots, k\}$ is its KNN in $\mathbf{y}_n$. The local interdependences $S_n^{(k)}(\mathbf{X}|\mathbf{Y})$ and global $S^{(k)}(\mathbf{X}|\mathbf{Y})$ are defined as

$$S_n^{(k)}(\mathbf{X}|\mathbf{Y}) = \frac{V_n(\mathbf{X})}{V_n^{(k)}(\mathbf{X}|\mathbf{Y})} \tag{1}$$

and

$$S^{(k)}(\mathbf{X}|\mathbf{Y}) = \frac{1}{N}\sum_{n=1}^{N} S_n^{(k)}(\mathbf{X}|\mathbf{Y}), \tag{2}$$

respectively. The quantity $S_n^{(k)}(\mathbf{X}|\mathbf{Y})$ (resp. $S^{(k)}(\mathbf{X}|\mathbf{Y})$) means the local (resp. global) variation rate of the mean distance influenced by $\mathbf{Y}$, and is called the *local* (resp. global) *similarity index*, LSI (resp. GSI).

To avoid spurious detection of synchronization due to short data, noise, bandpass filtering, and signal complexity, we developed a two-level process of computing GSI in order to get a more significant representation. The univariate difference of GSI between $\mathbf{X}$ and $\mathbf{Y}$ is defined as $S_{\mathrm{uni}}^{(k)}(\mathbf{X}|\mathbf{Y}) := \max\{S^{(k)}(\mathbf{X}|\mathbf{Y}) - \tilde{S}^{(k)}(\mathbf{X}|\mathbf{Y}), 0\}$, where $\tilde{S}^{(k)}(\mathbf{X}|\mathbf{Y})$ is the 95th percentile of distribution for 19 univariate surrogates of $\mathbf{Y}$ [20], generated by the iterative amplitude-adjusted Fourier transform algorithm (IAAFT) [21]. Fig. 1 illustrates signal processing with creation of uni-surrogate and phase reconstruction. Fig. 1(a) is two 68 s time series raw data recorded from two different selected sensors for a subject. Fig. 1(b) illustrates the bandpass filtered signals (delta band) and (c) is their corresponding phase-reconstructed data. Nineteen numbers of uni-surrogate data for each filtered data, F1 [resp. F2], are shown in Fig. 1(d) [resp. (e)], where the spectrums of the filtered data and their responding surrogate data are the same. The bivariate difference of GSI is then defined by

$$S_{\mathrm{bi}}^{(k)}(\mathbf{X}|\mathbf{Y}) := \begin{cases} \max\{S^{(k)}(\mathbf{X}|\mathbf{Y}) - \hat{S}^{(k)}(\mathbf{X}|\mathbf{Y}), 0\}, & \text{if } S_{\mathrm{uni}}^{(k)}(\mathbf{X}|\mathbf{Y}) > 0 \\ 0, & \text{if } S_{\mathrm{uni}}^{(k)}(\mathbf{X}|\mathbf{Y}) < 0 \end{cases}, \tag{3}$$

where $\hat{S}^{(k)}(\mathbf{X}|\mathbf{Y})$ is the 95th percentile of distribution for 19 bivariate surrogates [20], generated by IAAFT algorithm.

For each subject's MEG measurement, the mean bivariate difference of global similarity index (MBDGSI) for each frequency band (i.e., delta, theta, alpha, and beta band) was computed by the average of 110 values (i.e. $S_{\mathrm{bi}}^{(k)}(\mathbf{X}|\mathbf{Y})$) for channel pairs (i, j) where $i \neq j$ and $i, j = 1, \ldots, 11$. We employed in this study a two-way mixed ANOVA (2×2) analysis to investigate the group (patient vs. normal subjects) and gender (male vs. female) effects on MBDGSI values for each frequency band. The MBDGSI values between two groups or two genders were further compared by one-way ANOVA analysis for each frequency band if group or gender effect was found to be significant. A p-value below 0.01 was considered to be significant for both one-way and two-way ANOVA. Two kinds of correlations were provided. One is Kendall's rank correlation, and the other

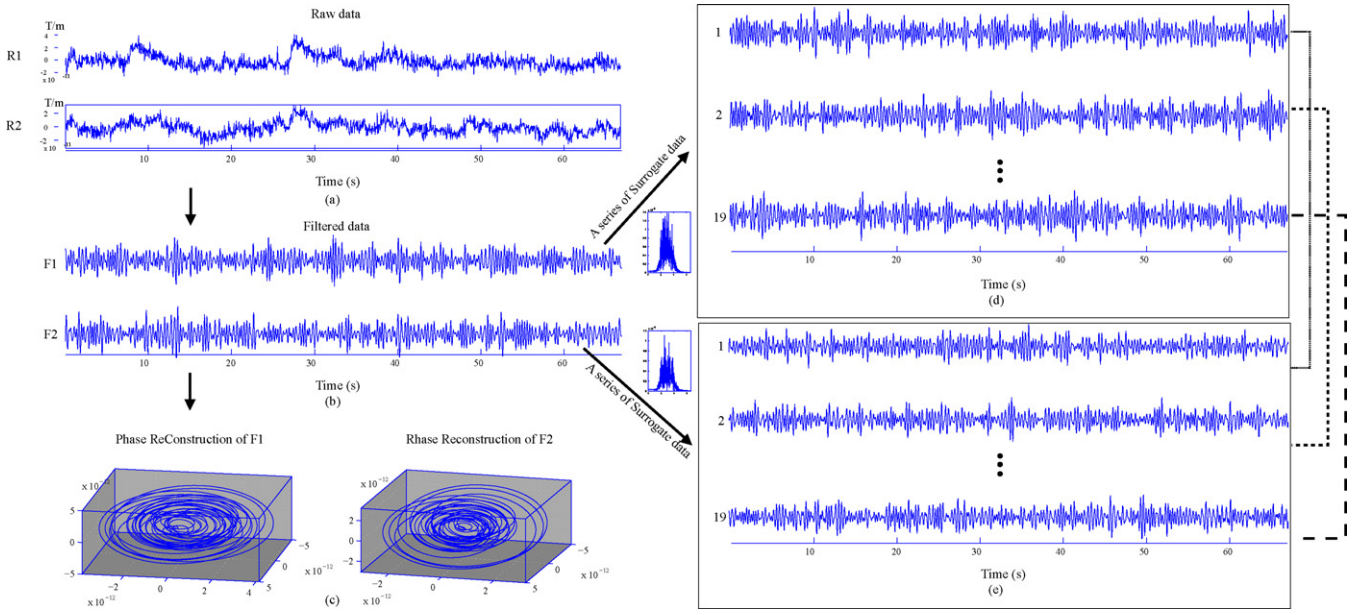

Fig. 1. Illustration of signal processing with creation of uni-surrogate and phase reconstruction. (a) Are two 68 s time series raw data recorded from two different sensors for a subject. (b) Illustrates the bandpass filtered signals (delta band) and (c) is their corresponding phase-reconstructed data. (d) [Resp. (e)] shows 19 numbers of uni-surrogate data for each filtered data, F1 [resp. F2], where the spectrums of the filtered data and their responding surrogate data are the same.

simple regression analysis. Kendall's rank correlation (denoted as τ) of clinical mood ratings, neuropsychological performance, and similarity index MBDGSI of different bands were calculated using software package SPSS version 13.0 (SPSS Inc., Chicago, IL). Simple linear regression analysis was used to provide the significance probability (denoted as p) between those indices as considered in Kendall's rank correlation.

The MBDGSIs for both groups and all four frequency bands are shown in Fig. 2(a). The MBDGSIs (i.e., delta, theta, alpha, and beta) were 0.0898 ± 0.0102, 0.0653 ± 0.0108, 0.0786 ± 0.0114, 0.0793 ± 0.0062 for normal subjects and 0.1092 ± 0.0169, 0.0637 ± 0.0122, 0.0675 ± 0.0103, 0.0662 ± 0.0114 for bipolar patients, respectively. The box has lines at the lower quartile, median and upper quartile values. Outliers ('+') are data with beyond the ends of the whiskers. The whiskers are to show the extent of the rest of the data. Two-way mixed ANOVA (2 groups $\times$ 2 genders) analysis for these four bands showed no significant main effect of group, gender, or interaction between group and gender, except the significant main effect of groups in beta band ($F[1, 16] = 14.72$; $p = 0.0015 < 0.01$). The gender effect was thus ignored. Compared with normal subjects by one-way ANOVA, BD patients had significantly higher MBDGSI values for delta band ($F[1, 18] = 8.75$; $p = 0.0084$) and significantly lower MBDGSI values for beta band ($F[1, 18] = 9.29$; $p = 0.0069$). For the theta and alpha bands, there were no significant group effects ($F[1, 18] = 0.08$; $p = 0.7773$ and $F[1, 18] = 4.75$; $p = 0.0448$). It means that BD patients had a significantly lower interdependence in the beta band and a significantly higher interdependence in the delta band.

Two neuropsychological tests revealed significant deficits of BD patients as compared with normal control ($p < 0.01$ by two-sample t-test), including 2-back omission in working memory (35 ± 6 vs. 38 ± 5) and divided attention (898 ± 95 vs. 801 ± 95). For normal subjects, there was no significant correlation between different bands. Positive correlations between beta and divided attention ($\tau = 0.479$, $p = 0.075$), and also 2-back omission ($\tau = 0.567$, $p = 0.059$) were found but did not reach statistical significance. For bipolar patients, there was a positive correlation between the MBDGSIs of delta and beta bands ($\tau = 0.539$, $p = 0.031$). The MBDGSI of theta band was negatively correlated with HAMD17 ($\tau = -0.596$, $p = 0.022$, near significant) ratings. As for correlation with neuropsychological performance, the MBDGSI of beta band was positively correlated with perseverative errors of WCST ($\tau = 0.506$, $p = 0.046$) and the MBDGSI of alpha band was negatively correlated with behavioral results of divided attention ($\tau = -0.42$, $p = 0.089$). Both did not reach statistical significance. Fig. 2(b) illustrated the results of simple regression analysis between (left panel) the MBDGSIs of beta and delta bands (positive correlation, $p = 0.0299$), (middle panel) HAMD17 and theta's MBDGSIs (negative correlation, $p = 0.0504$), and (right panel) perseverative errors of WCST and beta's MBDGSIs (positive correlation, $p = 0.0453$). These three results are consistent with those of Kendall's rank correlation.

In this study, we used the method based on 'similarity index' to investigate the synchronization of neural oscillations during resting condition without a task in the frontal regions of BD patients and normal controls. The measures of synchronization between different time series (from different channels of MEG or EEG) provide information about the interaction of these functional networks that can be modulated or altered under various cognitive challenges or diseased states, which in turn may be characterized by hypersynchronization (e.g., seizure attacks) or hypo-synchronization (e.g., neuro-degenerative disease). The changes can be discordant in different frequency band [24]. In the literature, cross correlation function and coherence function are two widely used methods for detecting interdependence between channel pairs in the time domain and the frequency domain, respectively. However, these methods are linear and hence are limited to the detection of linear features of biological signals. In our previous study using average relative power spectra analysis for all cortical regions, we found that only the delta power at frontal region in BD patients group was significantly increased [27]. Whereas, the results in this work showed that the patients with BD were characterized by not only increased synchronization of delta and but also decreased synchronization of beta oscillations in the frontal region, which is compatible with the assertion, and may implicate a dynamic change of various emotional status and cognitive impairment that can possibly be related to the clinical manifestations in patients with BD.

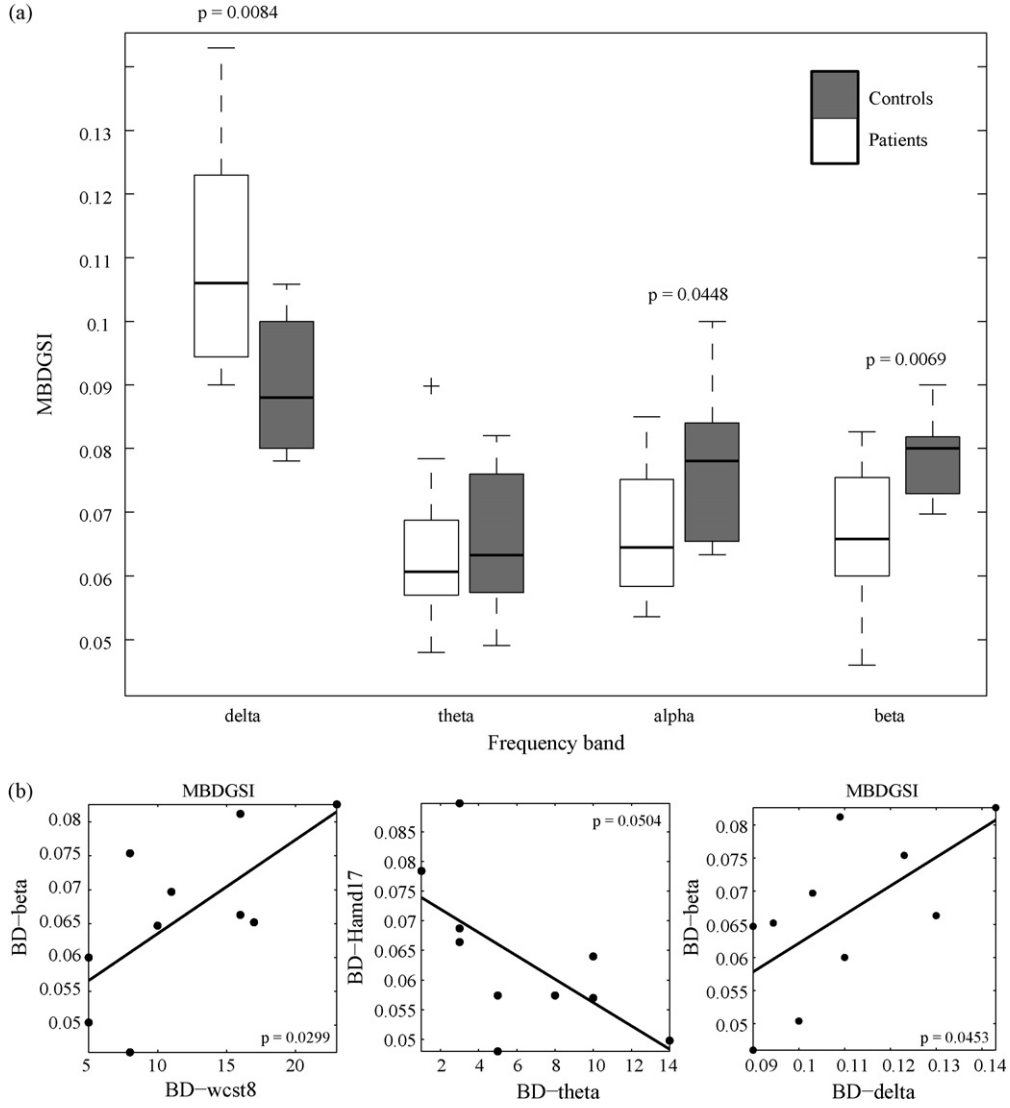

Fig. 2. Illustration of MBDGSIs difference between BD patients and healthy controls and the corresponding correlation with neuropsychological tests. (a) Shows the boxplot for the MBDGSIs of BD patients and control subjects for MEG data filtered at four bands, delta (2–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–24 Hz), respectively. BD patients have a significantly lower interdependence in beta band, and have a significantly higher interdependence in delta band. p values were shown in the plot. (b) Illustrates simple regression results between (left) the MBDGSIs of beta and delta bands (positive correlation, $p = 0.0299$), (middle) HAMD17 and the MBDGSIs of theta band (negative correlation, $p = 0.0504$), and (right) perserverative errors of WCST and the MBDGSIs of beta band (positive correlation, $p = 0.0453$) for BD patient group.

Previous studies have localized resting delta generators to the medial prefrontal, nucleus accumbens, and ventral tegmental areas [15,17]. These areas are believed to subserve the function of reward systems and can be modulated by dopamine. Increased delta activity was found in different states of reward deficiency and craving, in hypoglycemia induced by intravenous infusion of regular insulin, during sexual arousal, or after a single administration of testosterone [11,22,26]. In this study, our finding of significantly increased delta synchronization in BD patients might tentatively connote a possible subclinical dysfunction of motivation and reward system, which can be manifested by aggressiveness, impulsiveness or overt pleasure seeking during symptomatic episodes.

Theta oscillation was hypothesized to be a limbic rhythm and generated by the structures of anterior cingulate, and hippocampus. It was found to be closely related to emotional reactions in previous studies [1,2]. We in this study found theta synchronization was positive correlated with the mood ratings of HAMD17 but there was no significant difference of the MBDGSIs of theta band between normal subjects and bipolar patients. We thus hypothesized that theta synchronization might be more sensitive to state-related changes in emotions than trait related abnormalities in patents group.

Increased power of alpha oscillation was observed under various cognitive tasks requiring internal attention such as mental imagery, working memory and mental arithmatics [18]. Recent clinical observations showed that decreased alpha power could be associated with patients of attentional deficit disorder [7]. However, we failed to find significant decreased alpha synchronization or correlation between resting alpha synchronization and attentional performance in bipolar patients. The results may arise because previous studies used alpha power to correlate with cognitive measures, while here we used SIs (an index of disintegration among functionally concerted brain regions).

Delta and alpha oscillations are hypothesized to be reciprocally related to each other and the reciprocal relationship may reflect an inhibitory control of executive functions over motivational and emotional drives by prefrontal cortex [13]. Prefrontal cortex participates in balancing cognitive functions (associated with alpha oscillation) and motivational drives (linked with delta oscillations).

A deficient alpha and/or increased delta activity can be associated with cognitive deficits and a lack of inhibitory control. This is compatible with the results of various neuropsychological evaluations and clinical findings that decrease executive control and increased emotional reactivity in BD patients, even in euthymic phase [9]. Our findings of increased delta synchronization may pertain a neuronal correlate of prefrontal cortex dysfunction in our BD patients.

Beta band synchronization was also found to be decreased in the BD patients. In addition, there was a positive correlation between the MBDGSIs of delta and beta band in the patients group. Increased delta–beta coupling was found in people of high cortisol level in salivary or high anxious apprehension [14,22]. It was hypothesized that such coupling reflected a co-activation of behavioral activation and behavioral inhibition system and increased interaction of subcortical and cortical interaction. Our findings suggested that the characteristic symptoms of fluctuation between extreme high and low mood states in BD patients may be related to abnormal interaction of behavioral activation and inhibition system. Furthermore, a positive correlation between the MBDGSI of beta band and WCST perserverative errors was found in the patient group. It implicates that beta synchronization may be related to the deficit of executive function in the BD patients.

The aim of this study was to use MBDGSI to investigate neural dynamic modulation in BD. Our interpretation is constrained by several limitations. First, all of our patients used and wide range of anticonvulsant and antipsychotics of various dosages. Previous studies about the effects of lithium and anticonvulsants on EEG power provided inconsistent results [16,23]. Marciani et al. found that the EEG background activities of all frequency bands were not modified by the addition of the lamotrigine drug in the epileptic population [16]. Smith et al. evaluated the resting EEG of healthy adults and found lamotrigine reduced EEG power most prominently in the 6–12 Hz frequency range [23]. Although the influence of these medications on the MBDGSI is currently not certain, it can be a discernible confound. Furthermore because of the variety of medication and the small numbers of patients taking each drug combination, detailed analysis of the effects of each type of drug was difficult in our study. Further studies are needed to clarify the pharmacological effects. Second, the patients in our study were all in remission phase. Thus the proposed nonlinear measurements may reflect an organic trait in delta and beta bands, or state-related expression in theta band of brain dynamics. Studies on patients of different mood states are required to further elucidate the state-dependent factors in the neural synchronization of BD. Third, due to huge computation complexity, only sensors located at brain frontal regions were analyzed in this study. Further investigation of synchronization between different regions such as frontal and temporal regions would be needed.

We observed increased delta synchronization and decreased beta synchronization in the frontal regions of bipolar patient. Considering the respective functions subserved by different oscillations, the results implicated possible dysfunctions of inhibitory and executive control mechanisms. Our findings demonstrate the potentiality of using nonlinear dynamic approaches to disclose the subtle changes of neural dynamics in BD.

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References

[1] L.I. Aftans, S.V. Pavlov, N.V. Reva, A.A. Varlamov, Trait anxiety impact on the EEG theta band power changes during appraisal of threatening and pleasant visual stimuli, Int. J. Psychophysiol. 50 (2003) 205–212.
[2] L.I. Aftans, A.A. Varlamov, S.V. Pavlov, V.P. Makhnev, N.V. Reva, Affective picture processing: event-related synchronization within individually defined human theta band is modulated by valence dimension, Neurosci. Lett. 303 (2001) 115–118.
[3] L.L. Altshuler, S.Y. Bookheimer, J. Townsend, M.A. Proenza, N. Eisenberger, F. Sabb, J. Mintz, M.S. Cohen, Blunted activation in orbitofrontal cortex during mania: a functional magnetic resonance imaging study, Biol. Psychiatry 58 (2005) 763–769.
[4] J. Arnhold, P. Grassberger, K. Lehnertz, C.E. Elger, A robust method for detecting interdependencies: application to intracranially recorded EEG, Physica D 134 (1999) 419–430.
[5] B. Bahrami, R. Seyedsadjadi, B. Babadi, M. Noroozian, Brain complexity increases in mania, Neuroreport 16 (2005) 187–191.
[6] M. Breakspear, The nonlinear theory of schizophrenia, Aust. N. Z. J. Psychiatry 40 (2006) 20–35.
[7] A.R. Clarke, R.J. Barry, R. McCarthy, M. Selikowitz, Children with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder: an EEG analysis, Psychiatry Res. 111 (2002) 181–190.
[8] T. Glenn, P.C. Whybrow, N. Rasgon, P. Grof, M. Alda, C. Baethge, M. Bauer, Approximate entropy of self-reported mood prior to episodes in bipolar disorder, Bipolar Disord. 8 (2006) 424–429.
[9] M.J. Green, C.M. Cahill, G.S. Malhi, The cognitive and neurophysiological basis of emotion dysregulation in bipolar disorder, 103 (2007) 29–42.
[10] S.A. Gruber, J. Rogowska, D.A. Yurgelun-Todd, Decreased activation of the anterior cingulate in bipolar patients: an fMRI study, J. Affect. Disord. 82 (2004) 191–201.
[11] R.G. Heath, Pleasure and brain activity in man. Deep and surface electroencephalograms during orgasm, J. Nerv. Ment. Dis. 154 (1972) 3–18.
[12] M. Kameyama, M. Fukuda, Y. Yamagishi, T. Sato, T. Uehara, M. Ito, T. Suto, M. Mikuni, Frontal lobe function in bipolar disorder: a multichannel near-infrared spectroscopy study, Neuroimage 29 (2006) 172–184.
[13] G.G. Knyazev, Motivation, emotion, and their inhibitory control mirrored in brain oscillations, Neurosci. Biobehav. Rev. 31 (2007) 377–395.
[14] G.G. Knyazev, D.J.L.G. Schutter, J. van Honk, Anxious apprehension increases coupling of delta and beta oscillations, Int. J. Psychophysiol. 61 (2006) 283–287.
[15] L.S. Leung, C.Y. Yim, Rhythmic delta-frequency activities in the nucleus accumbens of anesthetized and freely moving rats, Can. J. Physiol Pharmacol. 71 (1993) 311–320.
[16] M.G. Marciani, F. Spanedda, M.A. Massetti, M. Maschi, G.L. Gigli, D. Mattia, G. Bernardi, Effect of lamotrigine on EEG paroxysmal abnormalities and background activity: a computerized analysis, Br. J. Clin. Pharmacol. 42 (1996) 621–627.
[17] C.M. Michel, D. Lehmann, B. Henggeler, D. Brandeis, Localization of the sources of EEG delta, theta, alpha and beta frequency bands using the FFT dipole approximation, Electroencephalogr. Clin. Neurophysiol. 82 (1992) 38–44.
[18] S. Palva, J.M. Palva, New vistas for alpha-frequency band oscillations, Trends Neurosci. 30 (2007) 150–158.
[19] M.P. Paulus, D.L. Braff, Chaos and schizophrenia: does the method fit the madness? Biol. Psychiatry 53 (2003) 3–11.
[20] E. Pereda, R. Rial, A. Gamundi, J. Gonzalez, Assessment of changing interdependencies between human electroencephalograms using nonlinear methods, Physica D 148 (2001) 147–158.
[21] T. Schreiber, A. Schmitz, Surrogate time series, Physica D 142 (2000) 346–382.
[22] D.J. Schutter, J. van Honk, Decoupling of midfrontal delta-beta oscillations after testosterone administration, Int. J. Psychophysiol. 53 (2004) 71–73.
[23] M.E. Smith, A. Gevins, L.K. McEvoy, K.J. Meador, P.G. Ray, F. Gilliam, Distinct cognitive neurophysiologic profiles for lamotrigine and topiramate, Epilepsia 47 (2006) 695–703.
[24] C.J. Stam, Nonlinear dynamical analysis of EEG and MEG: review of an emerging field, Clin. Neurophysiol. 116 (2005) 2266–2301.
[25] F. Takens, Dynamical Systems and Turbulence, Springer-Verlag, 1981, 366 pp.
[26] G. Tallroth, M. Lindgren, G. Stenberg, I. Rosen, C.D. Agardh, Neurophysiological changes during insulin-induced hypoglycaemia and in the recovery period following glucose infusion in type 1 (insulin-dependent) diabetes mellitus and in normal man, Diabetologia 33 (1990) 319–323.
[27] P. Tu, L.F. Chen, T.Y. Liu, Y.H. Chou, J.C. Hsieh, T.P. Su, Increased slow delta oscillations in frontal cortex of patients with bipolar disorder: a MEG study, in: Proceedings of the 13th Annual Meeting of the Organization for Human Brain Mapping, Chicago, IL, 2007.
[28] F. Varela, J.P. Lachaux, E. Rodriguez, J. Martinerie, The brainweb: phase synchronization and large-scale integration, Nat. Rev. 2 (2001) 229–239.