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qEEG / LORETA in Assessment of Neurocognitive Impairment in a Patient with Chronic Fatigue Syndrome: A Case Report

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Abstract

Importance: Chronic Fatigue Syndrome (CFS) is a chronic disease resulting in considerable and widespread cognitive deficits. Accurate and accessible measurement of the extent and nature of these deficits can aid healthcare providers and researchers in the diagnosis of this condition, choosing interventions and tracking treatment effects. Here, we present a case of a middle-aged man diagnosed with CFS which began following a typical viral illness.

Observations: LORETA source density measures of surface EEG connectivity at baseline were performed on 3 minutes of eyes closed de-artifacted19-channel qEEG. The techniques used to analyze the data are described along with the hypothesized effects of the deregulation found in this data set. Nearly all (>90%) patients with CFS complain of cognitive deficits such as slow thinking, difficulty in reading comprehension, reduced learning and memory abilities and an overall feeling of being in a "fog."Therefore, impairment may be seen in deregulated connections with other regions (functional connectivity); this functional impairment may serve as one cause of the cognitive decline in CFS. Here, the functional connectivity networks of this patient were sufficiently deregulated to cause the symptoms listed above.

Conclusions and significance: This case report increased our understanding of CFS from the perspective of brain functional networks by offering some possible explanations for cognitive deficits in patients with CFS. There are only a few reports of using source density analysis or qEEG connectivity analysis for cognitive deficits in CFS. While no absolute threshold exists to advise the physician as to when to conduct such analyses, the basis of his or her decision whether or not to use these tools should be a function of clinical judgment and experience. These analyses may potentially aid in clinical diagnosis, symptom management, treatment response and can alert the physician as to when intervention may be warranted.

Keywords: qEEG; LORETA; Source analysis; Chronic fatigue syndrome; Phase lag; Phase shift; Phase reset; Phase; Coherence; Cognitive impairment

Introduction

Chronic fatigue syndrome (CFS) is a major health condition that is associated with numerous body system dysregulation, including substantial cognitive deficits in more than 90% of patients, affecting over 17 million people worldwide, and about 1 million people in the United States alone [1-3]. As such, CFS represents a significant economic burden to society, greatly decreased quality of life for patients and considerable morbidity [4]. This contrasts with a relatively sparse neuropsychological research base for this disorder, documenting only modest levels of cognitive deficits [5-7] through neuropsychological testing [6] and other types of neuroimaging techniques [8]. These testing and imaging reports, however, do indicate some deficits involving attention and concentration, memory, and information processing speed [6,8-10], though patients tend to report much higher levels and more varied types of impairment than is reported in research literature.

Measures which address neural dynamics with a high time resolution can be co-registered to the MRI and PET and SPECT images, providing a millisecond analysis of brain neural activity, which can be easily compared to studies using other modalities. qEEG/LORETA measures are the only such modalities which capture this millisecond time scale activity [11-13]. A much more thorough understanding of cognitive deficits in neurocognitive disorders will require the depiction of the rapid coupling that takes place in neural oscillations on a millisecond timescale [14,15]. Using LORETA (source analysis of the qEEG signal) [16], the spatial resolution is about 1-3 cm and in qEEG the spatial resolution is about 1 cubic centimeter [17]. The maximum spatial resolution of fMRI is a little less than 1 cm, which is only slightly higher than qEEG or LORETA [16,18,19]. The advantage of using qEEG or LORETA is the greatly decreased cost and the considerably superior temporal resolution [11,18,20]. qEEG measures for connectivity analysis lack the spatial resolution of LORETA source analysis, but have the same temporal resolution, providing inexpensive and easy to interpret brain function [20].

qEEG and eLORETA measures [21-24] have found significantly deregulated delta sources (1-4 Hz) in widespread bi-lateral portions of the frontal lobe and limbic lobe regions as well as deregulated beta activity in posterior parietal regions in CFS. The co-occurrence of cortical hypoactivation in these brain regions provides empirical evidence for a neurobiological basis pertaining to patient symptomology including impairment in higher brain functions. Research [22] has found surface qEEG effects of peak alpha frequency (PAF), computed within the 8-12 Hz frequency band based on each participant's EEG indicating significantly decreased PAF over 58% of the entire cortex in patients with CFS when compared to controls (11 electrode sites, $p < 0.05$). These findings are consistent with previous reports of reduced efficiency of thalamocortical

connections in cognitive impairment [25-30] and suggest that EEG-PAF measurement may have both diagnostic and prognostic value in patients [31,32]. There is now a need to better capture dynamic relationships to understand a number of cognitive domains where CFS deficits have been found.

The human brain creates meaning, cognition and perception by way of continuous information flow which changes within milliseconds, and then evaluates matches and mismatches of those expectations against current sensory information available [13,15,33,34]. This process, based on prior experience (memories, learning history) and genetics, creates the expectations. Attention and arousal are produced when a novel event occur followed by excitation of the reticular formation which then promotes excitatory activity in the cortex [35,36]. During attention, the brain first filters out irrelevant information, then continues to process the relevant information [37-39]. This type of reductive decision making is essential to operate in the world. When this process is compromised in disease or injury, attention deficits, anxiety problems, and other negative states are created due to limited resource allocation efficiency. The switching dynamics-known as phase reset--phase shift and phase lock of rhythm patterns--form homeostasis to support normal brain function. Instabilities or disruptions in the homeostasis, in this system have been associated with pathology such as autism [40], epilepsy [41], cognitive deficits [42], and traumatic brain injury [43].

A review of the literature demonstrates that this system, known as EEG coherence (an overall functional connectivity measure) is related to a mixture of phase locking interrupted by phase shifts in the spontaneous EEG, operating through phase reset synchronization mechanisms (phase shift and phase lock duration) [44-49]. These fundamental brain mechanisms operate continually in flux at various frequencies across nodes of networks during the execution of any behavioral or cognitive task. Canavier and colleagues [50,51] demonstrate that phase-reset (phase lock followed by phase shift) represents our thoughts, feelings, and actions via coordination between mutually connected, phase coupled, brain regions. More importantly, Frey and colleagues [51] demonstrate the effect of phase reset on human cognition, especially in clinical disorders. Phase reset (phase shift and phase lock) are therefore fundamental brain mechanisms which underlie the physiological basis of the cycle described above.

Phase reset is made up of the two main physiological processes which make up phase reset [29,51]. Phase lock synchronizes millions of neurons across domains or networks within periods of 100-600 milliseconds. Phase shift then releases the locked synchronization and recruits a new set of neurons [17,40,51,52]. Phase shift allocates all available neurons for performing a given function and typically varies between 40 and 80 milliseconds in length. Longer phase lock periods have been found to be inversely correlated with intelligence due to the brief increase in committed neurons which create a momentary reduction in neurons, and phase shift has been shown to positively correlate with intelligence [52,53]. The following case report explores several of the issues reviewed above using qEEG/LORETA with a patient with CFS. We hypothesized that we would see overall, global deregulation, especially in the frontal, frontal-parietal and temporal lobes, as well as in limbic centers such as the anterior cingulate, along with disrupted surface connectivity.

Report of a Case

A 43-year-old male patient diagnosed with prior CFS was assessed with qEEG/LORETA as his request. This individual had been diagnosed with CFS by his physician, using the DePaul Symptom Inventory, and met the Canadian Clinical Case definition. Individuals with CFS typically report multiple cognitive complaints including many types of memory issues (working memory, metamemory, explicit memory, long-term storage and retrieval, etc.), decreased learning ability, slowed thought, difficulty with navigation (many cannot drive an automobile), problems with concentration and attention and general, overall decreased alertness known as "cognitive fog."This individual had these types of neurocognitive impairments, along with other classic CFS symptoms such as post-exertional malaise and sleep impairment. IRB approval from DePaul University was obtained to do this study.

Three minutes of eyes-closed resting EEG was recorded with Neuroguide software (version 2.7.4) with a 19-channel Electro-cap (Electro-Cap International, Easton, OH) positioned according to the International 10/20 system of electrode placement. Electrodes were referenced to linked ears with impedances below 5k ohms and the linked ears montage was used in data analysis. Data acquisition was obtained using a Discovery 24E amplifier (BrainMaster Technologies, Bedford, OH) at 256Hz sample rate with a 60Hz low-pass filter. Offline analysis was then conducted with Neuroguide software using automated detection and rejection of epochs containing any muscle, drowsiness, and movement artifact after "eyeballing" the data set to look for any type of gross abnormalities in the data. Raw data then was re-examined after the automatic processing of artifact removal. Two minutes and 37-seconds of artifact-free data were selected from the record, exceeding the 40-second minimum needed to obtain a high reliability coefficient of 0.90. Neuroguide was also used to compute reliability coefficients for each electrode site within each record; split half and test-retest reliability coefficients were kept above 0.95. After examining qEEG measures, we then computed LORETA to localize deeper cortical sources of scalp EEG activity with comparison to qEEG norms.

This case report outlines the cortical source effects for CFS. First, the LORETA source analysis illustrates abnormal source density at 2Hz (delta) (Figure 1), indicating an overall decrease of cortical activation associated with large-scale cortical integration which affects attention, arousal and more recently, greater psychological pain orthogonal to depression [54] operating through thalamocortical networks. It is important to note that all levels of consciousness (including sleep/coma) are comprised during slow cortical potentials (we found significant decreases in all rhythms, 1-30Hz but present only delta 2Hz and beta 12-15Hz here), creating overall deficits in arousal, attention, processing speed, integration and other cognitive processes [11,30]. We hypothesize that this overall decreased arousal may contribute to the often-reported state of brain fog in CFS. Second, the surface qEEG connectivity analysis illustrates a higher rate of phase resets per second than normal in beta (Figure 2) producing information transfer that is deregulated within neocortical local and long-distance circuits. For phase shift and phase lock duration, when both of these processes are significantly shorter, fewer neuronal resources are allocated for subsequent phase lock periods. These processes were authenticated in this data (Figure 2); i.e., too-fast phase shift followed by too-short phase lock which has been shown elsewhere to lead to inefficiency as a function of time.

Conclusions

Our case study confirmed the pattern of dysregulation in the cortex reviewed in the introduction. Furthermore, since both periods of phase shift/lock durations were found to be significantly shorter, that might contribute to an increased rate of phase reset, also seen in our data. Phase reset deregulation--phase locking periods being too brief and phase reset happening too often—appear to be consistent with the associated lower rate of information processing and reaction times found in the ME and CFS literature. These deregulated states represent the brain during non-optimal functioning, rendering it inefficient for most types of information processing functioning, whether it is executive functioning, memory, perceptual reasoning or information processing speed. When phase lock is significantly less than normal, as in this data set, the ability of the brain to

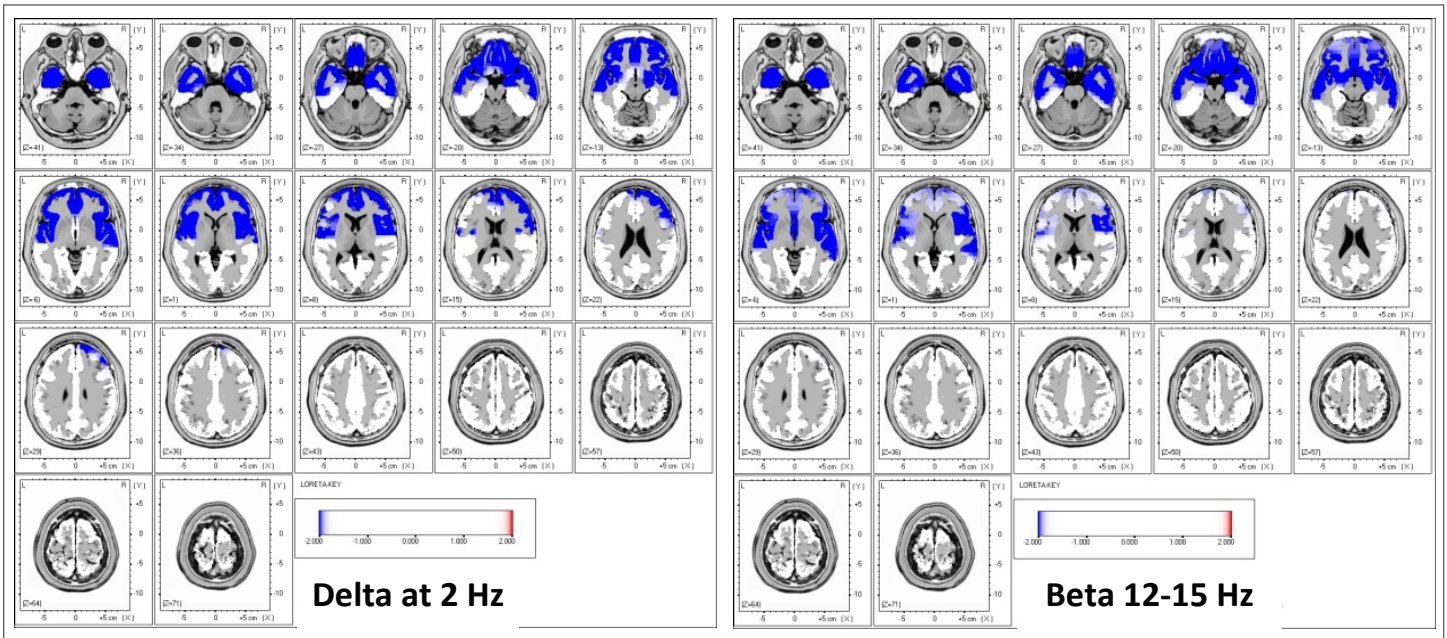

Figure 1: Results of LORETA current source density in a case with CFS showing widespread decreased current density for delta at 2 Hz and beta (12-15 Hz) demonstrating a global reduction in brain functioning (blue). The higher frequencies (beta) have been shown to be a function of delta frequencies. In other words, local oscillations are under constant influence of global brain dynamics (Buzsaki, 2006).

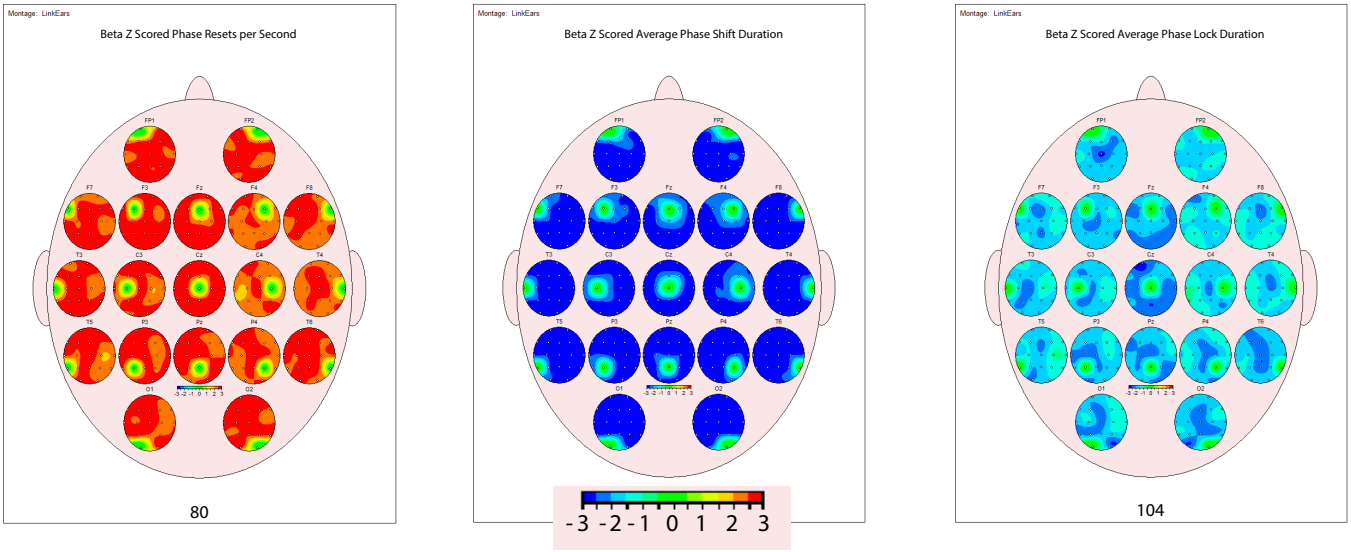

Figure 2: Surface qEEG connectivity topographs showing 3 aspects of phase reset in a case with CFS: z-scored resets per second, phase shift duration and phase lock duration. All three metrics were found to be significantly deviant from normal in beta (12-25 Hz). Red color indicates 3 standard deviations above, blue color indicates 3 standard deviations below. Rapid phase reset combined with shortened phase shifting and phase locking periods demonstrates a global decrease in neuronal resource allocation and inefficient information processing speed

sustain commitment of resources to mediate different functions is severely compromised. Phase shift duration in this data is also hypoactive, meaning that significantly less neurons are being recruited to perform a function than normal. The results here indicate slowed verbal comprehension, executive functions, perceptual reasoning, processing speed and memory, the sum total of which is known as cognitive impairment.

Patients with CFS often report premorbid functioning to be much more efficient, quicker, and complex than their functioning after becoming ill. Unfortunately, due to the sharp contrast between patient report and research findings, there is a pervasive lack of consistency in measurement of cognitive impairment in this population. This situation has stalled forward movement by fostering the incorrect notion that cognitive deficits faced by patients with CFS are created by psychological and emotional factors and have little or no physiological pathology [55]. Using qEEG/LORETA methods may provide a vehicle whereby the patients' symptoms and complaints can be validated by analyzing both surface and deeper

electric current sources occurring within the brain in 3 dimensions [56-58]. This study involved only one patient, so until it is replicated with larger samples, the results need to be considered preliminary.

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References

1. Grafman J, Schwartz V, Dale JK, Scheffers M, Houser C, et al. (1993) Analysis of neuropsychological functioning in patients with chronic fatigue syndrome. J Neurol Neurosurg Psychiatry. 56: 684-689.
2. Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, et al. (1999) A community-based study of chronic fatigue syndrome. Arch Intern Med 159: 2129-2137.
3. Komaroff AL, Buchwald D (1991) Symptoms and signs of chronic fatigue syndrome. Rev Infect Dis 13: S8-S11.
4. Jason LA, Benton MC, Valentine L, Johnson A, Torres-Harding S (2008) The economic impact of ME/CFS: individual and societal costs. Dyn Med. **7**: 6.
5. Attree EA, Arroll MA, Dancey CP, Griffith C, Bansal AS (2014) Psychosocial factors involved in memory and cognitive failures in people with myalgic encephalomyelitis/chronic fatigue syndrome. Psychol Res Behav Manag. **7**: 67-76.
6. Cockshell SJ, Mathias JL (2014) Cognitive functioning in people with chronic fatigue syndrome: a comparison between subjective and objective measures. Neuropsychology 28: 394-405.
7. Frank GH, John DeLuca (2007) Functional Neuroimaging in Clinical Populations. The Guilford Press, New York, London.
8. DeLuca J, Genova HM, Capili EJ, Wylie GR (2009) Functional neuroimaging of fatigue. Phys Med Rehabil Clin N Am. 20: 325-337.
9. Cockshell SJ, Mathias JL (2010) Cognitive functioning in chronic fatigue syndrome: a meta-analysis. Psychol Med. 40: 1253-1267.
10. Fumiharu Togo, Gudrun Lange, Benjamin H. Natelson, Karen S. Quigley (2013) Attention network test: Assessment of cognitive function in chronic fatigue syndrome. J Neuropsychol 9: 1-9.
11. Buzsaki G (2006) Rhythms of the Brain. Oxford University Press.
12. Zuo XN, Di Martino A, Kelly C, Shehzad ZE, Gee DG, et al. (2010) The oscillating brain: complex and reliable. Neuroimage 49: 1432-1445.
13. Rabinovich MI, Afraimovich VS, Bick C, Varona P (2012) Information flow dynamics in the brain. Phys Life Rev. 9: 51-73.
14. Menon V (2011) Large-scale brain networks and psychopathology: a unifying triple network model. Trends Cogn Sci. 15: 483-506.
15. Menon V (2012) Functional connectivity, neurocognitive networks, and brain dynamics. In: MI Rabinovich, KJ Friston, P Varona (eds) Principles of Brain Dynamics: Global State Interactions, MIT Press, Cambridge 27-47.
16. Pascual-Marqui RD, Michel CM, Lehmann D (1994) Low-resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. Int J Psychophysiol. 18: 49-65.
17. Thatcher RW (2012) Handbook of Quantitative Electroencephalography and EEG Biofeedback. Ani Publishing, St. Petersburg, FL.
18. Nunez PL, Srinivasan R, Fields RD (2014) EEG functional connectivity, axon delays and white matter disease. Clinical Neurophysiology. 26: 110-120.
19. Steriade M, Nunez A, Amzica F (1993) Intracellular analysis of relations between the slow (< 1 Hz) neocortical oscillation and other sleep rhythms of the electroencephalogram. J Neurosci. 13: 3266-3283.
20. Thatcher RW (2011) Neuropsychiatry and quantitative EEG in the 21st Century. Future Medicine 1: 495-514.
21. Zinn MA (2014) Cortical hypoactivation during resting EEG suggests central nervous system pathology in patients with Chronic Fatigue Syndrome. In Symposium conducted at the meeting of IACFS/ME 2014 Biennial Conference. San Francisco, CA, USA.
22. Zinn ML (2014) EEG Peak Alpha Frequency Correlates in Chronic Fatigue Syndrome: A Case-Control Observational Study. in IACFS/ME 2014 Biennial Conference. San Francisco, CA, USA.
23. Flor-Henry P, Lind JC, Koles ZJ (2010) EEG source analysis of chronic fatigue syndrome. Psychiatry Res. 181: 155-164.
24. Sherlin L, Budzynski T, Kogan Budzynski H, Congedo M, Fischer ME, et al. (2007) Low-resolution electromagnetic brain tomography (LORETA) of monozygotic twins discordant for chronic fatigue syndrome. Neuroimage. 34: 1438-1442.
25. Klimesch W (2012) α-band oscillations, attention, and controlled access to stored information. Trends Cogn Sci. 16: 606-617.
26. Klimesch W (1997) EEG-alpha rhythms and memory processes. Int J Psychophysiol. 26: 319-40.
27. Klimesch W (1999) EEG-alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev 29: 169-195.
28. Klimesch W, Doppelmayr M, Pachinger T, Ripper B (1997) Brain oscillations and human memory: EEG correlates in the upper alpha and theta band. Neurosci Lett. 238: 9-12.
29. Klimesch W, Freunberger R,Sauseng P (2010) Oscillatory mechanisms of process binding in memory. Neurosci Biobehav Rev. 34: 1002-1014.
30. Steriade M (2006) Grouping of brain rhythms in corticothalamic systems. Neuroscience 137: 1087-1106.
31. Angelakis E, Lubar JF, Stathopoulou S (2004) Electroencephalographic peak alpha frequency correlates of cognitive traits. Neurosci Lett 371: 60-63.
32. Angelakis E, Lubar JF, Stathopoulou S, Kounios J (2004) Peak alpha frequency: an electroencephalographic measure of cognitive preparedness. Clin Neurophysiol. 115: 887-897.
33. Deco G, Jirsa V, Friston KJ (2012) The dynamical structural basis of brain activity, In: Rabinovich MI, Friston K, Varona P (eds) Principles of Brain Dynamics: Global State Interactions, MIT Press: Cambridge, MA 1-23.
34. Rabinovich MI, Friston K, Varona P (2012) Principles of Brain Dynamics: Global State Interactions. The MIT Press, Cambridge, MA.
35. Steriade M, Gloor P, Llinás RR, Lopes de Silva FH, Mesulam MM (1990) Report of IFCN Committee on Basic Mechanisms. Basic mechanisms of cerebral rhythmic activities. Electroencephalogr Clin Neurophysiol. 76: 481-508.
36. Steriade M, McCarley RW (2005) Brain control of wakefulness and sleep. New York: Springer.
37. Fuster JM (2009) The Prefrontal Cortex. 4th edition, Elsevier.
38. Fuster JM (2006) The cognit: A network model of cortical representation. Int J Psychophysiol. 60: 125-132.
39. Fuster JM, Bressler SL (2012) Cognit activation: a mechanism enabling temporal integration in working memory. Trends Cogn Sci. 16: 207-218.
40. Thatcher RW, North DM, Neubrander J, Biver CJ, Cutler S, et al. (2009) Autism and EEG phase reset: deficient GABA-mediated inhibition in thalamo-cortical circuits. Dev Neuropsychol. 34: 780-800.
41. Chávez M, Le Van Quyen M, Navarro V, Baulac M, Martinerie J (2003) Spatio-temporal dynamics prior to neocortical seizures: amplitude versus phase couplings. IEEE Trans Biomed Eng. 50: 571-583.

42. Montez T, Linkenkaer-Hansen K, van Dijk BW, Stam CJ (2006) Synchronization likelihood with explicit time-frequency priors. Neuroimage 33: 1117-1125.

43. Thatcher RW, North DM, Curtin RT, Walker RA, Biver CJ, et al. (2001) An EEG severity index of traumatic brain injury. J Neuropsychiatry Clin Neurosci. 13: 77-87.

44. Agosta F, Pievani M, Geroldi C, Copetti M, Frisoni GB, et al. (2012) Resting state fMRI in Alzheimer's disease: beyond the default mode network. Neurobiol Aging 33: 1564-1578.

45. Filippi M, Agosta F, Scola E, Canu E, Magnani G, et al. (2013) Functional network connectivity in the behavioral variant of frontotemporal dementia. Cortex. 49: 2389-2401.

46. Canuet L, Ishii R, Pascual-Marqui RD, Iwase M, Kurimoto R, et al. (2011) Resting-state EEG source localization and functional connectivity in schizophrenia-like psychosis of epilepsy. PLoS One 6: e27863.

47. Knyazev GG (2013) Comparison of spatial and temporal independent component analyses of electroencephalographic data: A simulation study. Clin Neurophysiol. 124: 1557-1569.

48. Knyazev GG, Savostyanov AN, Volf NV, Liou M, Bocharov AV (2012) EEG correlates of spontaneous self-referential thoughts: a cross-cultural study. Int J Psychophysiol. 86: 173-181.

49. Knyazev GG, Slobodskoj-Plusnin JY, Bocharov AV, Pylkova LV (2011) The default mode network and EEG alpha oscillations: an independent component analysis. Brain Res. 1402: 67-79.

50. Canavier CC (2015) Phase-resetting as a tool of information transmission. Curr Opin Neurobiol. 31: 206-213.

51. Frey JN, Ruhnau P, Weisz N (2015) Not so different after all: The same oscillatory processes support different types of attention. Brain Res. 1626: 183-197.

52. Thatcher RW, North D, Biver C (2005) EEG and intelligence: relations between EEG coherence, EEG phase delay and power. Clin Neurophysiol 116: 2129-2141.

53. Thatcher RW, North DM, Biver CJ (2008) Biver, Intelligence and EEG phase reset: a two-compartmental model of phase shift and lock. Neuroimage. 42: 1639-1653.

54. Meerwijk EL, Ford JM, Weiss SJ (2015) Resting-state EEG delta power is associated with psychological pain in adults with a history of depression. Biol Psychol 105: 106-114.

55. Twisk FN (2014) The status of and future research into Myalgic Encephalomyelitis and Chronic Fatigue Syndrome: the need of accurate diagnosis, objective assessment, and acknowledging biological and clinical subgroups. Front Physiol 5: 109.

56. Pascual-Marqui RD, Esslen M, Kochi K, Lehmann D, et al. (2002) Functional imaging with low-resolution brain electromagnetic tomography (LORETA): a review. Methods Find Exp Clin Pharmacol. 24 Suppl C: 91-95.

57. Pascual-Marqui RD, Lehmann D, Koenig T, Kochi K, Merlo MC, et al. (1999) Low-resolution brain electromagnetic tomography (LORETA) functional imaging in acute, neuroleptic-naive, first-episode, productive schizophrenia. Psychiatry Res 90: 169-179.

58. Pascual-Marqui RD, Lehmann D, Koukkou M, Kochi K, Anderer P, et al. (2011) Assessing interactions in the brain with exact low-resolution electromagnetic tomography. Philos Trans A Math Phys Eng Sci. 369: 3768-3784.