



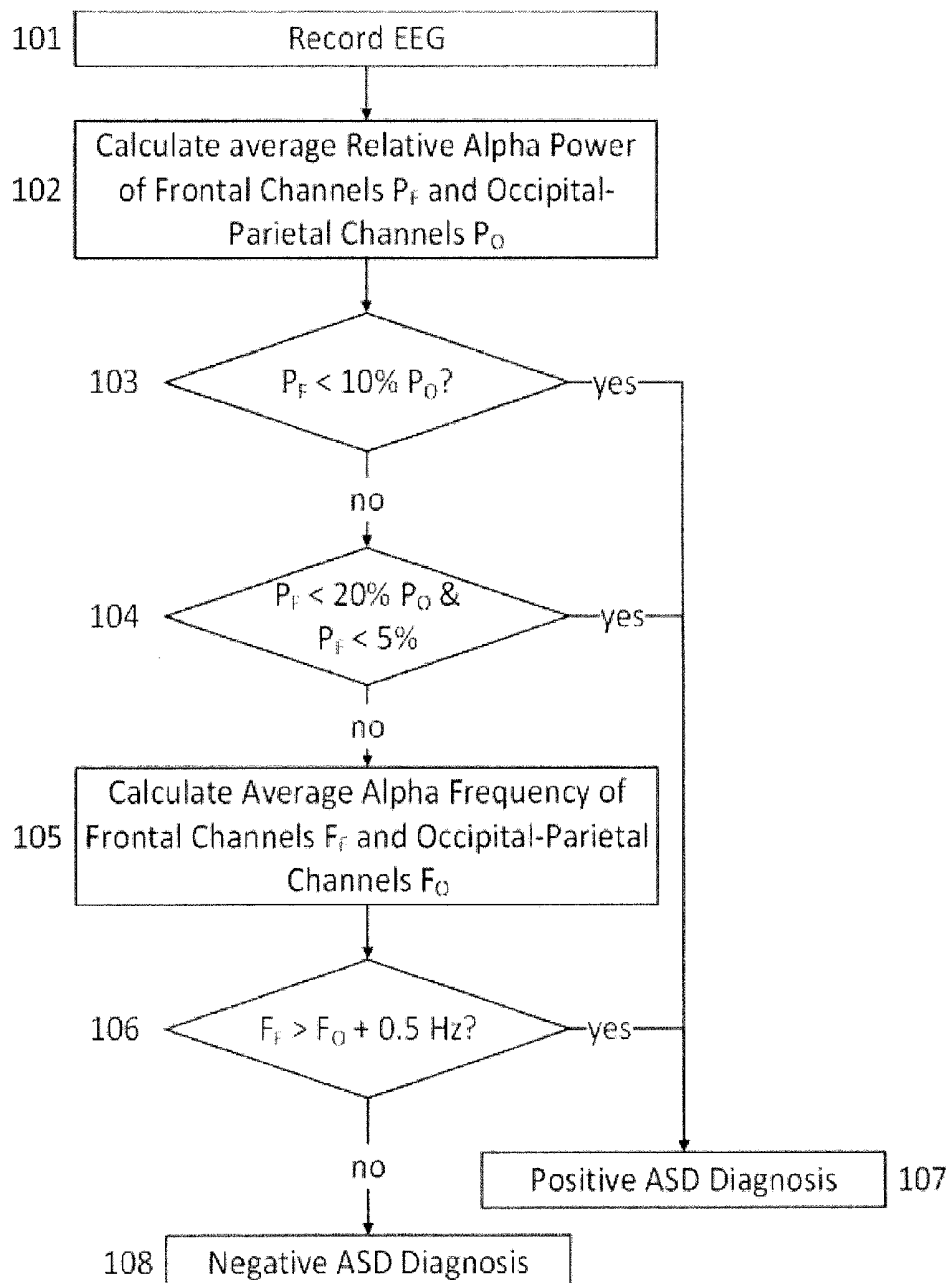
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(19) **United States**(12) **Patent Application Publication**
JIN(10) **Pub. No.: US 2017/0281030 A1**(43) **Pub. Date: Oct. 5, 2017**(54) **METHODS FOR DIAGNOSING MENTAL DISORDERS USING NEUROMETRICS****Publication Classification**(51) **Int. Cl.***A61B 5/048* (2006.01)*A61B 5/00* (2006.01)*A61B 5/16* (2006.01)(52) **U.S. Cl.**CPC *A61B 5/048* (2013.01); *A61B 5/165*(2013.01); *A61B 5/4088* (2013.01)(71) Applicant: **Kosivana Holdings Limited**, Limassol (CY)(72) Inventor: **Yi JIN**, Irvine, CA (US)(21) Appl. No.: **15/087,209**(22) Filed: **Mar. 31, 2016**

(57)

ABSTRACT

Described are novel methods for the diagnosis of specific mental disorders using neurometrics. EEG parameters are compared to thresholds to determine if a person is suffering from autism spectrum disorder, Alzheimer's disease, anxiety, depression, or schizophrenia.



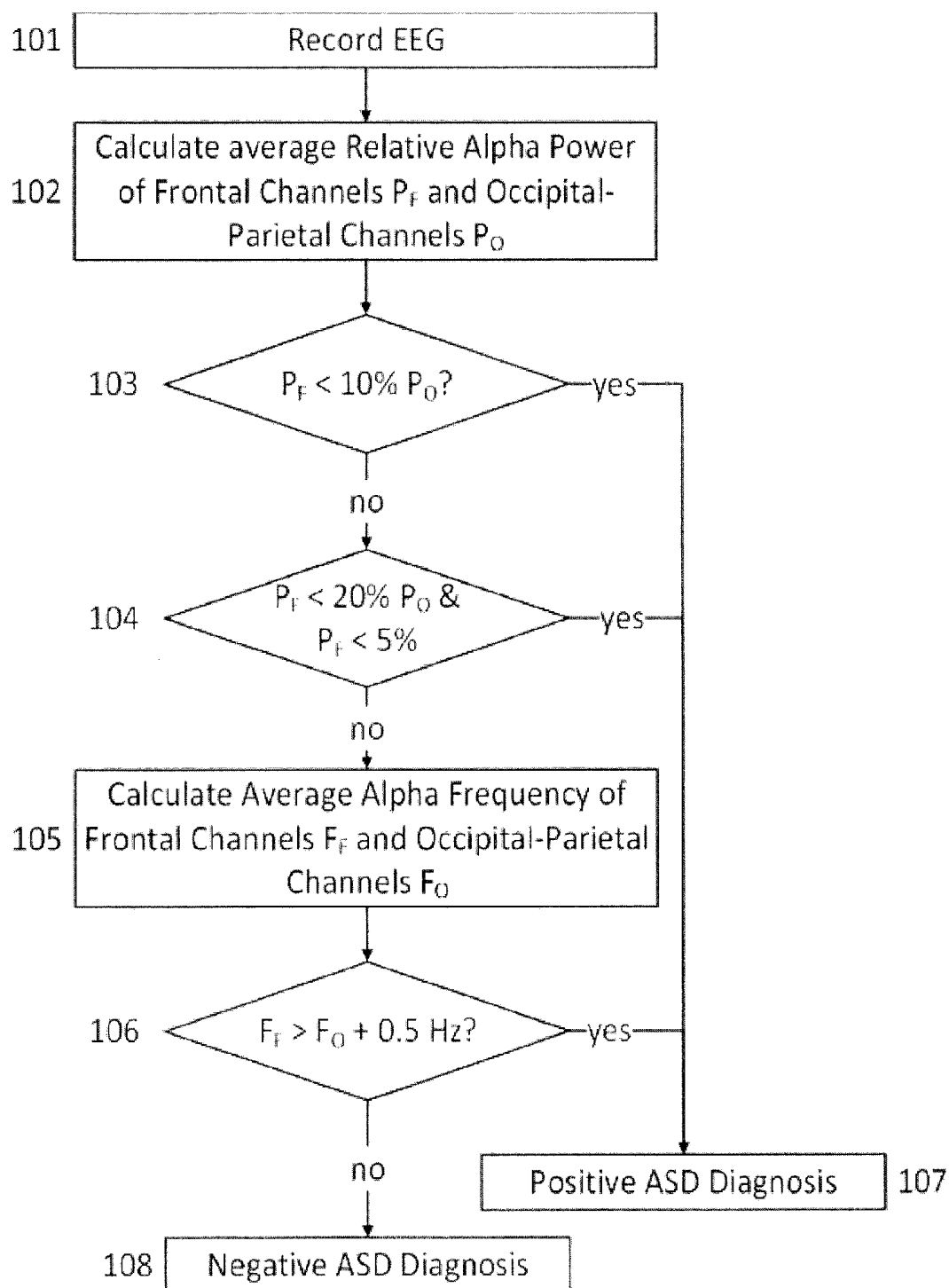


FIG. 1

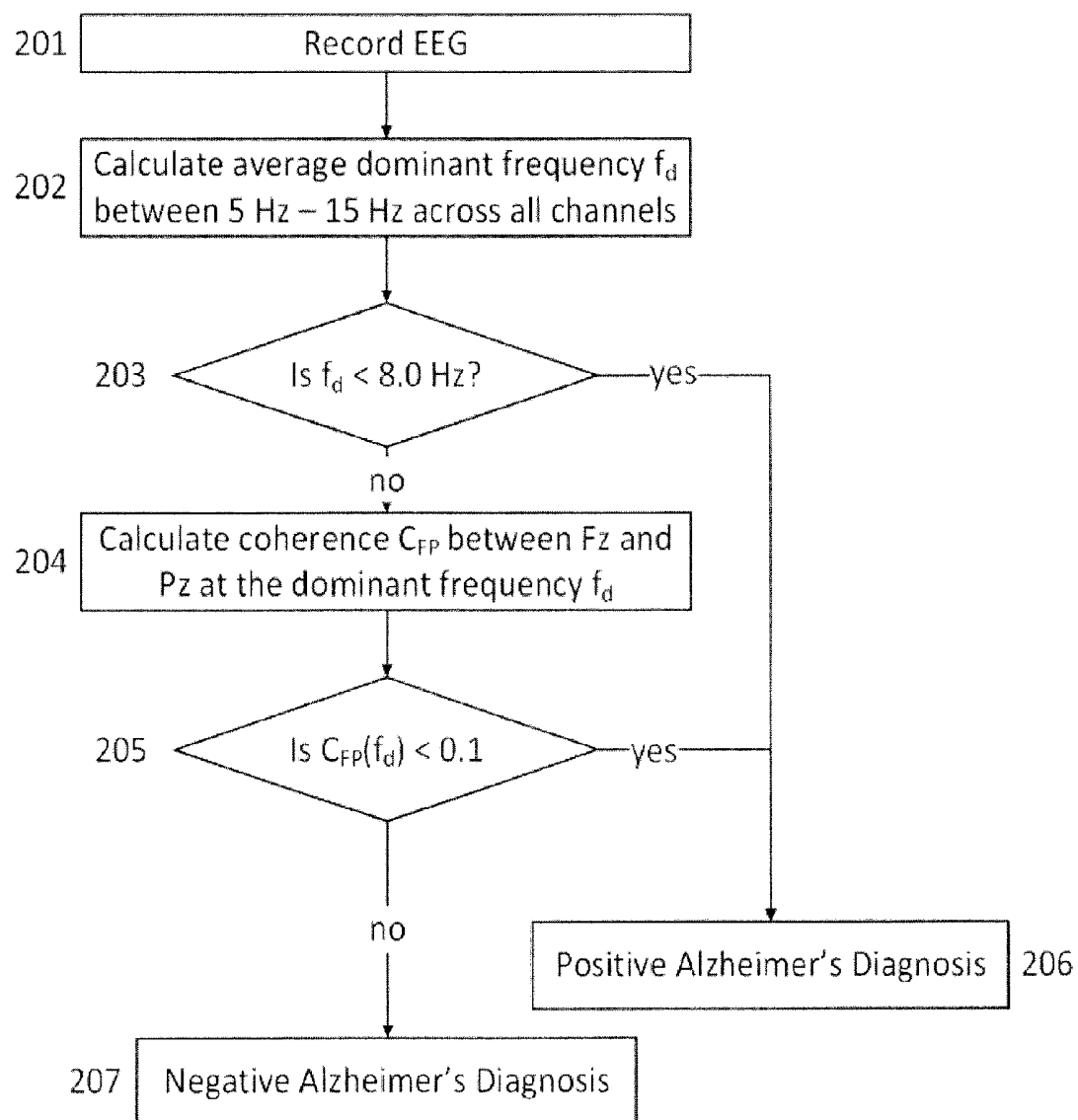


FIG. 2

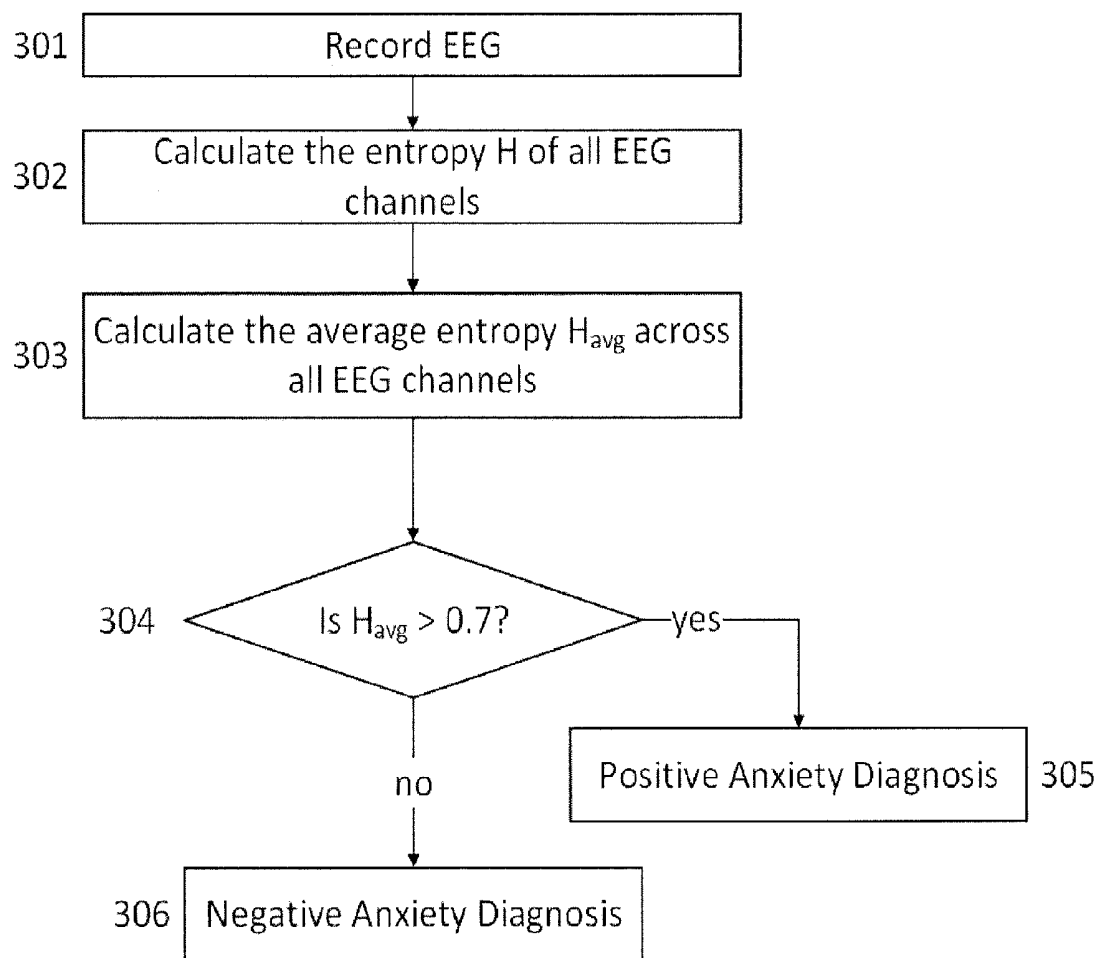


FIG. 3

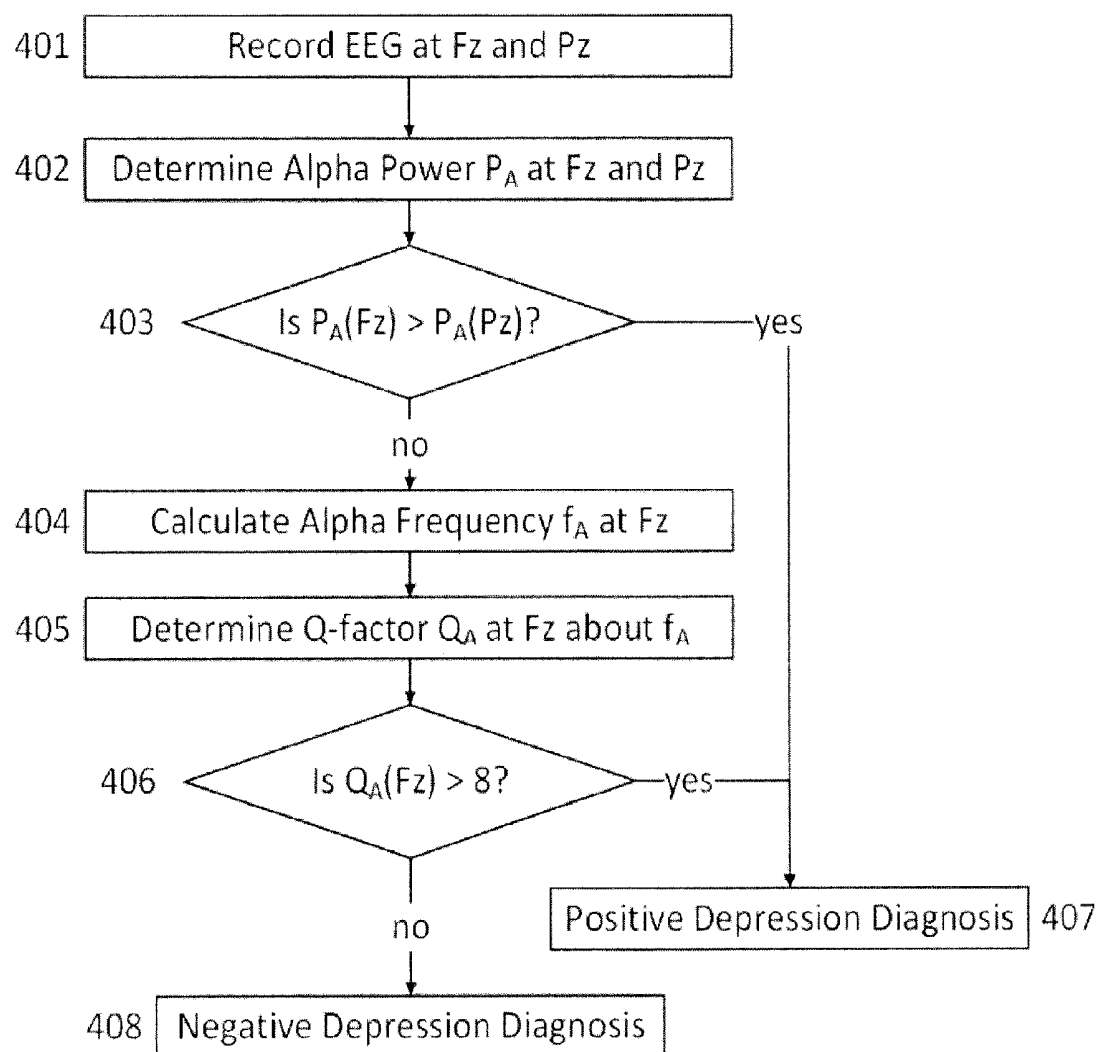


FIG. 4

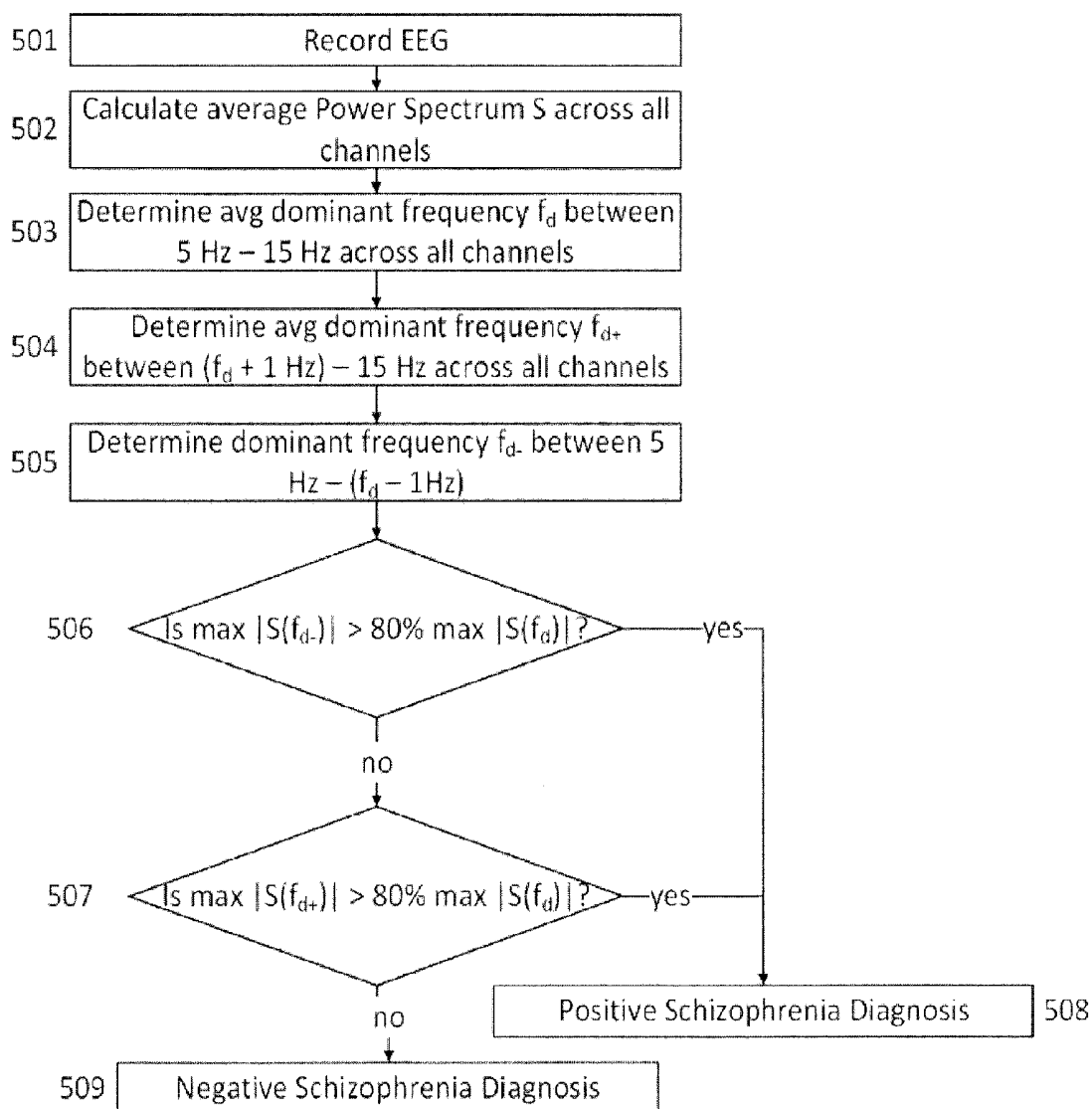
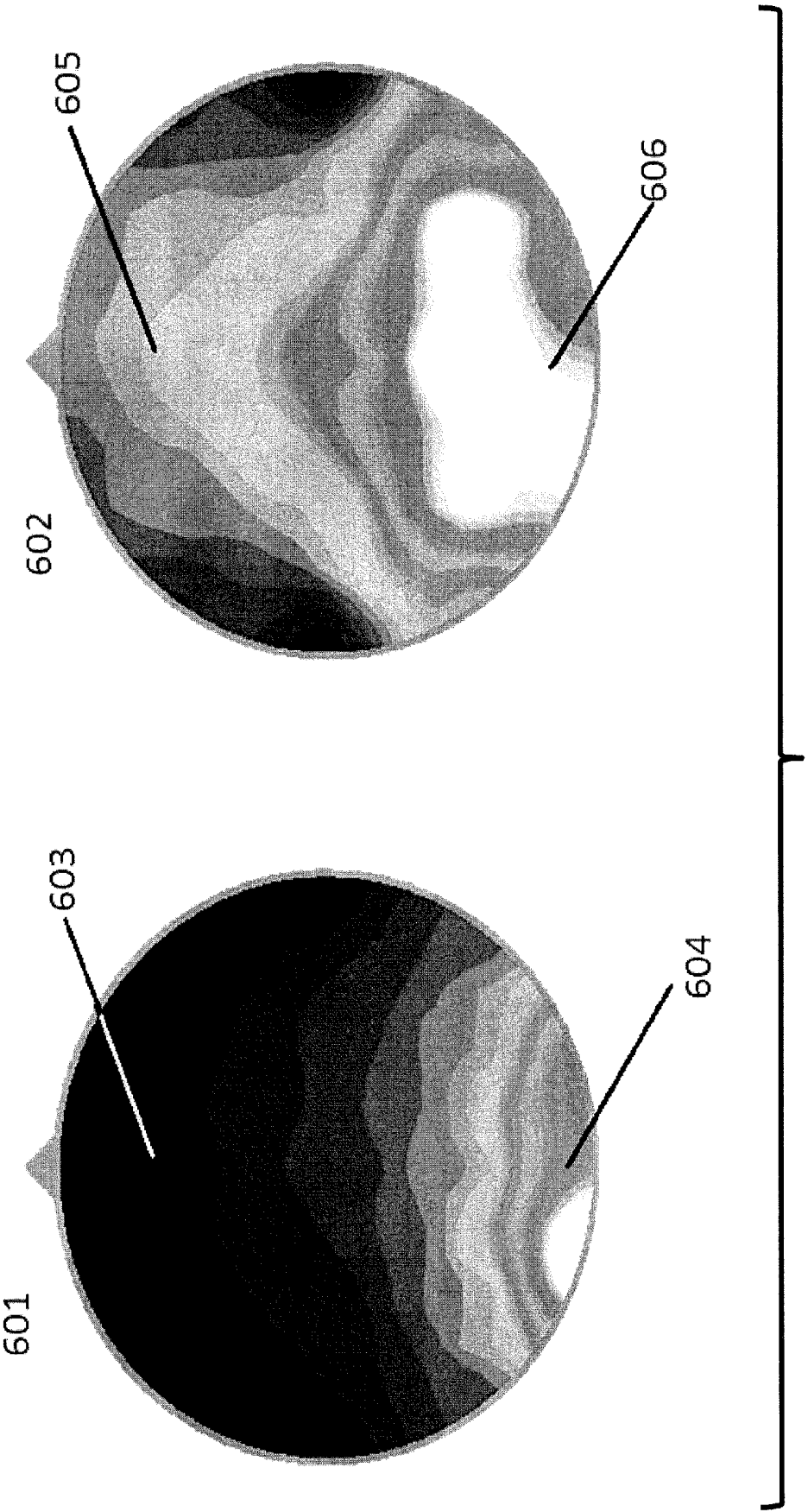


FIG. 5



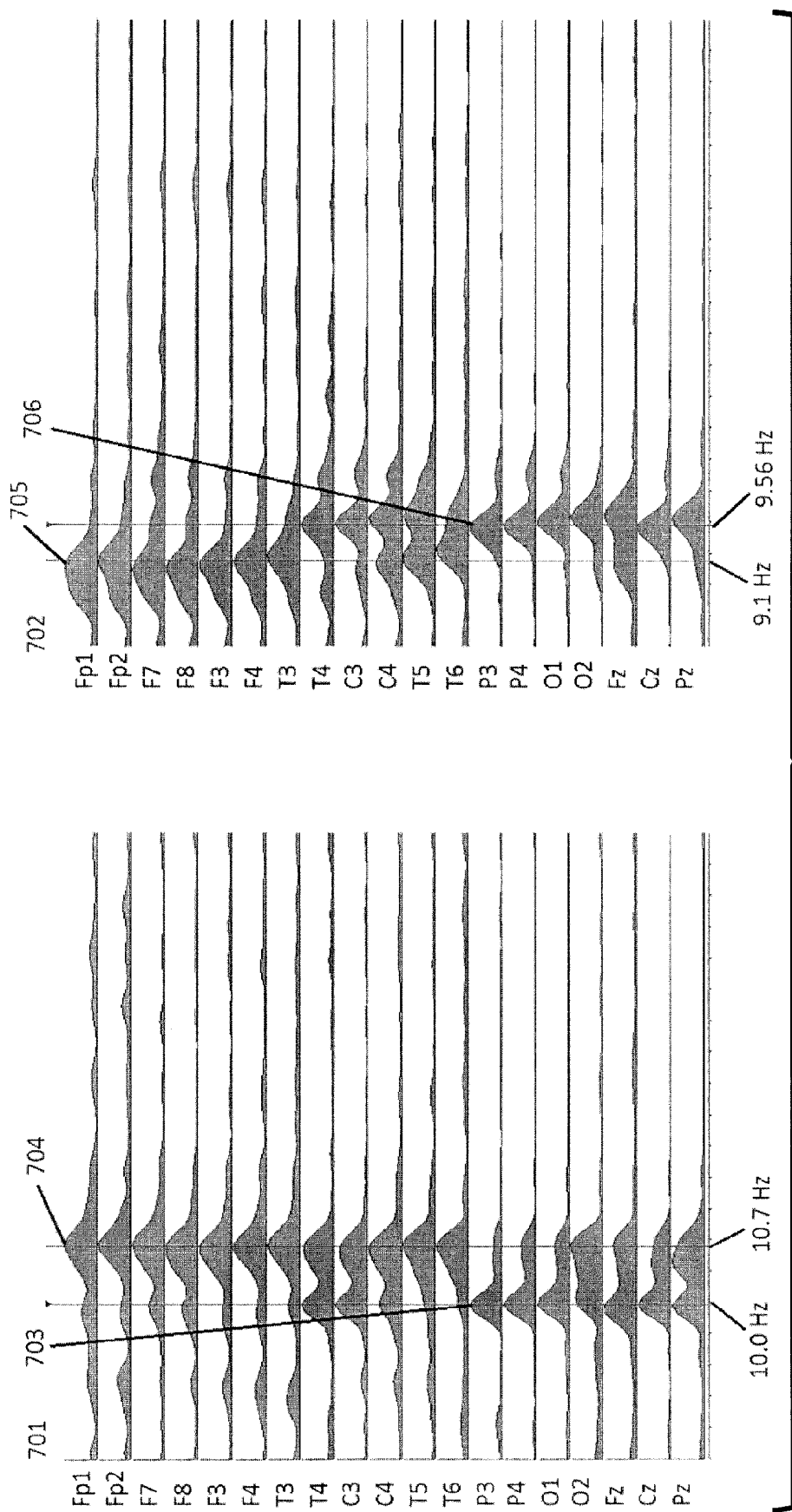


FIG. 7

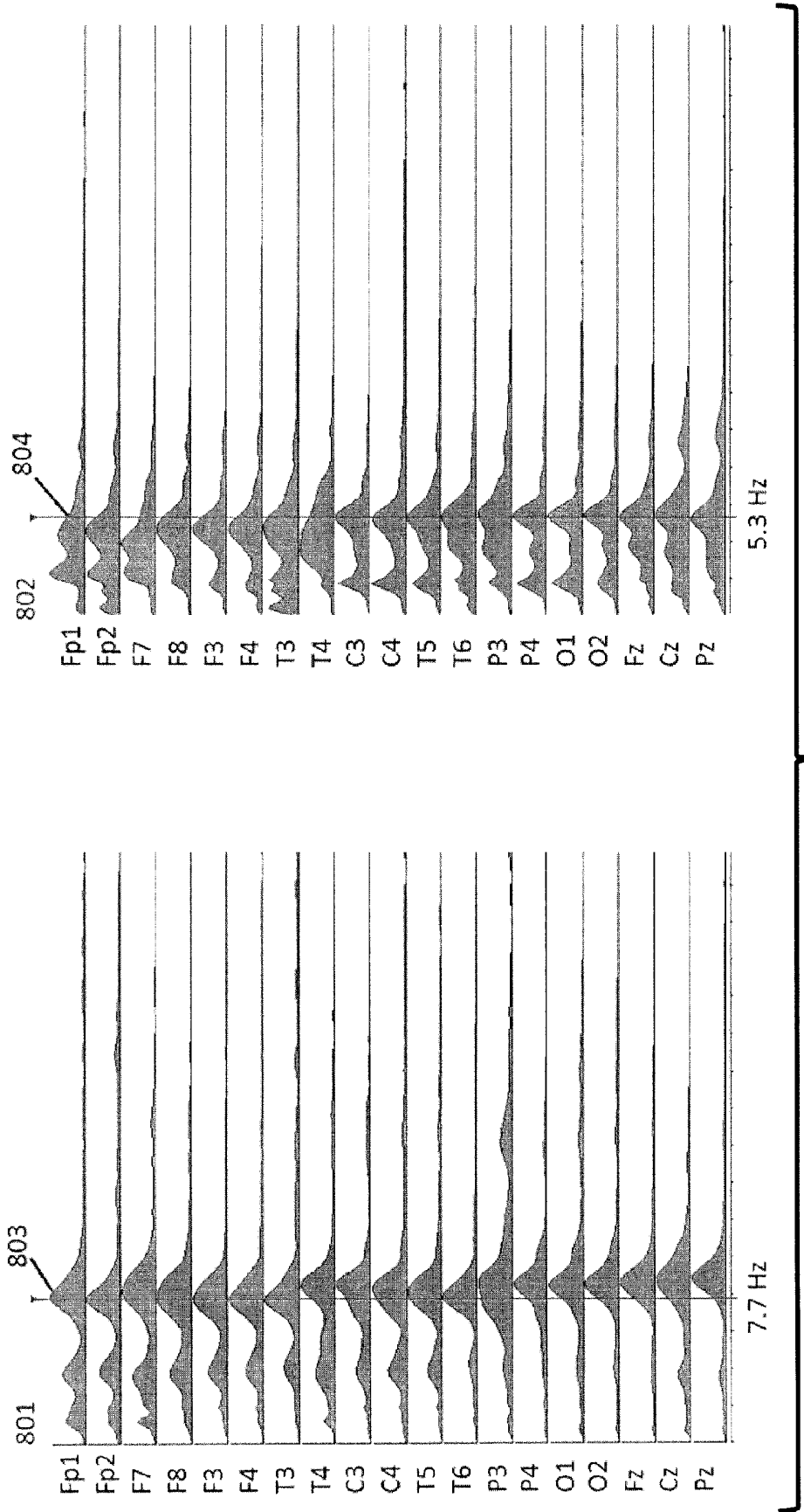


FIG. 8

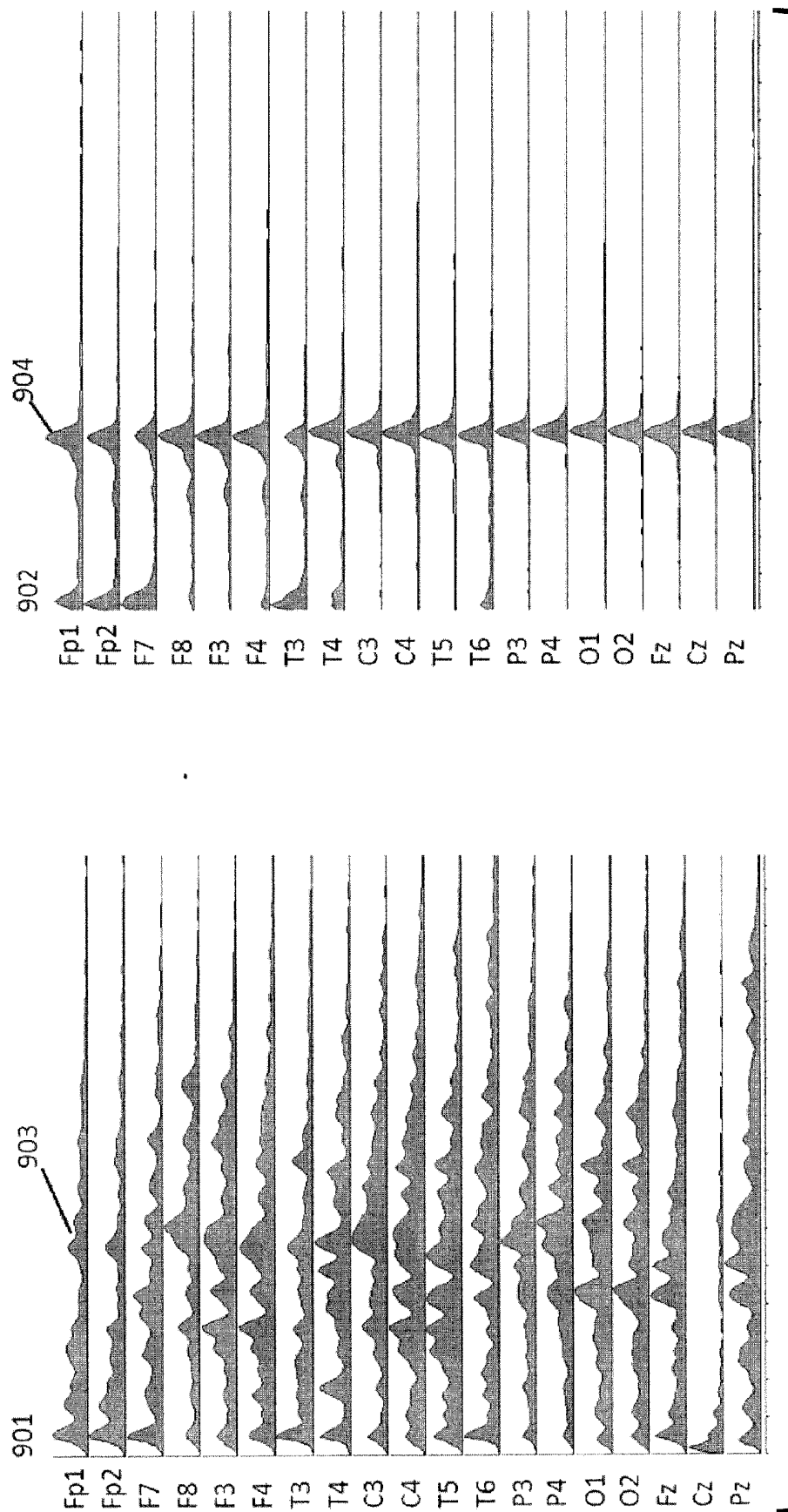


FIG. 9

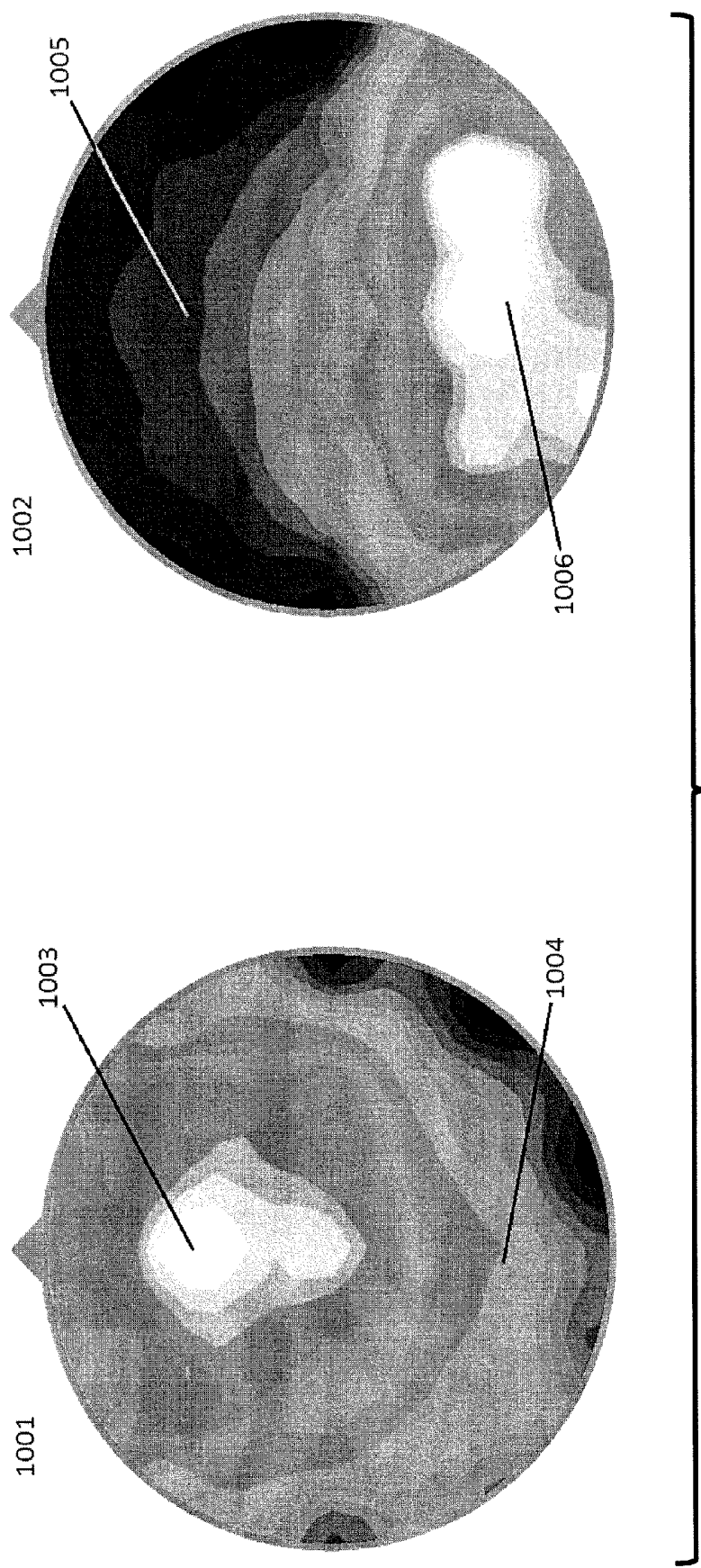


FIG. 10

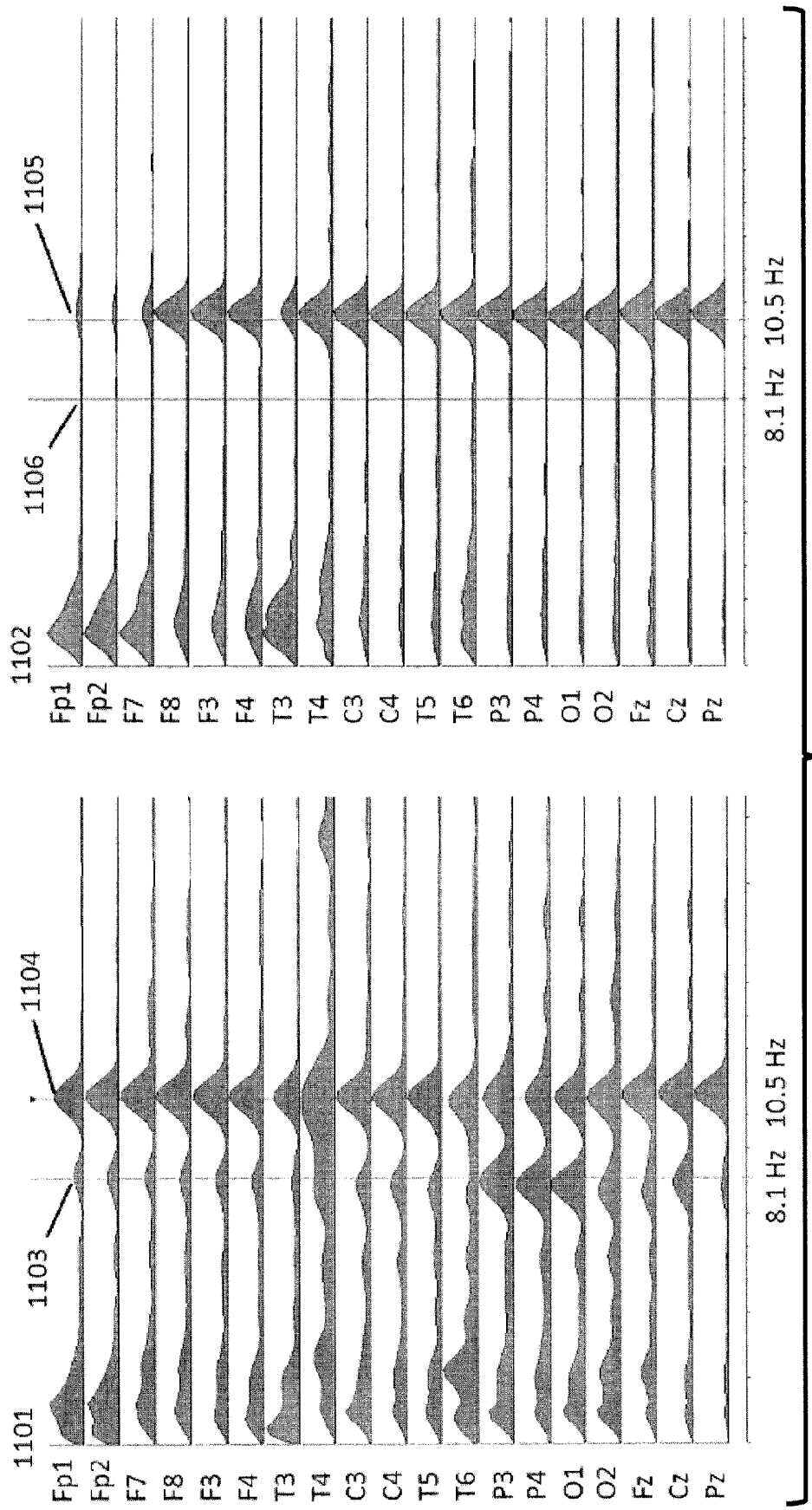


FIG. 11

METHODS FOR DIAGNOSING MENTAL DISORDERS USING NEUROMETRICS

BACKGROUND OF THE INVENTION

[0001] Mental disorders can be painful, debilitating, and very costly for the affected individual and their family. Approximately one in five adults in the US experiences a mental disorder in a given year. 18.1% of adults in the US experience an anxiety disorder, such as posttraumatic stress disorder, obsessive-compulsive disorder and specific phobias. 6.9% of adults in the US have at least one major depressive episode each year. 1.1% of adults in the US live with schizophrenia.

[0002] The consequences of lack of treatment are significant. Mental disorders are the third most common cause of hospitalization in the US for both youth and adults aged 18-44. Suicide is the 10th leading cause of death in the US, and the 2nd leading cause of death for those aged 15-24. Each day, approximately 18-22 veterans die by suicide.

[0003] A key factor in treatment of mental disorders is proper diagnosis. The standard method of diagnosing mental disorders has been with either the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Statistical Classification of Diseases and Related Health Problems (ICD), Chapter 5: Mental and behavioural disorders. Both standards primarily involve diagnosis using conversation with the patient regarding symptoms and behavior. This has the disadvantage of being subjective, based on the interviewer, which lessens the diagnostic reliability, sometimes resulting in two clinicians coming to different diagnoses of the same patient.

[0004] DSM and ICD are primarily concerned with the signs and symptoms of mental disorders, rather than the underlying causes. This reflects a general lack of pathophysiological understanding of mental disorders.

[0005] It is apparent that a repeatable and reliable method of diagnosing mental disorders that is based on measurable data, independent of the interpretation of an interviewer, would provide significant benefit to patients and to the psychiatric community.

SUMMARY

[0006] Certain terms are used which are necessary for a better understanding of the methods described herein. The definitions of these terms are given in the detailed description.

[0007] Described herein are novel methods to provide a diagnosis of mental disorders for a person using characteristics of the person's EEG. The methods described herein do not require any measurement other than the EEG, although the methods do not preclude the use of other measurements in order to confirm or validate the diagnosis. The methods described herein make use of the measurement locations described in the internationally recognized 10-20 system, although other, possibly higher resolution, systems could also be used.

[0008] In one aspect is a method of diagnosing autism spectrum disorder (ASD) that comprises: (a) recording the EEG of a person; and (b) calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the

average relative frontal Alpha Power is less than about ten percent of the average relative occipital-parietal Alpha Power.

[0009] In another aspect is a method of diagnosing ASD which comprises: (a) recording the EEG of a person; (b) calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the average relative frontal Alpha Power is less than about twenty percent of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

[0010] In another aspect is a method of diagnosing ASD that comprises: (a) recording the EEG of a person; (b) calculating the average Alpha Frequency of EEG signals from at least one of the frontal EEG channels and the average Alpha Frequency of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

[0011] The aspects described may be used individually or as a combination. By requiring more than one metric to be satisfied for a diagnosis, the confidence of the diagnosis may improve.

[0012] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about ten percent of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

[0013] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about ten percent of the average relative occipital-parietal Alpha Power and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

[0014] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about twenty percent of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5% and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

[0015] In one aspect is a method of diagnosing Alzheimer's disease that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; and (c) diagnosing the person with Alzheimer's Disease if the average dominant frequency is less than about 8 Hz.

[0016] In another aspect is a method of diagnosing Alzheimer's disease that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; and (c) calculating the average coherence at the dominant frequency between the EEG signals from at least one frontal EEG channel and at least one occipital-parietal EEG channel; and (d) diagnosing the person with Alzheimer's Disease if the average coherence is less than about 10%.

[0017] In some embodiments of at least one aspect described above, the person is diagnosed with Alzheimer's disease if the dominant frequency is less than about 8 Hz and the average coherence is less than about 10%.

[0018] In one aspect is a method of diagnosing Anxiety Disorder that comprises: (a) Recording the EEG of a person; (b) calculating the average entropy of the EEG signals from at least one EEG channel; and (c) diagnosing the person with Anxiety Disorder if the average entropy is greater than about 0.7.

[0019] In one aspect is a method of diagnosing Depression that comprises: (a) recording the EEG of a person; (b) calculating the average relative Alpha Power of at least one frontal EEG channel and the average relative Alpha Power of at least one occipital-parietal EEG channel; and (c) diagnosing the person with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power.

[0020] In another aspect is a method of diagnosing Depression that comprises: (a) recording the EEG of a person; (b) calculating the average frontal Alpha Frequency of EEG signals from at least one frontal EEG channel; (c) calculating the average relative Q-factor of EEG signals from at least one frontal EEG channel about the average Alpha Frequency; and (d) diagnosing the person with Depression if the average relative Q factor is greater than about 8.

[0021] In some embodiments of at least one aspect described above, the person is diagnosed with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power and the average relative Q factor is greater than about 8.

[0022] In one aspect is a method of diagnosing Schizophrenia that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency f_d between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; (c) calculating the average lower dominant frequency between about 5 Hz and about f_d-1 Hz of EEG signals from at least one EEG channel; (d) calculating the average upper dominant frequency between about f_d+1 Hz and about 15 Hz of EEG signals from at least one EEG channel; and (e) diagnosing the person with Schizophrenia if the magnitude of the average power spectrum from at least one EEG channel at the lower dominant frequency is at least about 80% of the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency or the magnitude of the average power spectrum from at least one EEG channel at the upper dominant frequency is at least about 80% of the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] A better understanding of the features and advantages of the methods provided will be obtained by reference to the following detailed description that sets forth illustrative embodiments and the accompanying drawings of which:

[0024] FIG. 1 shows an exemplary method in which a diagnosis of autism is determined based upon the relative Alpha Power of the frontal EEG channels and the occipital-parietal EEG channels, or based upon the difference between the frontal alpha frequency and the occipital-parietal alpha frequency.

[0025] FIG. 2 shows an exemplary method in which a diagnosis of Alzheimer's disease is determined based upon

the dominant frequency between 5 Hz-15 Hz, or based upon the EEG coherence between the Fz and Pz locations.

[0026] FIG. 3 shows an exemplary method in which a diagnosis of anxiety is determined based upon the average entropy across all EEG channels.

[0027] FIG. 4 shows an exemplary method in which a diagnosis of depression is determined based upon the EEG Alpha Power at Fz and Pz, or upon the Q-factor about the EEG alpha frequency at the Fz location.

[0028] FIG. 5 shows an exemplary method in which a diagnosis of schizophrenia is determined based upon the presence of multiple peaks in the FFT of the EEG channels greater than 1 Hz apart.

[0029] FIG. 6 shows an exemplary 2-D plot of the average relative Alpha Power distribution across all EEG channels for a person with ASD compared to a normal person.

[0030] FIG. 7 shows an exemplary graph of the FFT for all EEG channels for a person with ASD compared to a normal person, showing that the dominant peak frequency in the frontal EEG channels for a person with ASD is greater than 0.5 Hz higher than the dominant peak frequency of the occipital-parietal EEG channels, whereas the dominant peak frequency in the frontal EEG channels for a normal person is not higher than the dominant peak frequency of the occipital-parietal EEG channels.

[0031] FIG. 8 shows an exemplary graph of the FFT for all EEG channels for a person with mild Alzheimer's disease and a person with severe Alzheimer's disease, showing that the dominant frequency in both cases is less than 8 Hz.

[0032] FIG. 9 shows an exemplary graph of the FFT for all EEG channels for a person with anxiety compared to a normal person, showing that the average entropy across all EEG channels is much higher for a person with anxiety.

[0033] FIG. 10 shows an exemplary 2-D plot of the distribution of Alpha Power across all EEG channels for a person with depression compared to a normal person, showing that the Alpha Power in the frontal EEG channels is higher than the Alpha Power in the occipital-parietal EEG channels for a person with depression.

[0034] FIG. 11 shows an exemplary graph of the FFT for all EEG channels for a person with schizophrenia compared to a normal person, showing that the FFT for a person with schizophrenia contains two significant dominant peaks more than 1 Hz apart.

DETAILED DESCRIPTION

[0035] While certain embodiments have been provided and described herein, it will be readily apparent to those skilled in the art that such embodiments are provided by way of example only. It should be understood that various alternatives to the embodiments described herein may be employed, and are part of the invention described herein.

[0036] Described herein are methods for diagnosing mental disorders using characteristics of the EEG of a person. The methods described herein include diagnosis of autism spectrum disorder (ASD), Alzheimer's disease, anxiety, depression, and schizophrenia. The mental disorders described herein also encompass all subtypes derived from the mental disorder. For example, diagnosis of anxiety also comprises diagnosis of bulimia, anorexia nervosa, obsessive-compulsive disorder, post-traumatic stress disorder, generalized anxiety disorder, and panic disorder. Diagnosis of ASD also comprises diagnosis of Asperger's syndrome and childhood disintegrative disorder. Diagnosis of depres-

sion also comprises diagnosis of dysthymia, bipolar depression, seasonal depressive disorder, and depressive episode. Diagnosis of schizophrenia also comprises diagnosis of paranoid schizophrenia, disorganized schizophrenia, and catatonic schizophrenia. Diagnosis of Alzheimer's disease also comprises diagnosis of inflammatory, non-inflammatory, and cortical Alzheimer's disease, as well as dementia and mild cognitive impairment.

[0037] The term "diagnosis," when referring to the methods described herein, is the identification of the nature of a mental disorder by EEG analysis where the confidence that the diagnosis is correct is at least 90%.

[0038] The term "Fast Fourier Transform," or FFT, when referring to the methods described herein, is the calculation algorithm to determine the frequency spectrum of a signal from an EEG channel.

[0039] The term "Alpha Power," when referring to the methods described herein, is the sum of the magnitude squared of the FFT values in the alpha range (about 8 Hz to about 13 Hz).

[0040] The term "total power," when referring to the methods described herein, is the sum of the magnitude squared of the FFT values across the frequency spectrum from about 0 Hz to about half the sampling frequency.

[0041] The term "relative Alpha Power," when referring to the methods described herein, is the Alpha Power divided by the total power.

[0042] The term "average relative Alpha Power," when referring to the methods described herein, is the average value of the relative Alpha Power for at least one of the EEG channels.

[0043] The term "dominant frequency," when referring to the methods described herein, is the frequency associated with the highest spectral density within a specified range.

[0044] The term "alpha frequency," when referring to the methods described herein, is the dominant frequency within the alpha range.

[0045] The term "10-20 system," when referring to the methods described herein, is the internationally recognized method to describe the location of scalp electrodes in the context of an EEG recording. The locations are divided into frontal, central, temporal, parietal, and occipital regions. Each location has a label, based on the region where it is located.

[0046] The term "frontal channels," when referring to the methods described herein, is the set of EEG channels in locations above the frontal and pre-frontal region of the brain. For example, in the 10-20 system, the frontal channels comprise Fp1, Fp2, Fz, F3, F4, F7, and F8.

[0047] The term "occipital-parietal channels," when referring to the methods described herein, is the set of EEG channels in locations above the occipital and parietal regions of the brain. For example, in the 10-20 system, the occipital-parietal channels comprise Pz, P3, P4, O1, and O2.

[0048] The term "coherence," when referring to the methods described herein, is used to quantify common frequencies and evaluate the similarity of two signals. It is determined by dividing the magnitude-squared cross-spectral density between the two signals by the product of the spectral density of each signal at the frequency of interest.

[0049] The term "spectral density," when referring to the methods described herein, is a measure of the power of an EEG signal at a specified frequency, and is the Fourier transform of the auto-correlation function of the signal.

[0050] The term, "cross-spectral density," when referring to the methods described herein, is the Fourier transform of the cross-correlation of two EEG signals.

[0051] The term, "total spectral power," when referring to the methods described herein, is the total energy of an EEG signal, and is the sum of the spectral density over all frequencies.

[0052] The term "entropy," when referring to the methods described herein, is a measure of the system complexity. A high entropy EEG signal is a result of a large number of processes occurring in the brain. Entropy is determined for an EEG signal in two stages. First a normalized power spectrum is generated by dividing the spectral density by the total spectral power, as shown in the equation below:

$$S_n(f) = \frac{S(f)}{\sum_f S(f)}$$

[0053] where S_n is the normalized power spectrum and S is the spectral density. Then, the entropy is calculated as the sum across the frequency spectrum from 0 Hz to half the sampling frequency of the normalized spectrum multiplied by the log base two of the inverse power spectrum, as shown in the equation below:

$$E = \sum_f S_n(f) \log_2 \frac{1}{S_n(f)}$$

[0054] where E is the entropy.

[0055] The term "Q-factor," when referring to the methods described herein, is a measure of the frequency selectivity of the EEG signal about a specified frequency. A high Q-factor signal has a spectral distribution that is concentrated around the specified frequency, whereas a low Q-factor signal has a spectral distribution that is more widely spread about the specified frequency. Q-factor is calculated as the specified frequency divided by the half-power bandwidth. The half-power bandwidth is the width of the power spectrum at half the power spectrum value at the specified frequency.

[0056] Described herein are methods of diagnosing one or more mental disorders in a person using characteristics of the EEG of a person, which may include, but do not necessarily require, additional information, such as information regarding the person's symptoms, demographic data, genome analysis, vital signs, treatment history, or current medication.

[0057] The brain may be thought of as a physical system, where the goal, in addition to providing thought processes and autonomic function, includes minimization of energy consumption. The brain processes are brought about through electrochemical signaling between neurons. This electrochemical signaling is not random, but instead often occurs at or near a specified frequency. Therefore, the brain may also be thought of as a pseudo-resonant system, with the resonant frequency equal to its alpha frequency, or dominant EEG frequency between about 8 Hz to about 13 Hz.

[0058] A resonant system is lower energy than a non-resonant system, and it is this resonance that contributes to the minimization of energy consumption by the brain. Therefore, in the brain a tradeoff exists between complex neuronal behavior provided for rational thought and other

processes the brain must serve, and minimization of energy consumed by the brain. When the characteristics of resonant activity of the brain are altered from their "normal" values, symptoms of mental disorders may occur, based in part on the particular change in the EEG characteristics.

[0059] If the relative Alpha Power of the frontal region of the brain is significantly reduced compared to the Alpha Power in the occipital-parietal region, symptoms of ASD may occur, and a diagnosis of ASD is appropriate. Often, the alpha frequency measured in the occipital-parietal region of the brain is different than the alpha frequency in the frontal region of the brain. It is not uncommon for the occipital-parietal alpha frequency to be up to 1 Hz higher than the frontal alpha frequency. However, if the frontal alpha frequency is more than 0.5 Hz higher than the occipital-parietal alpha frequency, then symptoms of ASD may also occur, and a diagnosis of ASD is appropriate. If both EEG characteristics occur together, the confidence in the diagnosis may increase.

[0060] In one aspect the invention provides methods of diagnosing autism spectrum disorder (ASD) that comprise: (a) recording the EEG of a person; (b) calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the average relative frontal Alpha Power is less than about ten percent of the average relative occipital-parietal Alpha Power.

[0061] In another aspect is a method of diagnosing ASD that comprises: (a) recording the EEG of a person; (b) calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the average relative frontal Alpha Power is less than about twenty percent of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

[0062] In another aspect is a method of diagnosing ASD that comprises: (a) recording the EEG of a person; (b) calculating the average alpha frequency of EEG signals from at least one of the frontal EEG channels and the average alpha frequency of EEG signals from at least one of the occipital-parietal EEG channels; and (c) diagnosing the person with ASD if the average frontal alpha frequency is greater than about 0.5 Hz more than the average occipital-parietal alpha frequency.

[0063] The aspects described may be used individually or as a combination. By requiring more than one metric to be satisfied for a diagnosis, the sensitivity of the diagnosis may improve.

[0064] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

[0065] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average frontal alpha frequency is greater than about 0.5 Hz more than the average occipital-parietal alpha frequency.

[0066] In some embodiments of at least one aspect described above, the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 20% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5% and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

[0067] The dominant frequency in the range between about 5 Hz to about 15 Hz, in normal individuals who are awake, relaxed, with eyes closed, is equal to the alpha frequency. The alpha frequency has a normal range between 8 Hz-13 Hz, but if the alpha frequency drops below 8 Hz, then symptoms of dementia, mild cognitive impairment, or Alzheimer's may occur. In addition, these symptoms may occur if the coherence of brain EEG activity between the frontal and occipital-parietal regions of the brain drops to a low value, resulting in reduced communication between the regions of the brain and reduced cognitive performance. In either case, a diagnosis of Alzheimer's disease is appropriate.

[0068] In one aspect the subject invention provides a method of diagnosing Alzheimer's disease that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; and (c) diagnosing the person with Alzheimer's Disease if the average dominant frequency is less than about 8 Hz.

[0069] In another aspect is a method of diagnosing Alzheimer's disease that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; (c) calculating the average coherence at the dominant frequency between the EEG signals from at least one frontal EEG channel and at least one occipital-parietal EEG channel; and (d) diagnosing the person with Alzheimer's Disease if the average coherence is less than about 10%.

[0070] In some embodiments of at least one aspect described above, the person is diagnosed with Alzheimer's disease if the dominant frequency is less than about 8 Hz and the average coherence is less than about 10%.

[0071] The EEG of someone awake, relaxed, with eyes closed is normally rhythmic, with most of the energy in the signal centered around that alpha frequency. If the brain activity is more chaotic and contains energy that is distributed widely across multiple frequency bands, the person may have symptoms of anxiety, and an anxiety diagnosis is appropriate. The frequency distribution can be measured by determining the entropy of the power spectrum across all EEG channels. If the entropy is high, then an autism diagnosis is appropriate.

[0072] In one aspect is a method of diagnosing Anxiety Disorder that comprises: (a) recording the EEG of a person; (b) calculating the average entropy of the EEG signals from at least one EEG channel; and (c) diagnosing the person with Anxiety Disorder if the average entropy is greater than about 0.7.

[0073] In a normal person, the Alpha Power is concentrated around the posterior portion of the brain, with less Alpha Power present in the frontal region. If the concentration of Alpha Power is farther anterior in the brain, then the person may experience symptoms of depression, requiring a depression diagnosis. In addition, the brain of a depressed

person will often be highly rhythmic, and therefore have lower energy. A highly rhythmic brain can be shown by calculating the Q-factor of the EEG signal. A high Q-factor in the frontal region of the brain may result in symptoms of depression, and a depression diagnosis is appropriate.

[0074] In one aspect is a method of diagnosing Depression that comprises: (a) recording the EEG of a person; (b) calculating the average relative Alpha Power of at least one frontal EEG channel and the average relative Alpha Power of at least one occipital-parietal EEG channel; and (c) diagnosing the person with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power.

[0075] In another aspect is a method of diagnosing Depression that comprises: (a) recording the EEG of a person; (b) calculating the average frontal Alpha Frequency of EEG signals from at least one frontal EEG channel; (c) calculating the average relative Q-factor of EEG signals from at least one frontal EEG channel about the average Alpha Frequency; and (d) diagnosing the person with Depression if the average relative Q factor is greater than about 8.

[0076] In some embodiments of at least one aspect described above, the person is diagnosed with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power and the average relative Q factor is greater than about 8.

[0077] Normally, the power spectrum of the EEG of a person contains a single dominant frequency when relaxed, awake, with eyes closed, which is the alpha frequency. This frequency can be different between the occipital-parietal and frontal portions of the brain. However, if the EEG of the person contains multiple dominant frequencies at least about 1 Hz apart, each being of similar power, then the person may experience symptoms of schizophrenia, and is given a schizophrenia diagnosis.

[0078] In one aspect is a method of diagnosing Schizophrenia that comprises: (a) recording the EEG of a person; (b) calculating the average dominant frequency (f_d) between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; (c) calculating the average lower dominant frequency between about 5 Hz and about f_d-1 Hz of EEG signals from at least one EEG channel; (d) calculating the average upper dominant frequency between about f_d+1 Hz and about 15 Hz of EEG signals from at least one EEG channel; and (e) diagnosing the person with Schizophrenia if the magnitude of the average power spectrum from at least one EEG channel at the lower dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency or the magnitude of the average power spectrum from at least one EEG channel at the upper dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency.

[0079] FIG. 1 shows an exemplary flow diagram of a method to diagnose ASD. In this example, the EEG of the person is recorded (101) and the average relative Alpha Power of the frontal channels and occipital-parietal channels is found (102). If the frontal power is less than 10% the occipital-parietal power (103), then an ASD diagnosis is made (107). Otherwise, the criteria is changed such that if the frontal power is less than 20% the occipital-parietal power and the frontal power is less than 5% (104), then an ASD diagnosis is made. If both of these criteria are not met,

the average alpha frequency for the frontal EEG channels and the occipital-parietal channels is calculated (105), and an ASD diagnosis is made if the frontal alpha frequency is at least 0.5 Hz greater than the occipital-parietal alpha frequency. If no criteria are met, then an ASD diagnosis is not appropriate (108).

[0080] FIG. 2 shows an exemplary flow diagram of the method to diagnose Alzheimer's disease. In this example, the EEG of the person is recorded (201) and the average dominant frequency between about 5 Hz and about 15 Hz across all channels is determined (202). If the dominant frequency is less than 8.0 Hz (203), then a diagnosis of Alzheimer's disease is made (206). Otherwise, the coherence between the Fz EEG channel and the Pz EEG channel is found at the dominant frequency (204), and an Alzheimer's diagnosis is made if the coherence is less than 0.1 (205). If no criteria are met, then an Alzheimer's diagnosis is not appropriate (207).

[0081] FIG. 3 shows an exemplary flow diagram of the method to diagnose anxiety. In this example, the EEG of the person is recorded (301) and the entropy of each EEG channel is determined (302) and the average of those values is found (303). If this average is greater than 0.7 (304), an anxiety diagnosis is made (305). If not, then an anxiety diagnosis is not appropriate (306).

[0082] FIG. 4 shows an exemplary flow diagram of the method to diagnose depression. In this example, the EEG of the person is recorded, specifically at locations Fz and Pz (401). The Alpha Power at Fz and Pz is determined (402), and a depression diagnosis is made (407) if the alpha power at Fz is greater than the alpha power at Pz (403), then a depression diagnosis is made (407). Otherwise, the alpha frequency at Fz is found (404) and the Q-factor is determined at Fz about the alpha frequency (405), and a depression diagnosis is made if the Q-factor is greater than 8 (406). If no criteria are met, a depression diagnosis is not appropriate (408).

[0083] FIG. 5 shows an exemplary flow diagram of the method to diagnose schizophrenia. In this example, the EEG of the person is recorded at Fz (501), and the average power spectrum across all channels is found for the EEG at this location (502). The average dominant frequency is determined between 5 Hz-15 Hz across all channels (503). The average upper dominant frequency is found as the average dominant frequency between the dominant frequency+1 Hz and 15 Hz (504). The average lower dominant frequency is found as the average dominant frequency between 5 Hz and the dominant frequency+1 Hz (505). If the magnitude of the power spectrum at the lower dominant frequency is at least 80% the magnitude of the power spectrum at the dominant frequency (506), then a schizophrenia diagnosis is made (508). If the magnitude of the power spectrum at the upper dominant frequency is at least 80% the magnitude of the power spectrum at the dominant frequency (507), then a schizophrenia diagnosis is also made. Otherwise, a schizophrenia diagnosis is not appropriate (509).

[0084] FIG. 6 shows an exemplary 2-D plot of the average relative alpha power distribution across all EEG channels for a person with ASD (601) and a normal person (602). In the plots, the nose is at the top of the plot. The lighter regions in the plot show higher relative alpha power. As can be seen, in the normal person plot, the alpha power in the frontal region (605) is less than in the occipital parietal region (606), though not dramatically so. However, in the ASD

person's plot, the alpha power in the frontal region (603) is less than 10% of the alpha power in the occipital-parietal region (604).

[0085] FIG. 7 shows an exemplary graph of the FFT for all EEG channels for a person with ASD (701) compared to a normal person (702). For the person with ASD, it can be seen that the dominant frequency in the occipital parietal region (703) is 10.0 Hz, and the dominant frequency in the frontal region (704) is 10.7 Hz. In this, the alpha frequency in the frontal region is higher than in the occipital-parietal region. For the normal person, however, the reverse is true. The dominant frequency in the frontal region (705) is 9.1 Hz, and the dominant frequency in the occipital-parietal region (706) is 9.56 Hz.

[0086] FIG. 8 shows an exemplary graph of the FFT for all EEG channels for a person with mild Alzheimer's disease (801) and a person with severe Alzheimer's disease (802). The alpha frequency for the person with mild Alzheimer's disease (803) is 7.7 Hz. The alpha frequency for the person with severe Alzheimer's disease (804) is 5.3 Hz. Both are less than 8.0 Hz, which would result in an Alzheimer's diagnosis.

[0087] FIG. 9 shows an exemplary graph of the FFT for all EEG channels for a person with anxiety (901) compared to a normal person (902). In this, the distribution of activity (903) for the person with anxiety covers a much wider spectral range, resulting in a higher entropy value, whereas the distribution of activity (904) for the normal person is much more concentrated about the alpha frequency, and therefore has a lower entropy value.

[0088] FIG. 10 shows an exemplary 2-D plot of the distribution of Alpha Power across all EEG channels for a person with depression (1001) compared to a normal person (1002). In the plots, the nose is at the top of the plot. The lighter regions in the plot show higher Alpha Power. For the depressed person, the frontal Alpha Power (1003) is higher than the occipital-parietal Alpha Power (1004), indicating a diagnosis of depression. For the normal person, the frontal Alpha Power (1005) is less than occipital-parietal Alpha Power (1006).

[0089] FIG. 11 shows an exemplary graph of the FFT for all EEG channels for a person with schizophrenia (1101) compared to a normal person (1102). In this, two dominant peaks exist for the person with schizophrenia, one at 10.5 Hz (1104) and one at 8.1 Hz (1103). For the normal person, only one dominant peak (1105) exists, with no peak in another region in the 5-15 Hz band (1106).

[0090] Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise," "comprising," and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in a sense of "including, but not limited to." Words using the singular or plural number also include the plural or singular number respectively. Additionally, the words "herein," "hereunder," "above," "below," and words of similar import refer to this application as a whole and not to any particular portions of this application. When the word "or" is used in reference to a list of two or more items, that word covers all of the following interpretations of the word: any of the items in the list, all of the items in the list and any combination of the items in the list.

[0091] The above descriptions of illustrated embodiments of the system, methods, or devices are not intended to be exhaustive or to be limited to the precise form disclosed.

While specific embodiments of, and examples for, the system, methods, or devices are described herein for illustrative purposes, various equivalent modifications are possible within the scope of the system, methods, or devices, as those skilled in the relevant art will recognize. The teachings of the system, methods, or devices provided herein can be applied to other processing systems, methods, or devices, not only for the systems, methods, or devices described.

[0092] The elements and acts of the various embodiments described can be combined to provide further embodiments. These and other changes can be made to the system in light of the above detailed description.

[0093] In general, in the following claims, the terms used should not be construed to limit the system, methods, or devices to the specific embodiments disclosed in the specification and the claims, but should be construed to include all processing systems that operate under the claims. Accordingly, the system, methods, and devices are not limited by the disclosure, but instead the scopes of the system, methods, or devices are to be determined entirely by the claims.

[0094] While certain aspects of the system, methods, or devices are presented below in certain claim forms, the inventor contemplates the various aspects of the system, methods, or devices in any number of claim forms. Accordingly, the inventors reserve the right to add additional claims after filing the application to pursue such additional claim forms for other aspects of the system, methods, or devices.

Exemplary Embodiments

[0095] Specific embodiments of the invention include the following:

[0096] 1. A method of diagnosing autism spectrum disorder (ASD), wherein the method comprises:

[0097] a. recording the EEG of a person;

[0098] b. calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and

[0099] c. diagnosing the person with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power.

[0100] 2. A method of diagnosing ASD, wherein the method comprises:

[0101] a. recording the EEG of a person;

[0102] b. calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and

[0103] c. diagnosing the person with ASD if the average relative frontal Alpha Power is less than about 20% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

[0104] 3. A method of diagnosing ASD, wherein the method comprises:

[0105] a. recording the EEG of a person;

[0106] b. calculating the average Alpha Frequency of EEG signals from at least one of the frontal EEG channels and the average Alpha Frequency of EEG signals from at least one of the occipital-parietal EEG channels; and

- [0107] c. diagnosing the person with ASD if the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.
- [0108] 4. A method of embodiment 1 or 2 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.
- [0109] 5. A method of embodiment 1 or 3 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.
- [0110] 6. A method of embodiment 2 or 3 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 20% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5% and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.
- [0111] 7. A method of diagnosing Alzheimer's Disease, wherein the method comprises:
- [0112] a. recording the EEG of a person;
- [0113] b. calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; and
- [0114] c. diagnosing the person with Alzheimer's Disease if the average dominant frequency is less than about 8 Hz.
- [0115] 8. A method of diagnosing Alzheimer's Disease which comprises:
- [0116] a. recording the EEG of a person;
- [0117] b. calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel;
- [0118] c. calculating the average coherence at the dominant frequency between the EEG signals from at least one frontal EEG channel and at least one occipital-parietal EEG channel; and
- [0119] d. diagnosing the person with Alzheimer's Disease if the average coherence is less than about 10%.
- [0120] 9. A method of embodiment 7 or 8 wherein the person is diagnosed with Alzheimer's Disease if the dominant frequency is less than about 8 Hz and the average coherence is less than about 10%.
- [0121] 10. A method of diagnosing Anxiety Disorder, wherein the method comprises:
- [0122] a. recording the EEG of a person;
- [0123] b. calculating the average entropy of the EEG signals from at least one EEG channel; and
- [0124] c. diagnosing the person with Anxiety Disorder if the average entropy is greater than about 0.7.
- [0125] 11. A method of diagnosing Depression, wherein the method comprises:
- [0126] a. recording the EEG of a person;
- [0127] b. calculating the average relative Alpha Power of at least one frontal EEG channel and the average relative Alpha Power of at least one occipital-parietal EEG channel; and
- [0128] c. diagnosing the person with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power.
- [0129] 12. A method of diagnosing Depression, wherein the method comprises:
- [0130] a. recording the EEG of a person;
- [0131] b. calculating the average frontal Alpha Frequency of EEG signals from at least one frontal EEG channel;
- [0132] c. calculating the average relative Q-factor of EEG signals from at least one frontal EEG channel about the average Alpha Frequency; and
- [0133] d. diagnosing the person with Depression if the average relative Q factor is greater than about 8.
- [0134] 13. A method of embodiment 12 or 13 wherein the person is diagnosed with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power and the average relative Q factor is greater than about 8.
- [0135] 14. A method of diagnosing Schizophrenia, wherein the method comprises:
- [0136] a. recording the EEG of a person;
- [0137] b. calculating the average dominant frequency f_d between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel;
- [0138] c. calculating the average lower dominant frequency between about 5 Hz and about f_d-1 Hz of EEG signals from at least one EEG channel;
- [0139] d. calculating the average upper dominant frequency between about f_d+1 Hz and about 15 Hz of EEG signals from at least one EEG channel; and
- [0140] e. diagnosing the person with Schizophrenia if the magnitude of the average power spectrum from at least one EEG channel at the lower dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency or the magnitude of the average power spectrum from at least one EEG channel at the upper dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency.
- [0141] While embodiments of the present invention have been shown and described herein, such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.
- What is claimed is:
1. A method of diagnosing autism spectrum disorder (ASD), wherein the method comprises:
 - a. recording the EEG of a person;
 - b. calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and
 - c. diagnosing the person with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power.

2. A method of diagnosing ASD, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average relative Alpha Power of EEG signals from at least one of the frontal EEG channels and the average relative Alpha Power of EEG signals from at least one of the occipital-parietal EEG channels; and
- c. diagnosing the person with ASD if the average relative frontal Alpha Power is less than about 20% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

3. A method of diagnosing ASD, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average Alpha Frequency of EEG signals from at least one of the frontal EEG channels and the average Alpha Frequency of EEG signals from at least one of the occipital-parietal EEG channels; and
- c. diagnosing the person with ASD if the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

4. The method of claim 1 or 2 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5%.

5. The method of claim 1 or 3 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 10% of the average relative occipital-parietal Alpha Power and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

6. The method of claim 2 or 3 wherein the person is diagnosed with ASD if the average relative frontal Alpha Power is less than about 20% of the average relative occipital-parietal Alpha Power and the average relative frontal Alpha Power is less than about 5% and the average frontal Alpha Frequency is greater than about 0.5 Hz more than the average occipital-parietal Alpha Frequency.

7. A method of diagnosing Alzheimer's Disease, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel; and
- c. diagnosing the person with Alzheimer's Disease if the average dominant frequency is less than about 8 Hz.

8. A method of diagnosing Alzheimer's Disease, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average dominant frequency between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel;
- c. calculating the average coherence at the dominant frequency between the EEG signals from at least one frontal EEG channel and at least one occipital-parietal EEG channel; and
- d. diagnosing the person with Alzheimer's Disease if the average coherence is less than about 10%.

9. The method of claim 7 or 8 wherein the person is diagnosed with Alzheimer's Disease if the dominant frequency is less than about 8 Hz and the average coherence is less than about 10%.

10. A method of diagnosing Anxiety Disorder, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average entropy of the EEG signals from at least one EEG channel; and
- c. diagnosing the person with Anxiety Disorder if the average entropy is greater than about 0.7.

11. A method of diagnosing Depression, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average relative Alpha Power of at least one frontal EEG channel and the average relative Alpha Power of at least one occipital-parietal EEG channel; and
- c. diagnosing the person with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power.

12. A method of diagnosing Depression, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average frontal Alpha Frequency of EEG signals from at least one frontal EEG channel; and
- c. calculating the average relative Q-factor of EEG signals from at least one frontal EEG channel about the average Alpha Frequency; and
- d. diagnosing the person with Depression if the average relative Q factor is greater than about 8.

13. The method of claim 12 or 13 wherein the person is diagnosed with Depression if the average relative frontal Alpha Power is greater than the average relative occipital-parietal Alpha Power and the average relative Q factor is greater than about 8.

14. A method of diagnosing Schizophrenia, wherein the method comprises:

- a. recording the EEG of a person;
- b. calculating the average dominant frequency f_d between about 5 Hz and 15 Hz of EEG signals from at least one EEG channel;
- c. calculating the average lower dominant frequency between about 5 Hz and about f_d-1 Hz of EEG signals from at least one EEG channel;
- d. calculating the average upper dominant frequency between about f_d+1 Hz and about 15 Hz of EEG signals from at least one EEG channel; and
- e. diagnosing the person with Schizophrenia if the magnitude of the average power spectrum from at least one EEG channel at the lower dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency or the magnitude of the average power spectrum from at least one EEG channel at the upper dominant frequency is at least about 80% the magnitude of the average power spectrum from at least one EEG channel at the dominant frequency.

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专利名称(译)	使用神经测量学诊断精神障碍的方法		
公开(公告)号	US20170281030A1	公开(公告)日	2017-10-05
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[标]申请(专利权)人(译)	KOSIVANA控股		
申请(专利权)人(译)	KOSIVANA HOLDINGS LIMITED		
当前申请(专利权)人(译)	KOSIVANA HOLDINGS LIMITED		
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摘要(译)

描述了使用神经测定法诊断特定精神障碍的新方法。将EEG参数与阈值进行比较，以确定患者是否患有自闭症谱系障碍，阿尔茨海默病，焦虑症，抑郁症或精神分裂症。

