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(54) **METHOD FOR DETECTING NEUROLOGICAL AND CLINICAL MANIFESTATIONS OF A SEIZURE**

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(60) Provisional application No. 61/017,501, filed on Dec. 28, 2007.

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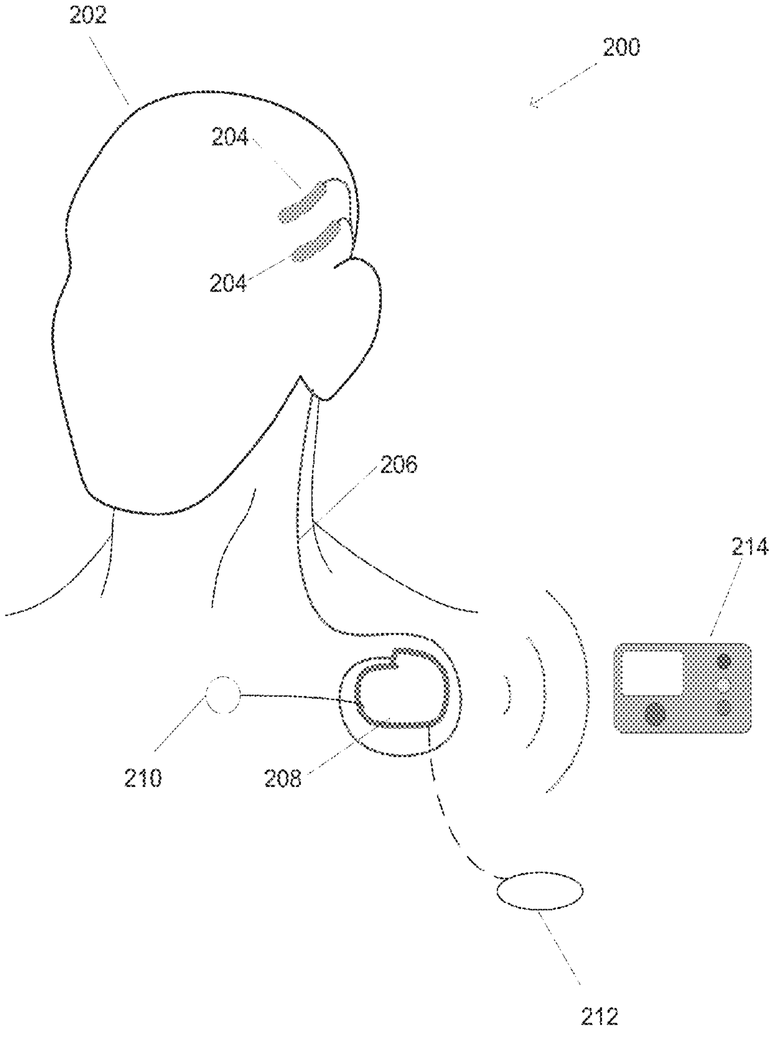
(57) **ABSTRACT**

Methods for detecting neurological and clinical manifestations of a seizure are provided. Systems are described including a monitoring device having a communication assembly for receiving neurological data transmitted external to a patient from a transmitter implanted in a patient; a processor that processes the neurological data to estimate the patient's brain state; and an assembly for automatically recording clinical manifestation data in response to a brain state estimate by the processor.



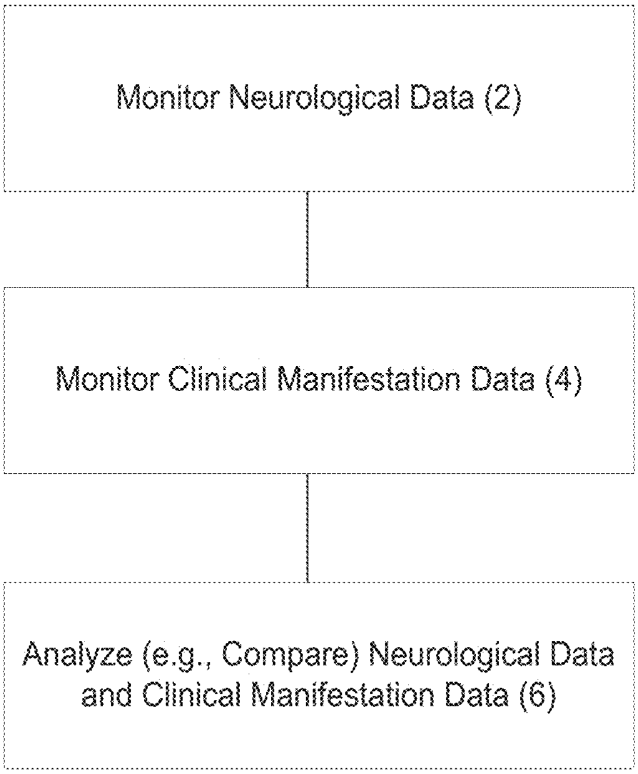

Monitor Neurological Data (2)
Monitor Clinical Manifestation Data (4)
Analyze (e.g., Compare) Neurological Data and Clinical Manifestation Data (6)

FIG. 1

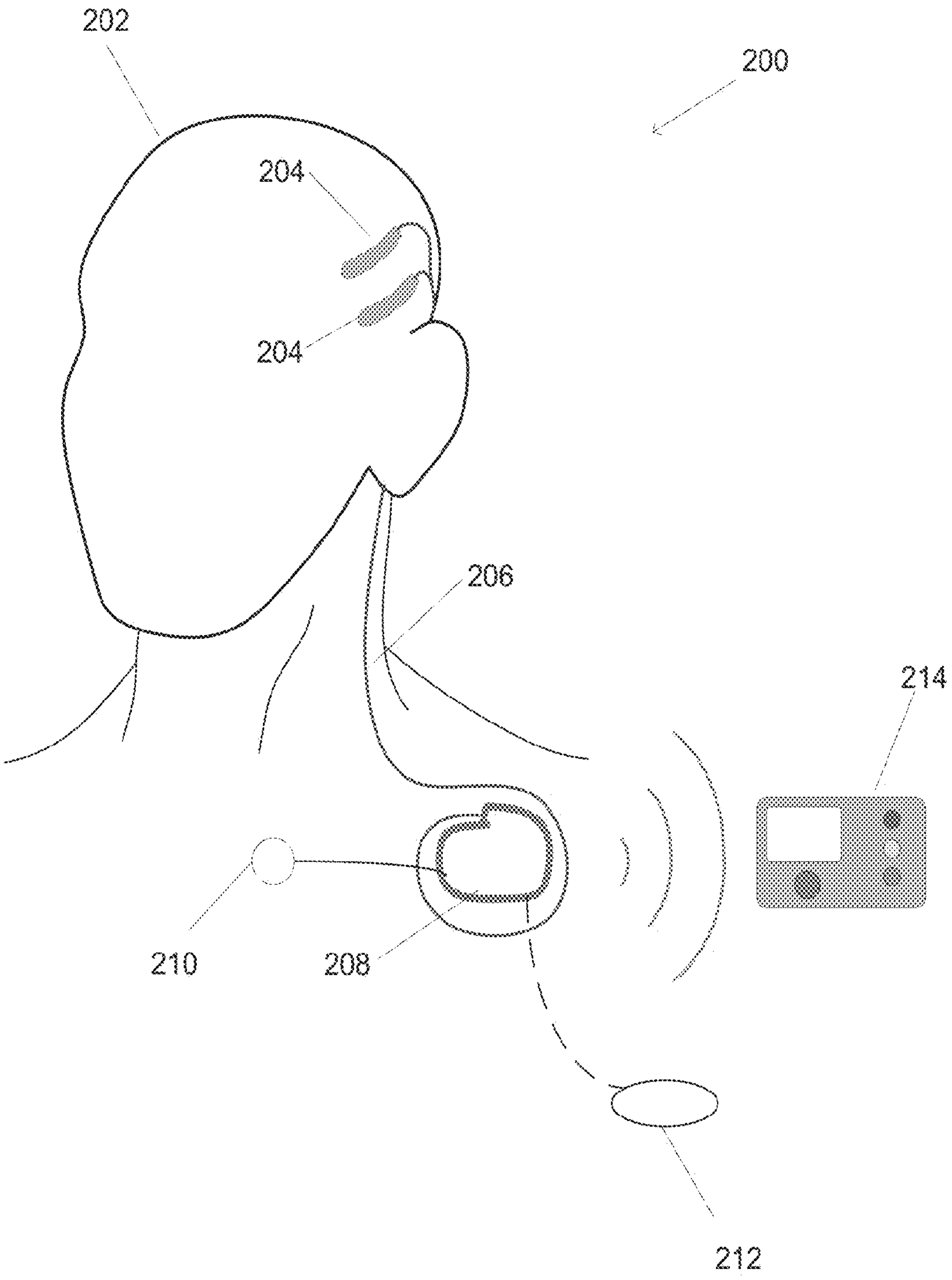


FIG. 2

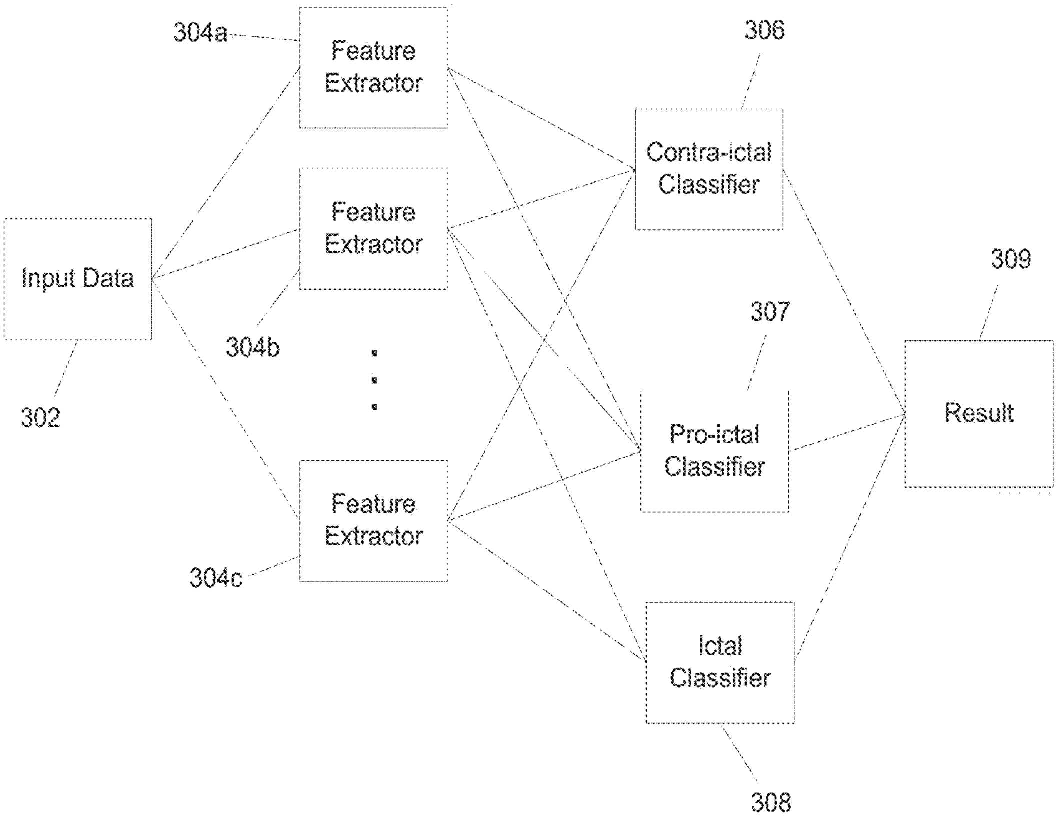

304a
Feature Extractor
306
Contra-ictal Classifier
309
Feature Extractor
Input Data
307
304b
302
Pro-ictal Classifier
Result
Feature Extractor
304c
Ictal Classifier
308

FIG. 3

Prediction algorithm output - Detection algorithm output

Safety algorithm output	0 0	0 1	1 1	1 0
0	Unknown "Yellow"	Seizure detected "Red flashing"	Seizure detected "Red flashing"	Seizure predicted "Red blinking"
1	Safe "Green"	Seizure detected "Red flashing"	Seizure detected "Red flashing"	Seizure predicted "Red blinking"

FIG. 4

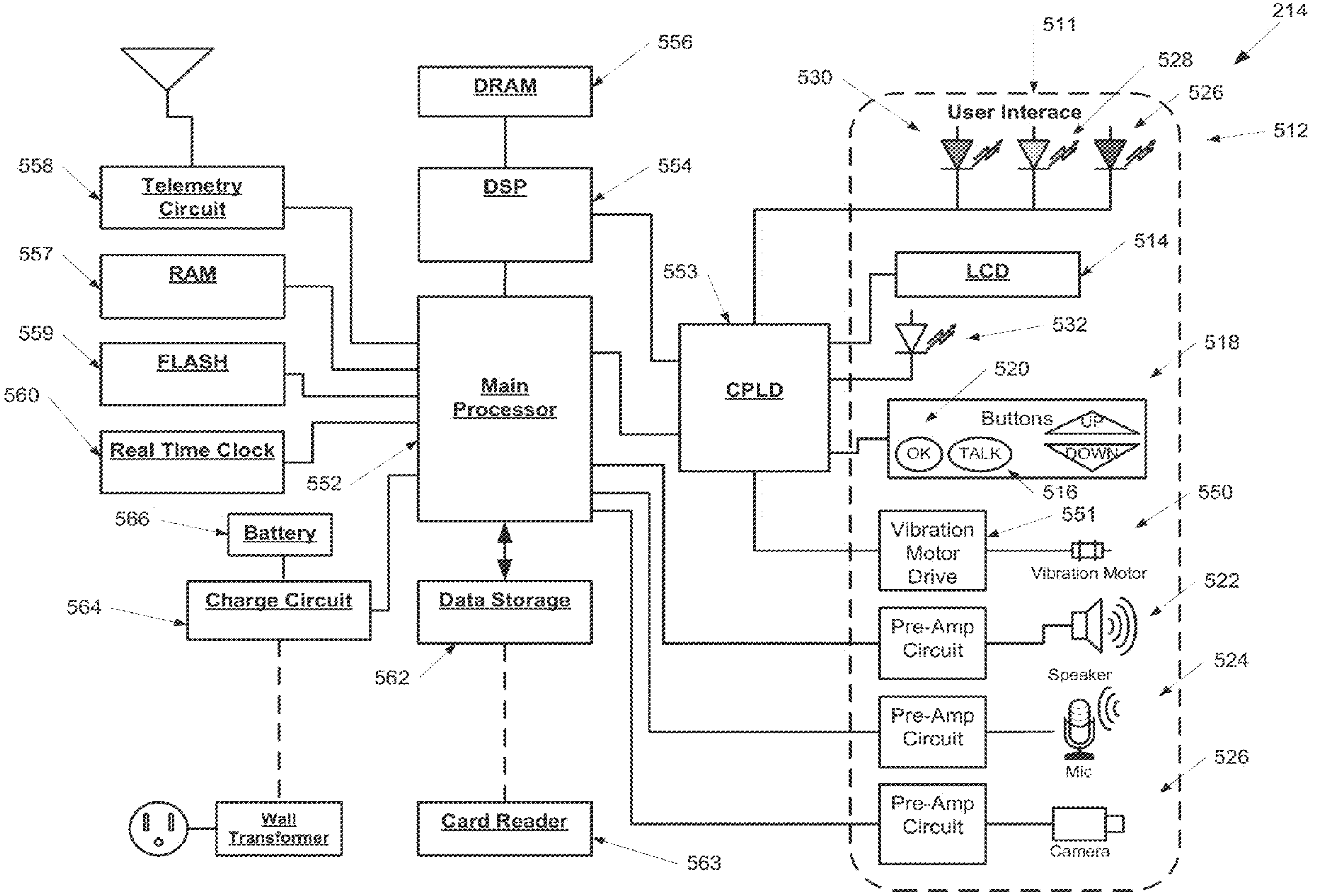

214
511
530
528
526
512
User Interace
556
DRAM
558
Telemetry Circuit
554
DSP
557
RAM
553
514
LCD
559
FLASH
532
518
520
Main Processor
CPLD
560
Real Time Clock
Buttons
UP
OK
TALK
DOWN
552
516
550
551
566
Battery
Vibration Motor Drive
Vibration Motor
564
Charge Circuit
Data Storage
522
Pre-Amp Circuit
Speaker
562
524
Pre-Amp Circuit
Mic
526
Pre-Amp Circuit
Camera
Wall Transformer
Card Reader
563

FIG. 5

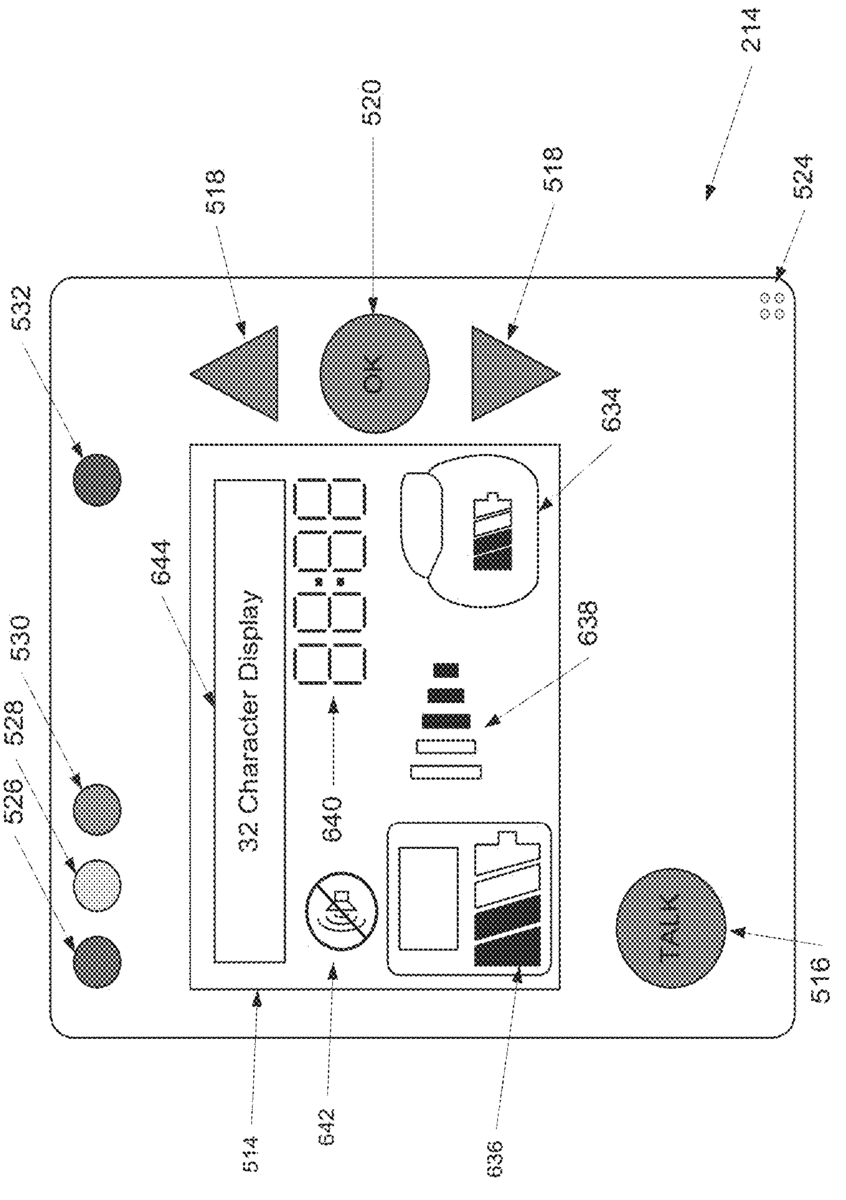

214
520
518
518
524
532
644
634
638
530
528
526
640
32 Character Display
OK
TALK
514
642
636
516

FIG. 6

METHOD FOR DETECTING NEUROLOGICAL AND CLINICAL MANIFESTATIONS OF A SEIZURE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation of U.S. patent application Ser. No. 12/343,376 filed Dec. 23, 2008, which claims the benefit of priority from U.S. Provisional Application No. 61/017,501, filed Dec. 28, 2007, both of which are incorporated by reference herein in their entirety.

INCORPORATION BY REFERENCE

[0002] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND OF THE INVENTION

[0003] Systems have been proposed that can monitor neurological data from a patient and use the data to detect a neurological event, such as the onset of an epileptic seizure. In such systems it may be desirable to additionally monitor a patient's notes and seizure logs to derive or change device settings.

[0004] Seizure logs, both written and electronic, have been used to monitor patient's seizure activity. However, conventional electronic seizure logs require the user, patient, or clinician, to take action to enter information into the seizure log. Examples of electronic seizure logs that require user activation are described in U.S. patent application Ser. No. 11/436,190 (US 2006/0212092), filed May 16, 2006, and U.S. patent application Ser. No. 11/412,230, filed Apr. 26, 2006 (US 2006/0235489), the disclosures of which are incorporated by reference herein in their entireties. However, as described in "Accuracy of Patient Seizure Counts," Christian Hoppe, PhD; Annkathrin Poepel, MD; Christian E. Elger, PhD, MD, Arch Neurol. 2007; 64(11):1595-1599, patient driven seizure logs are notoriously inaccurate, and provide only marginally useful data to both the physician and patient, and if used to derive new device settings may in fact detrimentally effect device performance. Additionally, clinical seizure activity that is monitored and/or recorded while the patient is in a hospital or other non-ambulatory setting requires the patient to be restricted to a confined location before the clinical manifestation data can be monitored and/or recorded. This prevents the patient from going about daily activities.

[0005] It would be beneficial to have a system that can automatically acquire data indicative of the occurrence of a clinical seizure without user intervention. It would also be beneficial to have a system wherein the acquisition of data indicative of the occurrence of a clinical seizure may be associated with the system's performance, and thereafter used to improve the performance of the system. It would additionally be beneficial to have an ambulatory system that can monitor and/or record data that is indicative of a clinical manifestation of a seizure without user intervention.

SUMMARY OF THE INVENTION

[0006] One aspect of the invention provides a method of comparing a patient's neurological data to data that is indicative of the patient's clinical manifestation of a seizure. In some embodiments, the method includes the steps of monitoring neurological data from a patient indicative of the patient's propensity for having a seizure; automatically recording clinical manifestation data from the patient that may be indicative of the occurrence of a clinical seizure; and analyzing the automatically recorded clinical manifestation data and the monitored neurological data to determine if one of the clinical manifestation data and the neurological data indicates the occurrence of a seizure while the other does not.

[0007] In some embodiments, the neurological data is EEG data, and the method includes the step of determining the patient's brain state based on the EEG data. The step of analyzing the clinical manifestation data with the neurological data may include the step of comparing the clinical manifestation data with the brain state to determine if one of the clinical manifestation data and the brain state indicates the occurrence of a seizure while the other does not. The step of determining the brain state may include the step of determining if the patient is in at least one of a pro-ictal state and an ictal state, and the step of automatically monitoring clinical manifestation data may include the step of automatically recording clinical manifestation data when the patient enters the pro-ictal or the ictal state. The method may also include the step of retraining an algorithm used in determining the patient's brain state if the determined brain state indicates seizure activity and the clinical manifestation data does not.

[0008] In some embodiments, the step of automatically monitoring clinical manifestation data includes the step of substantially continuously buffering clinical manifestation data during monitoring of neurological data from the patient. The method may also include the step of determining the patient's brain state based on the neurological data, and further comprising permanently storing in memory the monitored clinical manifestation data when the brain state indicates at least an increased likelihood of having a seizure.

[0009] In some embodiments, the step of automatically recording clinical manifestation data from the patient includes the step of annotating the monitored neurological data from a patient with an indication of the occurrence of the clinical manifestation of the seizure. The neurological data may be, e.g., an EEG recording, and annotating the neurological data may include the step of annotating the EEG data with an indication of the occurrence of the clinical manifestation of the seizure.

[0010] In some embodiments, the step of automatically recording clinical manifestation data includes the step of automatically recording convulsion activity in the patient. In other embodiments, the step of automatically recording clinical manifestation data includes the step of automatically recording audio of the patient. In still other embodiments, the step of automatically recording clinical manifestation data includes the step of automatically recording heart rate signals of the patient.

[0011] In some embodiments, the step of automatically recording clinical manifestation data includes the step of automatically recording video of the patient. In other embodiments, the method includes the step of transmitting in substantially real-time the neurological data from an implanted device to an external device, wherein automatically monitoring clinical manifestation data is performed by the external device when the step of monitoring the neurological data indicates a change from a first brain state to a second brain state. The step of automatically recording clinical manifestation data may include the step of recording clinical manifestation data in response to the occurrence of an event in the patient's condition. In some embodiments, the method is performed with an ambulatory patient monitoring device.

[0012] Another aspect of the invention provides a method of comparing a patient's estimated brain state to data that is indicative of clinical manifestation of a seizure. In some embodiments, the method includes the step of monitoring neurological data (such as, e.g., EEG data) from a patient; determining the patient's brain state based on the monitored neurological data, wherein the brain state indicates the patient's propensity for having a seizure; monitoring clinical manifestation data from the patient that is indicative of the occurrence of a clinical seizure; and comparing the monitored clinical manifestation data with the patient's determined brain state to determine if the brain state indicates the occurrence of a seizure while the clinical manifestation data does not. In some embodiments, the monitoring step is performed automatically, such as, e.g., in response to an occurrence of an event in the patient's condition. The method may be performed by an ambulatory patient monitoring device.

[0013] In some embodiments, the step of determining the brain state includes the step of determining if the patient is in at least one of a pro-ictal state and an ictal state or in at least one of a contra-ictal state, a pro-ictal state, and an ictal state. The method may also include the step of recording clinical manifestation data when the patient enters the pro-ictal or the ictal state. In some embodiments, the method includes the step of retraining an algorithm used in determining the patient's brain state if the determined brain state indicates seizure activity and the clinical manifestation data does not.

[0014] In some embodiments, the step of monitoring clinical manifestation data includes the step of substantially continuously buffering clinical manifestation data during monitoring of neurological data from the patient. The method may also include the step of permanently storing in memory the monitored clinical manifestation data when the brain state indicates at least an increased likelihood of having a seizure.

[0015] In some embodiments, the step of recording clinical manifestation data from the patient includes the step of annotating the monitored neurological data from a patient with an indication of the occurrence of the clinical manifestation of the seizure. In embodiments in which the neurological data includes an EEG recording, the step of annotating the neurological data may include the step of annotating the EEG data with an indication of the occurrence of the clinical manifestation of the seizure.

[0016] In various embodiments of the method, the step of recording clinical manifestation data may include recording convulsion activity in the patient, recording audio of the patient, recording heart rate signals of the patient, and/or recording video of the patient. The method may also include the step of transmitting in substantially real-time the neurological data from an implanted device to an external device, wherein monitoring clinical manifestation data is performed by the external device when monitoring the neurological data indicates a change from a first brain state to a second brain state.

[0017] Yet another aspect of the invention provides a method of automatically recording clinical manifestation data from a patient. In some embodiments, the method includes the steps of monitoring neurological data from a patient; estimating the patient's brain state based on the monitored neurological data; determining a change in the patient's brain state; and automatically recording clinical manifestation data from the patient using a device worn or held by the patient.

[0018] In some embodiments, clinical manifestation data is recorded when one or more specified changes in brain state occurs. In some embodiments, the step of determining a change in the patient's brain state includes the step of determining that the patient has entered into either a pro-ictal state or an ictal state or that the patient has gone from a contra-ictal state to a pro-ictal state or from a pro-ictal state to an ictal state. In some embodiments, the method includes the step of comparing either the neurological data or the brain state with the recorded clinical manifestation data to determine if one of the clinical manifestation data and the neurological data or brain state indicates the occurrence of a seizure while the other does not.

[0019] Still another aspect of the invention provides a monitoring device having a communication assembly for receiving neurological data transmitted external to a patient from a transmitter implanted in a patient; a processor that processes the neurological data to estimate the patient's brain state; and an assembly for automatically recording clinical manifestation data in response to a brain state estimate by the processor. In some embodiments, the assembly for automatically recording clinical manifestation data includes a data buffer configured to continuously buffer clinical manifestation data during monitoring of neurological data from the patient. Some embodiments of the invention also include an annotator configured to annotate monitored neurological data with an indication of the occurrence of clinical manifestation of a seizure.

[0020] In some embodiments, the assembly for automatically recording clinical manifestation data includes a convulsion detector, an audio input device, a heart rate detector, and/or a video camera. In some embodiments, monitoring device is adapted to be carried by an ambulatory patient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] The novel features of the invention are set forth with particularity in the claims that follow. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0022] FIG. **1** is a flow chart showing an embodiment of the invention.

[0023] FIG. **2** shows an embodiment of an ambulatory monitoring system according to an embodiment of the invention.

[0024] FIG. **3** is a schematic diagram showing aspects of a monitoring system according to an embodiment of the invention.

[0025] FIG. **4** is a schematic diagram showing other further aspects of a monitoring system according to an embodiment of the invention.

[0026] FIG. **5** is a block diagram showing aspects of a monitoring system according to an embodiment of the invention.

[0027] FIG. **6** shows aspects of a display for a monitoring system according to an embodiment of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0028] Described herein are systems and methods for determining if an observable clinical manifestation of a seizure is associated with the system's detection of a seizure or the system's determination of a patient's increased propensity for having a seizure (also referred to herein as "seizure prediction"). The system generally monitors a physiological signal (e.g., neurological data such as an electroencephalogram, or EEG) from the patient to detect the occurrence of a seizure and/or to estimate the patient's propensity for having a seizure. The correlation between observable clinical manifestation data of a seizure and the system's detection of a seizure and/or estimation of the patient's propensity for the seizure can assist in determining if the system is accurately estimating the propensity for having a seizure (or the detection of the seizure). The occurrence of an observable clinical manifestation of a seizure without the system's estimation of an increased propensity for the seizure or detection of a seizure suggests the system "missed" the seizure (i.e., a false negative), while the system's estimation of an increased propensity for a seizure or detection of a seizure without an observable clinical manifestation of a seizure may suggest a false positive or the detection or prediction of a sub-clinical seizure (i.e., an electrographic seizure that does not manifest clinically). Thus, the correlation between the two can be used to train the system (e.g., train an algorithm) to increase the accuracy of the system's estimation of the patient's propensity for a seizure and/or the system's detection capabilities. The correlation between the two can also help to create a system that is enabled with patient-specific algorithms (e.g., safety algorithm, prediction algorithm, detection algorithm).

[0029] The term "condition" as used herein refers generally to the patient's underlying disease or disorder—such as epilepsy, depression, Parkinson's disease, headache disorder, dementia, etc. The term "state" is used herein to generally refer to calculation results or indices that are reflective of a categorical approximation of a point (or group of points) along a single or multi-variable state space continuum. The estimation of the patient's state does not necessarily constitute a complete or comprehensive accounting of the patient's total situation. State typically refers to the patient's state within their neurological condition.

[0030] For example, for a patient suffering from epilepsy, at any point in time the patient may be in a different state along the continuum, such as an ictal state (a state in which a neurological event, such as a seizure, is occurring), a pre-ictal state (a state that immediately precedes the ictal state), a pro-ictal state (a state in which the patient has an increased risk of transitioning to the ictal state), an inter-ictal state (a state in between ictal states), a contra-ictal state (a protected state in which the patient has a low risk of transitioning to an ictal state within a calculated or predetermined time period), or the like. A pro-ictal state may transition to either an ictal or inter-ictal state. A pro-ictal state that transitions to an ictal state may also be referred to herein as a "pre-ictal state." The systems described herein may be adapted to be able to determine if the patient is in any or all of the above "states." Thus, the systems described herein may include systems designed to simply detect a seizure (i.e., to detect that the patient has entered an ictal state) as well as systems that are adapted to detect when the patient changes between at least two of the above described states. In addition, some systems may detect more than the states described herein.

[0031] The estimation and characterization of "state" may be based on one or more patient-dependent parameters from the a portion of the patient's body, such as neurological data from the brain, including but not limited to electroencephalogram signals "EEG" and electrocorticogram signals "ECoG" or intracranial EEG (referred to herein collectively as EEG"), brain temperature, blood flow in the brain, concentration of AEDs in the brain or blood, etc.). While parameters that are extracted from brain-based signals are preferred, the system may also extract parameters from other physiological signals of the body, such as heart rate, respiratory rate, chemical concentrations, etc.

[0032] An "event" is used herein to refer to a specific event, or change, in the patient's condition. Examples of such events include transition from one state to another state, e.g., an electrographic onset of seizure, an end of seizure, or the like. For conditions other than epilepsy, the event could be an onset of a migraine headache, a convulsion, or the like.

[0033] The occurrence of a seizure may be referred to as a number of different things. For example, when a seizure occurs, the patient is considered to have exited a "pre-ictal state" or "pro-ictal state" and has transitioned into the "ictal state". However, the clinical onset of a seizure is described herein to be a separate event from the electrographic onset of a seizure, but both may of course be occurring at the same time. The clinical onset of a seizure includes all clinical manifestations of a seizure. Clinical manifestations of a seizure, as used herein, includes an aura, a rhythmic jerking, stiffening or shaking of one or more limbs (referred to herein as "convulsion"), an ictal-moan, or any other commonly known clinical manifestation of a seizure, including any combination thereof.

[0034] A patient's "propensity" for a seizure is a measure of the likelihood of transitioning into the ictal state. The patient's propensity for seizure may be estimated by determining which "state" the patient is currently in. As noted above, the patient is deemed to have an increased propensity for transitioning into the ictal state (e.g., have a seizure) when the patient is determined to be in a pro-ictal state. Likewise, the patient may be deemed to have a low propensity for transitioning into the ictal state for a time period when it is determined that the patient is in a contra-ictal state. As stated above, the systems do not necessarily need to be able to determine the patient's propensity for a seizure, but can simply detect the occurrence of a seizure.

[0035] One exemplary simplified method is shown in FIG. **1**. The method comprises monitoring neurological data from a patient (e.g., EEG data) which is indicative of the patient's propensity for having a seizure (**2**). The method also includes monitoring clinical manifestation data from the patient that is indicative of the occurrence of a clinical seizure (**4**). Next, the method includes analyzing (e.g., comparing) the monitored clinical manifestation data and the neurological data to determine if one of the clinical manifestation data and the neurological data indicates the occurrence of a seizure while the other does not (**6**).

[0036] As used herein, "clinical manifestation data" may include any one or a combination of audio data (e.g., recording of an ictal moan), video data of the patient, data from an accelerometer provided on or in the patient's body (e.g., attached externally to or implanted in a patient's limb so as to record jerky rhythmic movements indicative of the patient's clinical seizure type), data from a heart rate monitor (e.g., to detect changes in heart rate, tachycardia, bradycardia, etc.), or data from other physiological or non-physiological sensors that are indicative of an occurrence of a seizure. While the remaining discussion highlights recording audio data, other types of clinical manifestation data may also be recorded.

[0037] FIG. **2** illustrates an exemplary simplified system that may be used to monitor a patient's neurological data and monitor clinical manifestation data from the patient. The system can also determine the patient's brain state based on the monitored neurological data.

[0038] The system **200** as shown comprises one or more electrodes **204** configured to measure neurological signals from patient **202**. Electrodes **204** may be located anywhere in or on the patient. In this embodiment, electrodes **204** are configured in one or more arrays and are positioned to sample electrical activity from the patient's brain. Electrodes **204** may be attached to the surface of the patient's body (e.g., scalp electrodes), attached to or positioned adjacent the skull (e.g., subcutaneous electrodes, bone screw electrodes, sphenoidal electrodes, and the like), or may be implanted intracranially in patient **202**. The electrode arrays include one or more macroelectrodes that are configured to monitor groups of neurons, or one or more microelectrodes that are configured to monitor a single neuron. In one embodiment, one or more of electrodes **204** will be implanted adjacent a previously identified epileptic focus, a portion of the brain where such a focus is believed to be located, or adjacent a portion of a seizure network.

[0039] Any number of electrodes **204** may be used, but electrodes **204** will preferably include between 1 electrode and 24 electrodes, and preferably between about 4 electrodes and 16 electrodes. The electrodes may take a variety of forms. The electrodes can comprise grid electrodes, strip electrodes and/or depth electrodes which may be permanently implanted through burr holes in the head.

[0040] In addition to measuring brain activity, other sensors may be employed to measure other physiological signals or non-physiological signals from patient **202** either for monitoring the patient's condition or to measure clinical manifestation data. For example, the system can include one or more of heart monitor **210** and accelerometer **212** that can be used to monitor data from the patient that is indicative of a seizure, or they can be used to monitor clinical manifestation data (e.g., heart rate and convulsion data, respectively) as described herein.

[0041] In an embodiment, electrodes **204** will be configured to substantially continuously sample the brain activity in the immediate vicinity of electrodes **204**. Electrodes **204** are shown electrically joined via leads **206** to implanted device **208**, but could be wirelessly coupled to implanted device **208** or other external device as is more fully described in the minimally invasive monitoring systems described in co-pending application Ser. No. 11/766,742, filed Jun. 21, 2007, the disclosure of which is incorporated herein by reference. In one embodiment, leads **206** and implanted device **208** are implanted inside patient **202**. For example, the implanted device **208** may be implanted in a sub-clavicular cavity or abdominal cavity of patient. In alternative embodiments, the leads **206** and implanted device **208** may be implanted in other portions of the patient's body (e.g., in the head) or attached to the patient **202** externally.

[0042] Implanted device **208** is configured to facilitate the sampling of low frequency and high frequency electrical signals from electrodes **204**. Sampling of brain activity is typically carried out at a rate above about 200 Hz, and preferably between about 200 Hz and about 1000 Hz, and most preferably at or above about 400 Hz. The sampling rates could be higher or lower, depending on the specific features being monitored, patient **202**, and other factors. Each sample of the patient's brain activity is typically encoded using between about 8 bits per sample and about 32 bits per sample, and preferably about 16 bits per sample. In alternative embodiments, implanted device **208** may be configured to measure the signals on a non-continuous basis. In such embodiments, signals may be measured periodically or aperiodically.

[0043] Patient Advisory Device ("PAD") **214** receives and optionally stores patient data. In one embodiment PAD **214** monitors, in substantially real-time, EEG signals and possibly other physiological signals from implanted device **208**. PAD **214** also may be used to record and/or store clinical manifestation data from the patient, such as audio data, heart rate data, accelerometer data, etc. In embodiments where the clinical manifestation data is in the form of audio and/or video recording, the PAD itself may be used to facilitate such monitoring. In other embodiments where the clinical manifestation data is monitored using a separate device such as heart monitor **210** and accelerometer **212**, the PAD is generally configured to receive the data monitored by the separate device and can thereafter record and/or store such clinical manifestation data. For example, heart rate data can be monitored by heart monitor **210**. The heart rate data can be transmitted to implanted device **208**, which can then transmit the heart rate data to PAD **214**.

[0044] In addition to the physiological signals from implanted unit **208** and the automatic recordings of the audio and/or video data, PAD **214** may also receive and store extracted features, classifier outputs, other patient inputs, and the like. Communication between PAD **214** and implanted device **208** may be carried out through wireless communication, such as a radiofrequency link, infrared link, optical link, ultrasonic link, or other conventional or proprietary wireless link. The wireless communication link between PAD **214** and implanted device **208** may provide a one-way or two-way communication link for transmitting data. Error detection and correction methods may be used to help insure the integrity of transmitted data. If desired, the wireless data signals can be compressed, encrypted, or otherwise processed prior to transmission to PAD **214**.

[0045] In use, electrode arrays **204** are used to sample neurological activity (e.g., EEG signals) from the patient's brain. The sampled brain activity is transmitted from electrode arrays **204** through leads **206** to implanted device **208**. In one embodiment implanted device **208** processes (e.g., filters, amplifies, digitizes, compresses, extracts features, and/or encrypts) the sampled brain activity signals and then wirelessly transmits a data signal with patient data to the PAD. As shown in FIG. **5** and described in more detail below, antenna and telemetry circuit **58** in PAD **214** receive the wireless signal from the implanted device with the patient data and transmit the patient data to main processor **552** and/or DSP **554** in the PAD. The patient data may be time stamped and stored in external storage device **562** for subsequent download to a physician computer (not shown). DSP **554** may process the patient data in substantially real-time with one or more brain state algorithms to estimate the patient's brain state, which is described below.

[0046] The system components shown in FIG. **2** are intended to be merely exemplary and the system may comprise one or more of those described herein. In addition, any data processing (neurological data or clinical manifestation data) that occurs is not limited to the locations described herein. Data processing may occur in almost any of the system components (e.g., in wireless electrode assemblies, implanted device **208**, or an external device such as PAD **214**) and it is not limited to the locations in which it is processed as described herein. For example, it may be desirable to perform much of the brain state analysis in implanted device **208** rather than in PAD **214**, or it may be desirable to analyze the clinical manifestation data and neurological data in implanted device **208**, PAD **214**, or other external device such as a physician's workstation.

[0047] In one exemplary embodiment of a system according to the instant invention in which the system estimates the patient's propensity for having a seizure, a plurality of brain state algorithms (e.g., safety algorithm, prediction algorithm, and detection algorithm) are optimized or enhanced for different purposes. While each of the algorithms will be optimized for different purposes, the algorithms may use one or more of the same features. For example, as shown in FIG. **3**, the PAD (or one of the implanted devices) may comprise a plurality of brain state algorithms which include one or more feature extractors and classifiers. The feature extractors **304***a*, **304***b*, **304***c* are each configured to extract the relevant features from the EEG signals (shown generically in FIG. **3** as "input data **302**"). The different brain state algorithms may take the features and use an optimized classifier **306**, **307**, **308** and attempt to classify the feature vector. For example, the contra-ictal classifier **306** will attempt to determine if the patient is in a brain state in which the patient is highly unlikely to transition into an ictal state within a predetermined time period. The pro-ictal classifier **307** will attempt to determine if the patient is in a pro-ictal brain state in which the patient has an elevated propensity for transitioning into the ictal state. The ictal classifier **308** will attempt to determine if the patient has already transitioned into the ictal state.

[0048] Exemplary brain state algorithms which may be used to determine the patient's brain state as described herein are described in U.S. patent application Ser. No. 12/020,450, filed Jan. 25, 2008, and U.S. patent application Ser. No. 12/035,335, filed Feb. 21, 2008, the disclosures of which are incorporated herein by reference. And while the above examples describe three separate algorithms to analyze the patient's brain state, it should be appreciated that a single algorithm may be used to perform the same function of the aforementioned algorithms. Also, there may be more or fewer than three algorithms used to classify the brain state into any number of brain states. The system may also include only one algorithm which is essentially a detection algorithm and could be the equivalent of the ictal classifier to determine if the patient has entered into the ictal state. The system could also only comprise the equivalent of the ictal and pro-ictal classifiers.

[0049] In embodiments in which the system provides an output to the patient (e.g., via PAD **214** or similar external device), the outputs of the three different algorithms may be combined in a logical manner to determine the type of output communication that is provided to the patient. FIG. **4** illustrates one example of how the output from three exemplary different brain state algorithms may be used to generate the communication output. In the illustrated embodiment, the output from the algorithms is illustrated as either "0" or "1". A "1" for the safety algorithm would mean that the safety algorithm determined that the patient was "safe" and unlikely to transition into the ictal state within a predetermined time period, whereas a "0" for the safety algorithm means that the patient is not "safe"—but that does not necessarily mean that the patient has an increased propensity for transitioning into the ictal state. A "1" for the prediction algorithm would mean that the prediction algorithm determined that the patient has an elevated propensity for transitioning into the ictal state (e.g., is in a pro-ictal state), whereas a "0" for the prediction algorithm means that the patient does not have an increased propensity for transitioning into the ictal state. A "1" for the detection algorithm would mean that the detection algorithm determined that the patient was in the ictal state, whereas a "0" for the detection algorithm means that the patient is determined to not be in the ictal state.

[0050] In the illustrated example of FIG. **4**, the possible brain state indicator outputs include a green light (safe brain state), a yellow light (unknown brain state), a blinking red light (pro-ictal brain state), and a flashing red light (ictal brain state). Of course, any type of visual, tactile, and/or audio output could be provided to indicate the patient's brain state, and the present invention is not limited to such outputs.

[0051] In the upper left corner of the chart in FIG. **4** is the combination of the outputs from the three algorithms in which the output of all three of the algorithms are "0". In such case, none of the algorithms are able to provide a positive determination and the patient's brain state would fall in the unknown state. Hence, the output to the patient would be the yellow light.

[0052] In the bottom left square of the left-most column, where the safety algorithm determines that the patient is safe (safety algorithm output is "1") and neither the prediction algorithm nor the detection algorithm determine that the patient is in a pro-ictal brain state or an ictal brain state (e.g., both are "0"), the patient is deemed to be in a safe brain state and the output to the patient is the green light.

[0053] In the middle four boxes—in which the seizure detection algorithm output is a "1", all of the output combinations are determined to be seizure detection and a red flashing light would be provided to the patient with PAD **214**. In this configuration, the seizure detection algorithm would take precedent over the seemingly inconsistent results from the safety algorithm and the prediction algorithm. Of course, in other configurations, where the results from the different algorithms are inconsistent, it may be desirable to estimate the patient to be in an "unknown" brain state and provide a yellow light (or similar output that is indicative of the unknown state).

[0054] The right column of the chart shows the situation where the seizure prediction algorithm has determined that the patient is in a pro-ictal brain state and the detection algorithm has determined that the patient is not yet in the ictal brain state. In such situations, the output from the prediction algorithm would take precedent over the output from the safety algorithm and the output to the patient would be that of "seizure predicted" and a red flashing light would be provided. In other configurations, in the situation where the safety algorithm is inconsistent with the prediction algorithm (e.g., both are "1"), it may be desirable to estimate the patient to be in an "unknown" brain state and provide a yellow light (or similar output).

[0055] Thus, depending on the output(s) from the brain state algorithms, the appropriate brain state indicator is illuminated on PAD and/or an audible or tactile alert is provided to the patient when the patient's brain state changes. The PAD may also include an "alert" or "information" indicator (such as an LED, or tone) that alerts the patient that a change in brain state or system component state has occurred, or that user intervention is required. This alert indicator may occur in conjunction with another alert, and may simply be used as a universal indicator to the patient that the user needs to pay attention to the PAD and/or intervene.

[0056] The brain state indicators on PAD **214** allow the patient to substantially continuously monitor the brain state on a real-time basis. Such brain state indicators may be used by the patient to assess which activities "trigger" their brain to move them from a "safe" state to an "unknown" or "pro-ictal state." Consequently, over time the patient may be able to avoid the particular triggers.

[0057] FIG. **5** shows a simplified block diagram of an exemplary embodiment of a PAD which is part of a system designed to receive a patient's neurological data and receive and/or monitor clinical manifestation data. As noted above, the patient's neurological data may be processed to determine the patient's propensity for having a seizure while the clinical manifestation data may be used subsequently to confirm the occurrence of the seizure (or determine that a seizure did not occur), and such data may thereafter be used to adjust one or more parameters of the system.

[0058] The illustrated PAD shows a user interface **511** that includes a variety of indicators for providing system status and alerts to the patient. User interface **511** may include one or more indicators **512** that indicate the patient's brain state. In the illustrated embodiment, the output includes light indicators **512** (for example, LEDs) that comprise one or more discrete outputs that differentiate between a variety of different brain states. In the illustrated embodiment, the brain state indicators **512** include a red light **526**, yellow/blue light **528**, and a green light **530** for indicating the patient's different brain states. In some configurations the lights may be solid, blink or provide different sequences of flashing to indicate different brain states. If desired, the light indicators may also include an "alert" or "information" light **532** that is separate from the brain state indicators so as to minimize the potential confusion by the patient. In other embodiments the PAD is part of a system that is merely a detection system, or part of a system that can indicate detection and an increased likelihood of having a seizure (pro-ictal), but does not necessarily determine when the patient is in a contra-ictal brain state. In other embodiments, the system may only be used for a "safety monitor" and may only indicate when the patient is in the contra-ictal brain state. Exemplary methods and systems for providing alerts to the patient can be found in a commonly owned U.S. patent application filed concurrently with this application entitled "Patient Advisory EEG Analysis Method and Apparatus" (Attorney Docket No. 10003-733.100), the disclosure of which is incorporated herein by reference.

[0059] PAD **214** may also include a liquid crystal display ("LCD") **514** (which can be seen in more detail in FIG. **6**) or other display for providing system status outputs to the patient. The LCD **514** generally displays the system components' status and prompts for the patient. For example, as shown in FIG. **6**, LCD **514** can display indicators, in the form of text or icons, such as, for example, implantable device battery strength **634**, PAD battery strength **636**, and signal strength **638** between the implantable device and the PAD. If desired, the LCD may also display the algorithm output (e.g., brain state indication) and the user interface **511** may not require the separate brain state indicator(s) on other portions of the PAD. The output on the LCD can be continuous, but in some embodiments may appear only upon the occurrence of an event or change of the system status and/or the LCD may enter a sleep mode until the patient activates a user input. LCD **514** is also shown including clock **640**, audio status **642** (icon shows PAD is muted), and character display **644** for visual text alerts to the patient—such as an estimated time to seizure or an estimated "safe" time. While not shown in FIG. **6**, LCD **514** may also indicate the amount of free memory remaining on the memory card.

[0060] Referring again to FIG. **5**, PAD **214** may also include speaker **522** and a pre-amp circuit to provide audio outputs to the patient (e.g., beeps, tones, music, recorded voice alerts, etc.) that may indicate brain state, change in brain state, or system status outputs to the patient. User interface **511** may also include a vibratory output device **550** and vibration motor drive **551** to provide a unique tactile alert to the patient that indicates a specific brain state, which may be used separately from or in conjunction with the visual and audio outputs provided to the patient. Depending on the desired configuration any of the aforementioned outputs may be combined to provide information to the patient.

[0061] PAD **214** typically comprises at least one input device that allows the PAD to monitor and/or record clinical manifestation data which is indicative of the occurrence of a clinical seizure. The input device can be automatically activated, user-activated, or a combination thereof. PAD **214** may include a circular buffer in RAM **557** to buffer the clinical manifestation data. If a seizure is detected and/or predicted, the clinical manifestation data may then be written and permanently stored in data storage **562**. While SRAM is one preferred embodiment of the type of memory for storing the clinical manifestation data files, other types of conventional types of memory (e.g., FLASH **559**) may also be used.

[0062] Inputs include, for example, one or more physical inputs (e.g., buttons **516**, **518**, **520**) that may be used to activate an audio input (in the form of a microphone **524** and a pre-amp circuit) and/or a video input (in the form of a video capture device **526** and a pre-amp circuit). In some uses, the inputs can be used by the patient to make time-stamped notes or annotations that may be overlaid on the patient's EEG data file. Such notes could include, occurrence of a clinical seizure (e.g., clinical manifestation data), feeling of an aura (a different feeling, smell, taste, etc.), taking of an anti-epileptic drug, indication of sleep state ("I'm going to sleep," "I just woke up," "I'm tired," etc.) Such notes or annotations may be stored in a separate data file or as part of the patient's EEG or brain state files.

[0063] For example, in some embodiments the PAD comprises a dedicated user activated input button that allows the user to simply depress the input button to indicate that that the patient is experiencing a clinical manifestation of a seizure or an aura. Upon user-activation a separate clinical manifestation data file can be created, receive a date and time-stamp, and can be stored on the PAD and/or transmitted in substantially real-time to another device, such as a physician's computer system over a wireless network. Alternatively, the neurological data (e.g., EEG data) which is being processed by the system can simply be automatically annotated with the date and time and type of input (e.g., "user-activated aura indicator," or "automatic convulsion indicator"). If the clinical manifestation information is saved as a separate data file, it can be subsequently analyzed with the neurological data to determine if one of the clinical manifestation data and the neurological data indicate the occurrence of a seizure while the other does not. If this is the case, the system, such as an algorithm in the system, can be re-trained to improve the accuracy of the system in predicting and/or detecting seizures. This process is described in more detail below.

[0064] In some embodiments, a user-activated input may be configured to allow the patient to record any type of audio, such as voice data using the microphone. As shown in FIG. **5**, a dedicated voice recording user input **516** may be activated to allow for voice recording. In preferred embodiments, the voice recording may be used as an audio patient seizure diary. Such a diary may be used by the patient to record when a seizure has occurred, when an aura or prodrome has occurred, when a medication has been taken, to record patient's sleep state, stress level, etc. Such voice recordings may be time stamped and stored in data storage of the PAD and may be transferred along with recorded EEG signals to the physician's computer. Such voice recordings may thereafter be overlaid over the EEG signals and used to interpret the patient's EEG signals and improve the training of the patient's customized algorithm(s), if desired.

[0065] Such user activated inputs may thereafter be compared to the outputs of the brain state algorithms to assess a number of different things. For example, the number of seizures detected by the detection algorithm may be compared to the number of auras that the patient experienced. Additionally, the number of seizures detected by the detection algorithm may be compared to the patient's seizure log to assess how many of the seizures the patient was able to log. In other aspects, the physician may ask that the patient make a notation in the log every time an anti-epileptic drug is taken. Such a log could be used to monitor the patient's compliance, as we as to determine the effect of the anti-epileptic drug on the patient's EEG.

[0066] In other embodiments, the PAD (or other device within the system) may be adapted to include automatic inputs for automatically monitoring and/or recording clinical manifestation data which is indicative of the occurrence of a seizure. Exemplary automatic inputs include a microphone and pre-amp circuit (which can automatically monitor and/or record audio data from the patient such as an ictal-moan), a convulsion detector (e.g., accelerometer which can automatically monitor and/or record a patient's rhythmic movement or jerking that is indicative of the patient's clinical seizure), a heart rate monitor (which can automatically monitor and/or record a patient's heart rate or the like), and/or a video recording unit (similar to those in cellular phones) which can automatically record video of the patient.

[0067] The different inputs can be disposed within the PAD, a separate device external to the patient, or they may be disposed within or on the patient. If the input device is disposed in the PAD, the PAD can monitor the clinical manifestation data and either store the data in the PAD or transmit it to a separate external device such as a physician's computer. If the input device is disposed within or on the patient, or in a separate external device, the monitored clinical manifestation data, processed or unprocessed, can be transmitted to the PAD, where it can be stored or further transmitted to a separate external device such as a physician's computer. As described above, the devices used to automatically monitor and/or record the clinical manifestation data can be disposed in any of the system components described herein, and the data can be processed and/or stored in any of the system components described herein. For example, a microphone can be disposed within the PAD to monitor and record audio data while a heart rate monitor can be disposed on or within the patient to monitor the patient's heart rate.

[0068] In an exemplary embodiment, a convulsion detector, such as an accelerometer, can be built into the PAD or other external device worn or held by the patient, or it can be disposed internally within the patient, such as in the implanted device **208** or implanted elsewhere in the patient's body as illustrated as detector **212** in FIG. **2**. The convulsion detector is shown in communication with implanted device **208**, which is in communication with PAD **214**, via conventional wired and wireless communication links. The convulsion detector (wherever it may be disposed) can detect a convulsion associated with a seizure and transmit a data signal to the PAD that a convulsion/seizure has occurred. The PAD may then automatically date and time-stamp the convulsion occurrence, which can then be annotated on the EEG data or which can then be stored as a separate data file. Again, the occurrence of this clinical manifestation of the occurrence of a seizure can then be compared to the stored EEG data, or the brain state estimation, for training purposes.

[0069] In a second example of automatically recording clinical manifestation data, as shown schematically in FIG. **2** the heart rate monitor **210** may be in communication with the implanted device **208** or PAD **214** via conventional wired or wireless communication links. Heart rate monitor **210** may be used to monitor a change in heart rate (e.g., autonomic tone via R-R interval variability) that is indicative of a seizure and transmits a data signal to the PAD that a change in heart rate that is indicative of seizure has occurred. The PAD may then automatically date and time-stamp the occurrence, which can then be annotated on the EEG data or which can then be stored as a separate data file. Again, the occurrence of this clinical manifestation of the occurrence of a seizure can then be compared to the stored EEG data, or the brain state estimation, for training purposes.

[0070] In a third example of automatically recording clinical manifestation data, the automatic input device is a microphone on the PAD and is automatically activated to record audio data from the patient. This can be used to record audio clinical manifestations of a seizure, such as, for example, a so-called "ictal moan" or "ictal gasp" that may be caused by tonic contraction of muscles. This is a distinguishable sound to a practiced clinician and can be discerned by listening to the recorded audio data. In some configurations, it may be desirable to use speech recognition software to automatically determine if there is an audio recording of the clinical manifestation of the patient's seizure. Such speech recognition software would be made patient specific by training on the patient's previous occurrence of a seizure.

[0071] In this third example (but may be applied to any of the embodiments described herein), the microphone may be configured to automatically continuously record audio data in a first-in first-out (FIFO) manner where the current audio data over-writes the oldest data as memory storage capacity is exceeded. In the event that the system determines that a neurological event has occurred or the patient's brain state has changed (e.g., the system determined that a seizure has been detected or predicted, the patient has changed from a safe-state to a pro-ictal state, the system has predicted the onset of a seizure, etc.), the PAD automatically begins to permanently store the monitored audio data for a specific period of time preceding (e.g., the "pre-trigger timer period" anywhere from a few seconds (10 seconds to 5 minutes) and/or following the trigger ("post trigger) while continuing to monitor and store the patient's EEG information. If an audio clinical manifestation has occurred, it will be recorded via the microphone and stored in memory. As described above, the monitored EEG data or determined brain state can then be annotated with the indication of the occurrence (including date/time stamp) of the clinical manifestation of the seizure (e.g., "ictal moan automatically recorded"), or the clinical manifestation data can be stored as a separate file, date and time-stamped, and stored in the PAD memory or transmitted to another device. It can then be compared to the EEG data or brain state.

[0072] In an alternative embodiment in which the clinical manifestation data is automatically monitored and/or recorded, the clinical manifestation data is not continuously monitored and recorded. Rather, the PAD or other device may automatically initiate audio monitoring and/or recording upon the occurrence of an event in the patient's condition or upon the occurrence of a change in the patient's brain state. Examples of events that can trigger the automatic monitoring and/or recoding of clinical manifestation data include, without limitation, when the system detects a seizure, when the system detects a change from a safe-state to pro-ictal state, the system predicts the onset of a seizure, the system detects an increased likelihood of having a seizure, etc.). The data can be time-stamped and used for training or retraining purposes as described above. To avoid missing the recordation of a clinical manifestation, it would likely be beneficial for the PAD to initiate recording as soon as the system detects an event. For example, the PAD can start recording the clinical manifestation data when the system estimates a change from a safe-state to a pro-ictal state or when the onset of a seizure is predicted.

[0073] In some configurations, the PAD is adapted to automatically switch from a first mode (where clinical manifestation data is continuously recorded) to a second mode in which the clinical manifestation data is recorded only upon the occurrence of a change in the patient's condition. This can be advantageous if the remaining storage in the device falls below a certain threshold. In other embodiments, the PAD may always be set in the second mode.

[0074] In a fourth example of the automatic input device the video recording unit **526** (the video recording unit may alternatively be disposed in a device other than the PAD) may be configured to continuously record video data in a first-in first-out (FIFO) manner where the current video data overwrites the oldest data as memory storage capacity is exceeded, in a manner similar to that described above for the automatic audio recording. In an alternative embodiment of automatic video recording, the video data may not always be continuously monitored and recorded, rather, the video data may be automatically initiated upon the occurrence of an event, as described above (e.g., the system detects a seizure, a change from safe-state to pro-ictal state, the system predicts the onset of a seizure, etc.).

[0075] While it has been previously proposed to use accelerometer data and video data to detect an onset of a clinical seizure in a hospital setting, such data has not been collected with an ambulatory device and such data does not appear to be used to confirm the electrographic onset of a seizure for assessing performance and possible retraining of a seizure monitoring system. One exemplary advantage of an ambulatory system with such capabilities is that a seizure detection system can be retrained and yet the patient does not have to be confined to a hospital or other non-ambulatory setting.

[0076] Recording the clinical manifestation data can also assist in the classification of the monitored electrographic seizure activity as either sub-clinical (not manifesting clinically) or clinical (associated with a clinical manifestation), which is described in more detail below.

[0077] While the above describes preferred physiological and non-physiological data that may be used to confirm the clinical onset of a seizure, there are other types of clinical manifestation data that may be used. For example, it may be possible to monitor the patient's respiration via impedance pneumograph, a skin temperature, electrical impulses of muscles via electromyography (EMG) sensors, or the like.

[0078] Referring again to FIG. **5**, similar to conventional cellular phones, inputs **516**, **518**, **520** may be used to toggle between the different types of outputs provided by the PAD. For example, the patient can use buttons **516**, **518** to choose to be notified by tactile alerts such as vibration rather than audio alerts (if, for example, a patient is in a movie theater). Or the patient may wish to turn the alerts off altogether (if, for example, the patient is going to sleep). In addition to choosing the type of alert, the patient can choose the characteristics of the type of alert. For example, the patient can set the audio tone alerts to a low volume, medium volume, or to a high volume.

[0079] The one or more inputs may also be used to acknowledge system status alerts and/or brain state alerts. For example, if PAD **214** provides an output that indicates a change in brain state, one or more of the LEDs **512** may blink, the vibratory output may be produced, and/or an audio alert may be generated. In order to turn off the audio alert, turn off the vibratory alert and/or to stop the LEDs from blinking, the patient may be required to acknowledge receiving the alert by actuating one of the user inputs (e.g., acknowledge/okay button **520**).

[0080] While the PAD is shown having inputs **516**, **518**, **520**, any number of inputs may be provided on PAD. For example, in one alternate embodiment, the PAD may comprise only two input buttons. The first input button may be a universal button that may be used to scroll through output mode options. A second input button may be dedicated to voice recording. When an alert is generated by the PAD, either of the two buttons may be used to acknowledge and deactivate the alert. In other embodiments, however, there may be a dedicated user input for acknowledging the alerts.

[0081] PAD **214** may comprise main processor **552** and complex programmable logic device (CPLD) **553** that control much of the functionality of the PAD. In the illustrated configuration, main processor and/or CPLD **553** control the outputs displayed on LCD **514**, generates the control signals delivered to vibration device **550** and speaker **522**, and receives and processes the signals from buttons **516**, **518**, **520**, microphone **524**, video assembly **526**, and real-time clock **560**. Real-time clock **560** may generate the timing signals that are used with the various components of the system.

[0082] The main processor may also manage data storage device **562** and manage telemetry circuit **558** and charge circuit **564** for a power source, such as battery **566**.

[0083] While main processor **552** is illustrated as a single processor, the main processor may comprise a plurality of separate microprocessors, application specific integrated circuits (ASIC), or the like. Furthermore, one or more of microprocessors **552** may include multiple cores for concurrently processing a plurality of data streams.

[0084] CPLD **553** may act as a watchdog to main processor **552** and DSP **554** and may flash LCD **514** and brain state indicators **512** if an error is detected in DSP **554** or main processor **552**. Finally, CPLD **553** controls the reset lines for main microprocessor **552** and DSP **554**.

[0085] Telemetry circuit **558** and antenna may be disposed in PAD **214** to facilitate one-way or two-way data communication with the implanted device. Telemetry circuit **558** may be an off the shelf circuit or a custom manufactured circuit. Data signals received from the implanted device by telemetry circuit **558** may thereafter be transmitted to at least one of DSP **554** and main processor **552** for further processing.

[0086] DSP **554** and DRAM **556** receive the incoming data stream from main processor **552**. In embodiments in which the PAD comprises the brain state algorithms, the brain state algorithms process the data (for example, EEG data) and estimate the patient's brain state, and can be executed by DSP **554** in the PAD. In other embodiments, however, the brain state algorithms may be implemented in the implanted device, and the DSP may be used to generate the communication to the patient based on the data signal from the algorithms in the implanted device. The algorithms can also be stored in a device remote from the patient, such as a physician's computer system. The implanted device and the PAD could primarily transmit the monitored data to the remote device for subsequent processing.

[0087] Main processor **552** is also in communication with data storage device **562**. Data storage device **562** preferably has at least about 7 GB of memory so as to be able to store data from about 16 channels at a sampling rate of between about 200 Hz and about 1000 Hz. With such parameters, it is estimated that the 7 GB of memory will be able to store at least about 1 week of patient data. Of course, as the parameters (e.g., number of channels, sampling rate, etc.) of the data monitoring change, so will the length of recording that may be achieved by the data storage device **562**. Furthermore, as memory capacity increases, it is contemplated that the data storage device will be larger (e.g., 10 GB or more, 20 GB or more, 50 GB or more, 100 GB or more, etc.). Examples of some useful types of data storage device include a removable secure digital card or a USB flash key, preferably with a secure data format. The storage device can be used to store raw neurological data (e.g., EEG data), processed neurological data (e.g., determined brain states), clinical manifestation data, raw or processed neurological data annotated with the occurrence of the clinical manifestation of a seizure, etc.

[0088] "Patient data" as used herein may include one or more of raw analog or digital EEG signals, compressed and/or encrypted EEG signals or other physiological signals, extracted features from the signals, classification outputs from the algorithms, monitored clinical manifestation data, etc. Data storage device **562** can be removed when full and read in card reader **563** associated with the patient's computer and/or the physician's computer. If the data card is full, (1) the subsequent data may overwrite the earliest stored data as described above, or (2) the subsequent data may be processed by DSP **554** to estimate the patient's brain state (but not stored on the data card). While preferred embodiments of data storage device **562** are removable, other embodiments of the data storage device may comprise a non-removable memory, such as FLASH memory, a hard drive, a microdrive, or other conventional or proprietary memory technology. Data retrieval off of such data storage devices **562** may be carried out through conventional wired or wireless transfer methods.

[0089] The power source used by PAD **214** may comprise any type of conventional or proprietary power source, such as a non-rechargeable or rechargeable battery **566**. If a rechargeable battery is used, the battery is typically a medical grade battery of chemistries such as a lithium polymer (LiPo), lithium ion (Li-Ion), or the like. Rechargeable battery **566** will be used to provide the power to the various components of PAD **214** through a power bus (not shown). Main processor **552** may be configured to control charge circuit **564** that controls recharging of battery **566**.

[0090] In addition to being able to communicate with an implanted device, the PAD may have the ability to communicate wirelessly with a remote device—such as a server, database, physician's computer, manufacturer's computer, or a caregiver advisory device (all interchangeably referred to herein as "CAD"). In the exemplary embodiment, the PAD may comprise an additional communication assembly (not shown) in communication with main processor **552** that facilitates the wireless communication with the CAD. The communication assembly may be a conventional component that is able to access a wireless cellular network, pager network, wifi network, or the like, so as to be able to communicate with the remote device. Any of the information stored in PAD **214** may be transmitted to the remote device.

[0091] In some embodiments, PAD **214** is able to deliver a signal through the communication assembly that is received by a remote device, in either real-time or non-real-time. Real-time transfer of data could include the real-time transfer of the patient's brain state, clinical manifestation data, patient notes (e.g., seizure log, etc.) so as to inform a caregiver of the occurrence of a seizure or the patient's brain state or change in brain state, as determined by the PAD. The CAD would allow the caregiver to be away from the patient (and give the patient independence), while still allowing the caregiver to monitor the occurrence of clinical manifestation data, seizures, the patient's brain state, and the patient's propensity for seizure. Thus, if the patient's brain state indicates a high propensity for a seizure or the occurrence of a seizure, the caregiver would be notified via the CAD, and the caregiver could facilitate an appropriate treatment to the patient (e.g., small dosage of an antiepileptic drug, make the patient safe, etc.).

[0092] In other embodiments, the communication assembly could be used to facilitate either real-time or non-real time data transfer to the remote server or database. If there is real time transfer of data, such a configuration could allow for remote monitoring of the patient's brain state, recorded EEG data, and/or clinical manifestation data. Non-real time transfer of data could expedite transfer and analysis of the patient's recorded EEG data, clinical manifestation data, extracted features, or the like. Thus, instead of waiting to upload the brain activity data from the patient's data storage device, when the patient visits their physician, the physician may have already had the opportunity to review and analyze the patient's transferred brain activity data and clinical manifestation data prior to the patient's visit.

[0093] Some embodiments include a system which can be toggled between two or more different modes of operation. In one example, a first mode of operation of the PAD (or other device) may be primarily data collection and algorithm training, in which the monitored neurological signals (e.g., EEG signals), brain state estimations, and clinical manifestation data are transmitted or transferred to a remote device (e.g., to the physician). It may be desirable to also run a generalized (i.e., not patient-specific) seizure detection algorithm in conjunction with the automatic clinical manifestation recording means (e.g., record audio, video, heart rate, movement). It can then be determined if there is an association between a clinical manifestation of a seizure and the neurological signals and/or brain state estimations. It should be noted that in some embodiments the clinical manifestation data can be compared to the raw EEG data, while in other embodiments the clinical manifestation data can be compared with the determined brain states or the extracted features (or compared to all of the different data).

[0094] In a second mode of operation, after the brain state algorithms have been trained (either using the monitored clinical manifestation data and neurological data that was collected during the first mode of operation, or simply by using collected neurological data), the brain state algorithms may be implemented to process substantially real-time data signals to determine the patient's brain state. The brain state indicators may also be enabled to inform the patient of their substantially real-time brain state status. The system can, however, continue to automatically record the clinical manifestation data upon the occurrence of a change in the patient's condition. The recorded clinical manifestation data can then be compared to the neurological data or determined brain state to determine if the system is accurately predicting seizure activity. The system can then be retrained as necessary. This process can occur as frequently as desired. In fact, system can be set up to automatically record clinical manifestation data for the life of the system.

[0095] In a third mode of operation, it may be desirable to only receive and process the data signals from the implanted device and the PAD, but no longer store the monitored data signals in a memory of the PAD. For example, if the brain state algorithms are performing as desired, the brain data signals and the clinical manifestation data will not have to be stored and analyzed. Consequently, the patient would not have to periodically replace the data card in the PAD as frequently. However, it may still be desirable to store clinical manifestation data and/or neurological data signals that immediately precede and follow any detected seizure. Consequently, in the third mode such seizure data signals may optionally be stored.

[0096] As noted above, the PAD will typically comprise one or more brain state algorithms. In one embodiment, the brain state algorithms will generally characterize the patient's brain state as either "Safe or Low Propensity," "Unknown," "Prediction or Elevated Propensity" or "Detection." It is intended that these are meant to be exemplary categories only and are in no way to be limiting and additional brain states or fewer brain state indicators may be provided. There may be different types of algorithms which are configured to characterize the brain state into more or less discrete states. "Safe" generally means that brain activity indicates that the patient is in a contra-ictal state and has a low susceptibility to transition to an ictal state for an upcoming period of time (for example, 60 minutes to 90 minutes). This is considered positive information and no user lifestyle action is required. A "prediction" state generally means that the algorithm(s) in the PAD are determining that the patient is in a pro-ictal state and has an elevated propensity for a seizure (possibly within a specified time period). A "detection" state generally means that brain activity indicates that the patient has already transitioned into an ictal state (e.g., occurrence of an electrographic seizure) or that there is an imminent clinical seizure. User actions should be focused on safety and comfort. An "unknown" state generally means the current type of brain activity being monitored does not fit within the known boundaries of the algorithms and/or that the brain activity does not fit within the contra-ictal state, pro-ictal state, or ictal state. Therefore no evaluation can be reliably made. "Unknown" can also indicate there has been a change in the status of the brain activity and while the patient does not have an elevated propensity and no seizure has been detected, it is not possible to reliable tell the patient they are substantially safe from transitioning into an ictal state for a period of time. This state is considered cautionary and requires some cautionary action such as limiting exposure to risk. The two different types of "unknown" may have separate brain state indicators, or they may be combined into a single brain state indicator, or the user interface may not provide the "unknown" state to the patient at all.

[0097] In one method, the physician (or software, as the training can be partially automated) first determines if a clinical manifestation of a seizure occurred by investigating or analyzing the clinical manifestation data (e.g., ictal moan in an audio file, a convulsion indication from a convulsion detection file, a change in heart rate from the heart monitor file, video indication from a video file, etc.). As discussed above, in some embodiments the clinical manifestation data is stored in a separate data file, while is some embodiments the monitored EEG data or a recordation of the determined brain state is annotated with an indication of the occurrence of a clinical manifestation of a seizure. Either way, the physician can determine when the clinical manifestation occurred. The physician can then analyze the estimated brain state output from the algorithm(s) before and after the occurrence of the documented clinical manifestation. The physician can then determine if the system accurately estimated the brain state before and/or during the seizure. For example, if the physician observes a recorded ictal moan, preferably the system had estimated a pro-ictal state for a period of time before the ictal moan. In addition, the system would have preferably estimated an ictal state at or near in time to the occurrence of the ictal moan.

[0098] If the system did not detect either a pro-ictal state or an ictal state (or predict a seizure), the algorithm(s) may need to be reprogrammed/re-trained using the patient's EEG data before and near the point in time the clinical manifestation was detected. This technique can also be used in an initial step in programming of the system to train the algorithms for patient-specific prediction and/or detection. In a system designed simply to predict the onset of a seizure or to detect the onset of a seizure, the clinical manifestation data can similarly be used to determine if the system correctly determined if a seizure occurred or predicted the onset of the seizure.

[0099] In a second method, the physician (or software) may first determine when the system determined a neurological event occurred (e.g., a detected seizure, an increased likelihood of having a seizure, a change in brain state, etc.), and then looks for clinical manifestation data that was recorded near in time to the event to determine if there was any recorded clinical manifestation associated with the estimated neurological activity. Similar to the above method, the algorithms can then be retrained as necessary to improve their accuracy.

[0100] In this second method, an absence of clinical manifestation data does not necessarily mean the algorithm(s) which detected or predicted a seizure was incorrect, as there may not have been, for example, an ictal moan associated with the clinical seizure that in fact occurred. Alternatively, a convulsion may not have been forceful enough to trigger the convulsion detector. Or, in some situations, the patient may have had an electrographic seizure with no clinical manifestation (i.e., sub-clinical). However, in such situations the physician might consider the alert a false positive, and determining an absence of a clinical manifestation of a seizure can assist in the determination of false positives and such information may thereafter be used in metrics for assessing the specificity and sensitivity of the algorithm, which may later lead to retraining of the algorithm(s) to reduce the occurrence of such false positives. Exemplary methods and systems that can be used in the comparing and/or analyzing steps described herein can be found in a commonly owned U.S. patent application filed concurrently with this application entitled "Patient Advisory EEG Analysis Method and Apparatus" (Attorney Docket No. 10003-733.100), the disclosure of which is incorporated herein by reference.

[0101] A lack of detected clinical manifestation data could, however, also necessitate an adjustment of the parameters used to monitor and record clinical manifestations of the occurrence of a seizure. For example, the audio recording sensitivity may need to be increased to record very soft audio data which is indicative of the occurrence of a seizure. Or the convulsion detector (e.g., accelerometer positioned somewhere in or on the patient) may need to be adjusted to a more sensitive setting. Adjusting the sensitivity and parameters used to automatically monitor and record clinical manifestation data may therefore be required after analyzing the clinical manifestation data with the neurological data or the patient's brain state.

[0102] Additional features which can be incorporated in a PAD or other system device as described herein are described in co-pending U.S. patent application Ser. No. 12/180,996, filed Jul. 28, 2008, the entire disclosure of which is incorporated by reference herein.

[0103] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that 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.

What is claimed is:

1. A method of detecting a neurological status of a subject, the method comprising:

acquiring a neurological signal from the subject;

using a processor to perform a first determination of a neurological state of the subject based on the neurological signal;

acquiring a clinical manifestation signal from the subject contemporaneously with the neurological signal, the clinical manifestation signal comprising an accelerometer signal;

using the processor to perform a second determination of the neurological state of the subject based on the clinical manifestation signal;

comparing the first and second determinations to identify a preferred determination selected from at least one of the first and second determinations; and

identifying the neurological status of the subject based on the preferred determination.

2. The method of claim **1**, wherein the neurological signal is at least one of an EEG signal and an ECoG signal.

3. The method of claim **1**, wherein the first and second determinations are consistent with each other.

4. The method of claim **1**, wherein the first and second determinations are inconsistent with each other.

5. The method of claim **4**, wherein the first determination indicates that the subject is not experiencing a seizure and the second determination indicates that the subject is experiencing a seizure.

6. The method of claim **4**, wherein the first determination indicates that the subject is experiencing a seizure and the second determination indicates that the subject is not experiencing a seizure.

7. The method of claim **1**, wherein one of the first and second determinations does not indicate an occurrence of a seizure.

8. The method of claim **1**, wherein the preferred determination is the first determination, and wherein the comparing of the first and second determinations includes confirming an accuracy of the first determination with the second determination.

9. The method of claim **1**, wherein the preferred determination is the second determination, and wherein the comparing of the first and second determinations includes confirming an accuracy of the second determination with the first determination.

10. The method of claim **1**, wherein the first determination is associated with a first accuracy value of the first determination and the second determination is associated with a second accuracy value of the second determination, and wherein the preferred determination is in part based on the first or second determination that has a greater accuracy value.

11. The method of claim **1**, wherein the comparing of the first and second determinations includes identifying a deficiency in at least one of the first and second determinations.

12. A method of detecting a seizure status of a subject, the method comprising:

detecting a first seizure state using a neurological signal obtained from a neurological sensor monitoring the subject;

contemporaneously detecting a second seizure state using a clinical manifestation signal obtained from a clinical manifestation sensor monitoring the subject, the clinical manifestation signal comprising an accelerometer signal;

comparing the detection using the neurological signal and the detection using the clinical manifestation signal to identify a preferred detection selected from the detection using the neurological signal and the detection using the clinical manifestation signal; and

identifying the seizure status of the subject based on the preferred detection.

13. The method of claim **12**, wherein the neurological sensor is disposed to monitor the subject's brain, and wherein the neurological signal is at least one of an EEG signal and an ECoG signal.

14. The method of claim **12**, wherein the first seizure state and the second seizure state are consistent with each other.

15. The method of claim **12**, wherein the first seizure state and the second seizure state are inconsistent with each other.

16. The method of claim **15**, wherein the first seizure state is a non-seizure state of the subject and the second seizure state is a seizure state of the subject.

17. The method of claim **15**, wherein the first seizure state is a seizure state of the subject and the second seizure state is a non-seizure state of the subject.

18. The method of claim **12**, wherein one of the first seizure state and the second seizure state does not indicate a seizure status of the subject.

19. The method of claim **12**, wherein the preferred detection is the detection of the first seizure state, and wherein the comparing of the detection using the neurological signal and the detection using the clinical manifestation signal includes confirming an accuracy of the detection of the first seizure state with the detection of the second seizure state.

20. The method of claim **12**, wherein the preferred detection is the detection of the second seizure state, and wherein the comparing of the detection using the neurological signal and the detection using the clinical manifestation signal includes confirming an accuracy of the detection of the second seizure state with the detection of the second seizure state.

21. The method of claim **12**, wherein the detection of the first seizure state is associated with a first accuracy value and the detection of the second seizure state is associated with a second accuracy value, and wherein the preferred determination is in part based on the greater of the first and second accuracy values.

22. The method of claim **12**, wherein the comparing of the detection using the neurological signal and the detection using the clinical manifestation signal includes identifying a deficiency in at least one of the detection of the first seizure state and the detection of the second seizure state.

23. A method of detecting a neurological status of a subject, the method comprising:

acquiring a neurological signal from the subject;

using a processor to identify a first parameter from the neurological signal, the first parameter associated with a first characterization of the neurological status of the subject;

acquiring a clinical manifestation signal from the subject contemporaneously with the neurological signal, the clinical manifestation signal comprising an accelerometer signal;

using the processor to identify a second parameter from the clinical manifestation signal, the second parameter associated with a second characterization of the neurological status of the subject;

comparing the first and second characterizations to identify a preferred characterization selected from at least one of the first and second characterizations; and

identifying the neurological status of the subject based on first and/or second parameter associated with the preferred determination.

24. The method of claim **23**, wherein the neurological signal is at least one of an EEG signal and an ECoG signal.

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摘要(译)

提供了用于检测癫痫发作的神经学和临床表现的方法。描述了包括监视设备的系统，该监视设备具有通信组件，用于接收从植入患者体内的发射器发送到患者体外的神经数据;处理神经系统数据以估计患者大脑状态的处理器;以及用于响应于处理器的大脑状态估计自动记录临床表现数据的组件。