(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 April 2004 (29.04.2004)

PCT

(10) International Publication Number
WO 2004/036765 A2

(51) International Patent Classification[7]: H04B

(21) International Application Number:
PCT/US2003/032599

(22) International Filing Date: 15 October 2003 (15.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/271,394 15 October 2002 (15.10.2002) US

(71) Applicant *(for all designated States except US)*: **NORTHSTAR NEUROSCIENCE, INC.** [US/US]; 2401 - 4th Avenue, Suite 500, Seattle, WA 98121 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **GLINER, Bradford, Evan** [US/US]; 4368 230th Way SE, Sammamish, WA 98075 (US).

(74) Agent: **PARKER, Paul, T.**; Perkins Coie LLP, P.O. Box 1247, Seattle, WA 98111-1247 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/036765 A2

(54) Title: NEURAL STIMULATION SYSTEM AND METHOD RESPONSIVE TO COLLATERAL NEURAL ACTIVITY

(57) Abstract: A neural stimulation system responsive to collateral neural activity that may arise in association with a neural stimulation procedure includes a stimulation interface configured to deliver stimulation signals to a target neural population, a monitoring interface positioned to receive signals corresponding to a neural activity within the target neural population, a stimulus unit coupled to deliver stimulation singals to the stimulation interface, and a sensing unit coupled to the monitoring device and the stimulus unit. The neural stimulation procedure may be directed toward rehabilitating, restoring, and/or enhancing one or more neural functions by facilitating and/or effectuating a neuroplastic change or reorganization; and/or affecting a neurological condition that exists on a continuous or essentially continuous basis absent the stimulation procedure. The sensing unit determines whether evidence of an collateral neural activity exists, whereupon the stimulus unit attempts to abate the collateral neural activity.

NEURAL STIMULATION SYSTEM AND METHOD RESPONSIVE TO COLLATERAL NEURAL ACTIVITY

CROSS-REFERENCE TO RELATED APPLICATION(S)

[0001] This application is a Continuation-in-Part of U.S. Application No. 09/978,134, entitled "Systems and Methods for Automatically Optimizing Stimulus Parameters and Electrode Configurations for Neuro-Stimulators," filed October 15, 2001, which is incorporated herein by reference.

TECHNICAL FIELD

[0002] The present disclosure is related to systems and methods for detecting and responding to collateral neural activity that may arise in association with or as a result of stimulation applied to a region of the cortex or other area of the brain.

BACKGROUND

[0003] A wide variety of mental and physical processes are controlled or influenced by neural activity in particular regions of the brain. For example, the neural-functions in some areas of the brain (i.e., the sensory or motor cortices) are organized according to physical or cognitive functions. There are also several other areas of the brain that appear to have distinct functions in most individuals. In the majority of people, for example, the areas of the occipital lobes relate to vision, the regions of the left interior frontal lobes relate to language, and the regions of the cerebral cortex appear to be consistently involved with conscious awareness, memory, and intellect.

[0004] Many problems or abnormalities with body functions can be caused by damage, disease and/or disorders in the brain. Effectively treating such abnormalities may be very difficult. For example, a stroke is a very common condition that damages the brain. Strokes are generally caused by emboli (*e.g.*, obstruction of a vessel), hemorrhages (*e.g.*, rupture of a vessel), or

thrombi (*e.g.*, clotting) in the vascular system of a specific region of the brain, which in turn generally cause a loss or impairment of a neural function (*e.g.*, neural functions related to facial muscles, limbs, speech, etc.). Stroke patients are typically treated using various forms of physical therapy to rehabilitate the loss of function of a limb or another affected body part. Stroke patients may also be treated using physical therapy plus drug treatment. For most patients, however, such treatments are not sufficient, and little can be done to improve the function of an affected body part beyond the limited recovery that generally occurs naturally without intervention.

[0005] The neural activity in the brain can be influenced by electrical energy that is supplied from a waveform generator or other type of device. Various patient perceptions and/or neural functions can thus be promoted or disrupted by applying an electrical current to the cortex or other region of the brain. As a result, researchers have attempted to treat various neurological conditions using electrical or magnetic stimulation signals to control or affect brain functions.

[0006] Neural activity is governed by electrical impulses or "action potentials" generated in and propagated by neurons. While in a quiescent state, a neuron is negatively polarized, and exhibits a resting membrane potential that is typically between -70 and -60 mV. Through electrical or chemical connections known as synapses, any given neuron receives from other neurons excitatory and inhibitory input signals or stimuli. A neuron integrates the excitatory and inhibitory input signals it receives, and generates or fires a series of action potentials in the event that the integration exceeds a threshold potential. A neural firing threshold may be, for example, approximately –55 mV. Action potentials propagate to the neuron's synapses, where they are conveyed to other neurons to which the neuron is synaptically connected.

[0007] A neural stimulation signal may comprise a series or train of electrical or magnetic pulses that deliver an energy dose to neurons within a target neural population. The stimulation signal may be defined or described in accordance with stimulation signal parameters including pulse amplitude, pulse frequency, duty cycle, stimulation signal duration, and/or other parameters. Electrical or

magnetic stimulation signals applied to a population of neurons can depolarize neurons within the population toward their threshold potentials. Depending upon stimulation signal parameters, this depolarization can cause neurons to generate or fire action potentials. Neural stimulation that elicits or induces action potentials in a functionally significant proportion of the neural population to which the stimulation is applied is referred to as supra-threshold stimulation; neural stimulation that fails to elicit action potentials in a functionally significant proportion of the neural population is defined as sub-threshold stimulation. In general, supra-threshold stimulation of a neural population triggers or activates one or more functions associated with the neural population, but sub-threshold stimulation by itself fails to trigger or activate such functions. Supra-threshold neural stimulation can induce various types of measurable or monitorable responses in a patient. For example, supra-threshold stimulation applied to a patient's motor cortex can induce muscle fiber contractions.

[0008] While electrical or magnetic stimulation of neural tissue may be directed toward producing an intended type of neural activity, such stimulation may result in unintended collateral neural activity. In particular, neural stimulation for treating a condition can induce seizure activity or other types of collateral neural activity. It will be appreciated that such collateral neural activity is undesirable and/or inconvenient in a neural stimulation situation.

[0009] Seizure activity may originate at a seizure focus, which is typically a collection of neurons (*e.g.*, on the order of 1000 neurons) exhibiting a characteristic type of synchronous firing activity. In particular, each neuron within a seizure focus exhibits a firing response known as a paroxysmal depolarizing shift (PDS). The PDS is a large magnitude, long duration depolarization that triggers a neuron to fire a train or burst of action potentials. Properly functioning feedback and/or feed-forward inhibitory signaling mechanisms cause afterhyperpolarization through which the neuron's membrane potential returns to a hyperpolarized state below its firing threshold. Following afterhyperpolarization, the neuron may undergo another PDS.

[0010] Afterhyperpolarization limits the duration of the PDS, thereby helping to ensure that synchronous neural firing activity remains localized to the seizure

focus. Inhibitory feedback signaling provided by neurons surrounding a seizure focus, commonly referred to as "surround inhibition," is particularly important in constraining seizure activity to the seizure focus. In the event that inhibitory signaling mechanisms fail and/or are unable to overcome or counter PDS activity, neurons within the seizure focus recruit other neurons to which they are synaptically coupled into their synchronous firing pattern. As a result, synchronous firing activity spreads beyond the seizure focus to other areas of the brain. This can lead to a cascade effect in which seizure activity becomes increasingly widespread, and accompanying clinical manifestations become increasingly significant.

[0011] In view of the foregoing, it may be important to detect and/or respond to seizure activity. Various systems and/or devices directed toward treating neurological conditions exist, including those capable of detecting and responding to particular types of neurological events. For example, some neural stimulators attempt to treat involuntary motion disorders such as Parkinson's disease by applying stimulation signals to the thalamus or other area of a patient's brain. As another example, U.S. Patent No. 6,134,474 describes an implantable device capable of detecting a neurological event, such as seizure activity, and generating a responsive electrical signal intended to terminate the detected event. Additionally, European Patent Application Publication EP1145736 describes an implantable device capable of detecting electrical activity in the brain; applying a nonresponsive signal to reduce the likelihood of a seizure occurring; and applying a responsive signal in the event that epileptiform activity is detected.

[0012] Unfortunately, present neural stimulation systems and methods fail to automatically detect and/or respond to seizure activity or other collateral neural activity induced in association with and/or as a result of neural stimulation procedures directed toward purposes other than epileptic seizure management. In particular, conventional neural stimulation systems fail to automatically detect seizure activity induced by neural stimulation procedures directed toward patient neural function rehabilitation and/or enhancement, or modulation of patient sensory perceptions.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] Figure 1 is a schematic illustration of a neural stimulation system responsive to specific neural activity according to an embodiment of the invention.

[0014] Figure 2 is a graph illustrating several parameters that may describe or characterize a stimulation signal.

[0015] Figure 3A is a plan view of a grid electrode configured as a stimulation interface according to an embodiment of the invention.

[0016] Figure 3B is a plan view of an implantable stimulation and monitoring interface configured for stimulating a target neural population and detecting signals corresponding to specific neural activity according to an embodiment of the invention.

[0017] Figure 4 is a flowchart of a neural stimulation process responsive to specific neural activity according to an embodiment of the invention.

[0018] Figure 5 is a flowchart of a neural stimulation process responsive to specific neural activity according to another embodiment of the invention.

[0019] Figure 6 is a flowchart of a neural stimulation process responsive to specific neural activity according to another embodiment of the invention.

DETAILED DESCRIPTION

[0020] The following disclosure describes a system and method for detecting and responding to collateral neural activity that may arise in association with and/or as a result of a neural stimulation procedure. In the context of the present invention, a neural stimulation procedure may involve the application of stimuli to one or more target neural populations within a patient, and may be directed toward rehabilitating, restoring, and/or enhancing one or more neural functions in the patient by facilitating and/or effectuating a neuroplastic change or reorganization. A neural stimulation procedure may alternatively or additionally be directed toward modulating or ameliorating a patient sensory perception such as pain, or affecting a neurological condition that is present on a continuous or essentially continuous basis in the absence of the applied

stimuli. Collateral neural activity may comprise seizure activity, migraine activity, and/or essentially any other type of neural activity that may be undesirable, unwanted, unintended, and/or counterproductive relative to an intended or desired neural activity or outcome associated with the neural stimulation procedure.

[0021] Figure 1 is a schematic illustration of a neural stimulation system 100 for detecting and responding to collateral neural activity according to an embodiment of the invention. In one embodiment, the system 100 comprises a stimulus unit 140 configured to deliver stimulation signals to a patient 190 using a stimulation interface 110. The system 100 may additionally comprise a sensing unit 180 configured to identify or detect parameters associated with collateral neural activity in the patient 190 using a monitoring interface 112. The sensing unit 180 is configured to communicate with the stimulus unit 140 upon detection of collateral neural activity and/or periodically throughout a stimulation procedure. The stimulus unit 140 may be coupled to the stimulation interface 110 by a first link 114; the monitoring interface 112 may be coupled to the sensing unit 180 by a second link 116; and the sensing unit 180 may be coupled to the stimulus unit 140 by a third link 118, where one or more of such links 114, 116, 118 may be wire-based or wireless.

[0022] The stimulus unit 140 generates and outputs stimulation signals. As considered herein, stimulation signals may include treatment signals and/or response signals. Treatment signals may comprise electrical and/or magnetic stimuli applied to one or more target neural populations and directed toward treating and/or rehabilitating one or more neurological conditions. The treatment signals may also affect or influence particular types of neurological activity. In general, treatment signals may be directed toward affecting or altering one or more neurological conditions that exist within the patient 190 on a continuous, essentially continuous, or nearly continuous basis (*i.e.*, non-intermittent or essentially non-intermittent through potentially cyclical) in the absence of the treatment signal. Treatment signals may be directed toward facilitating and/or effectuating neuroplasticity in the patient 190, for example, in a manner described in U.S. Patent Application No. 09/978,134, which is

incorporated herein by reference. Treatment signals may alternatively or additionally be directed toward affecting or modulating a patient sensation such as pain; or eliminating or ameliorating the effects of neurodegenerative disorders, for example, involuntary movements and/or other symptoms associated with Parkinson's disease.

[0023] In general, response signals may comprise electrical, magnetic, and/or other (*e.g.*, sonic or vibratory) stimuli directed toward disrupting, desynchronizing, abating, and/or eliminating collateral neural activity arising in association with or as a result of the application of treatment signals to the patient 190. Depending upon their nature, response signals may be applied proximate or directly to one or more target neural populations and/or particular patient sensory systems or body locations. The description that follows considers electromagnetic response signals; however, the present invention may employ other or additional types of response signals in a manner understood by those skilled in the art.

[0024] Figure 2 is a graph illustrating several parameters that may define, describe, or characterize stimulation signals. A stimulus start time t_0 defines an initial point at which a stimulation signal is applied to the stimulation interface 110. In one embodiment, the stimulation signal may be a biphasic waveform comprising a series of biphasic pulses, and which may be defined, characterized, or described by parameters including a pulse width t_1 for a first pulse phase; a pulse width t_2 for a second pulse phase; and a pulse width t_3 for a single biphasic pulse. The parameters can also include a stimulus repetition rate $1/t_4$ corresponding to a pulse repetition frequency; a stimulus pulse duty cycle equal to t_3 divided by t_4; a stimulus burst time t_5 that defines a number of pulses in a pulse train; and/or a pulse train repetition rate $1/t_6$ that defines a stimulus burst frequency. Other parameters include a peak current intensity I_1 for the first pulse phase and a peak current intensity I_2 for the second pulse phase. Those skilled in the art will understand that pulse intensity or amplitude may decay during one or both pulse phases, and a pulse may be a charge-balanced waveform. Those skilled in the art will further understand that in an alternate embodiment, pulses can be monophasic or polyphasic. Additional

stimulation parameters may include applying the stimulation to selected configurations of the stimulation interface 110 for any given stimulation signal and/or time.

[0025] In one embodiment, the stimulus unit 140 comprises a controller 150, a pulse system 160, and a set of controls/indicators 170. The controller 150 may include a processor, a memory, and a programmable computer medium. The controller 150 may be implemented as a computer or microcontroller, and the programmable medium can be hardware and/or memory resident software that performs, directs, and/or facilitates neural stimulation procedures in accordance with the present invention. The controls/indicators 170 can include a graphic user interface, an input/output device, and/or other types of interface elements for exchanging commands and/or output with the controller 150.

[0026] The pulse system 160 selectively generates stimulation signals and sends, directs, or delivers such stimuli to the stimulation interface 110. The pulse system 160 may be implanted into the patient 190, in a manner described in U.S. Application No. 09/802,808 incorporated herein by reference. Alternatively, the pulse system 160 may be an external unit capable of delivering stimulation signals to the stimulation interface 110 using RF energy, electromagnetism, or wire terminals exposed on the patient's scalp. The stimulation interface 110 may comprise one or more stimulus delivery devices configured to apply treatment signals and/or response signals to the patient 190. The stimulation interface 110 may comprise a type of neural-stimulation device described in U.S. Application No. 09/802,808.

[0027] In one embodiment, the pulse system 160 is a component of a Transcranial Magnetic Stimulation (TMS) device that delivers magnetic stimulation signals to a patient 190. The stimulation interface 110 in this embodiment may comprise an electromagnetic coil arrangement in a manner understood by those skilled in the art. In another embodiment, the pulse system 160 forms a portion of an electrical stimulation device. The stimulation interface 110 of this embodiment may comprise an electrode arrangement or configuration capable of delivering electrical stimulation signals to the patient 190. In such an embodiment, the stimulation interface 110 may be implanted

into the patient 190 to provide cortical stimulation, deep brain stimulation, and/or other types of neural stimulation.

[0028] Various portions or elements of the stimulation interface 110 may be configured to deliver treatment signals only, response signals only, or either treatment or response signals. One or more portions of the stimulation interface 110 may reside upon or proximate to one or more target neural populations in and/or through which a) neuroplasticity may be occurring and/or may be expected to occur; and/or b) a patient sensation such as pain may be modulated or influenced.

[0029] Figure 3A is a plan view of an exemplary grid electrode 120 capable of implementing one or more portions of a stimulation interface 110 according to an embodiment of the invention. The grid electrode 120 comprises a support member or substrate 122 that carries a plurality of electrical contacts 124. Those skilled in the art will understand that the number of contacts 124 may vary in accordance with embodiment details. The grid electrode 120 further comprises a set of leads (not shown) that couple the contacts 124 to the pulse system 160 in a manner understood by those skilled in the art. A grid electrode 120 of the type shown in Figure 3A is available from AdTech Medical Instrument Corporation of Racine, WI (www.adtechmedical.com).

[0030] The contacts 124 can be divided so that one group of contacts 124 delivers treatment signals while another group of contacts 124 delivers response signals. For example, a central contact group 126 may deliver treatment signals to a target neural population while an outer contact group 128 may deliver response signals in a manner that may enhance or promote surround inhibition. In such an embodiment, response signals may be delivered in a time-shared or a concurrent manner relative to treatment signal delivery. Alternatively, the grid electrode 120 may be configured to deliver treatment signals or response signals to all contacts 124 in a time-shared manner, or configured to deliver treatment signals only or response signals only.

[0031] The sensing unit 180 comprises a system, device, or apparatus configured to detect or identify collateral neural activity or parameters of such

activity that occur in association with and/or as a result of a neural stimulation procedure. The sensing unit 180 may include a processor, a memory, and a programmable computer medium. The programmable medium of the sensing unit 180 can comprise hardware and/or software capable of analyzing signals corresponding to neural activity and determining whether collateral neural activity or evidence of such activity exists. The sensing unit 180 may communicate with the stimulus unit 140 upon detecting collateral neural activity so that the stimulus unit 140 may respond to the sensing unit 180. The sensing unit 180 may monitor for collateral neural activity or evidence of such activity on a periodic or continuous basis. The sensing unit 180, for example, can operate under the direction of or in cooperation with the controller 150. Communication between the stimulus unit 140 and the sensing unit 180 may occur through the third link 118. Such communication may involve the exchange of operational parameters, synchronization information, status information, and/or information associated with the detection of collateral neural activity.

[0032] The sensing unit 180 may receive from the monitoring interface 112 one or more types of physiological signals and/or physiological correlate signals useful for indicating the presence of collateral neural activity. In general, a meaningful, significant and/or sustained change in a physiological or physiological correlate signal relative to the signal's normal or background behavior can indicate the onset and/or occurrence of collateral neural activity. The sensing unit 180 may comprise hardware and/or software that performs signal filtering, processing, and/or analysis operations. Depending upon the nature of the physiological and/or physiological correlate signals under consideration, the sensing unit 180 and/or the monitoring interface 112 may exhibit various embodiments.

[0033] The monitoring interface 112 can have several embodiments. For example, one or more portions of the monitoring interface 112 may be oriented or positioned relative or proximate to a set of target neural populations to which a neural stimulation procedure is directed so that the monitoring interface 112 may detect or receive signals corresponding or related to such neural

populations. Alternatively or additionally, one or more portions of the monitoring interface 112 may be oriented or positioned within or upon the patient's body to detect one or more types of patient responses correlated to neural activity.

[0034] In one embodiment, the sensing unit 180 comprises an electroencephalogram (EEG) monitoring and/or analysis device and the monitoring interface 112 comprises one or more surface, cortical, and/or subcortical electrodes, electrode arrays, and/or electrical probes capable of receiving or detecting EEG signals. The sensing unit 180 may analyze EEG signals received from the monitoring interface 112 and determine whether collateral neural activity or evidence of such activity exists. Those skilled in the art will recognize that particular types of EEG activity, such as interictal spikes and/or energy spectrum shifts, may be indicative of seizure activity.

[0035] In addition to EEG signals, other types of physiological signals and/or physiological correlate signals may be useful for providing evidence of collateral neural activity. For example, signals corresponding to cerebral blood flow (CBF) may be used to indicate the onset or occurrence of seizure activity, as described by M. E. Weinand et al. in an article entitled "Cerebral blood flow and temporal lobe epileptogenicity" (J. Neurosurg. 1997 Feb; 86(2): 226-32). In one embodiment, the monitoring unit 112 may comprise a CBF monitor, which may include a set of electrodes, a thermistor, and/or a thermal diffusion probe; a set of near infrared sources and sensors; a set of piezoelectric ultrasonic emitters and sensors (to facilitate, for example, transit time measurements); and/or one or more other types of CBF monitoring devices. In such an embodiment, the sensing unit 180 may comprise a CBF signal analysis system or device. In a related alternate embodiment, the monitoring unit 112 may comprise a neural tissue oxygenation monitor, and the sensing unit 180 may correspondingly comprise a neural tissue oxygenation analysis system or device.

[0036] Particular types of muscle fiber activity may also be indicative of collateral neural activity (*e.g.*, extremely rapid muscle fiber contractions, particularly when sustained). In one embodiment, the sensing unit 180

comprises an electromyography (EMG) device configured to detect, monitor, and/or analyze motor evoked potentials (MEPs) associated with muscle fiber innervation, in a manner understood by those skilled in the art. The monitoring interface 112 correspondingly comprises a set of surface, percutaneous, and/or implanted electrodes or probes that may be positioned or configured to measure electrical activity associated with the innervation of one or more muscles and/or muscle groups. In another embodiment, the sensing unit 180 comprises a motion analysis system and the monitoring interface 112 comprises a set of motion detectors, strain gauges, and/or accelerometers configured to detect or monitor one or more types of patient movements. The sensing unit 180 may analyze motion signals received from the monitoring interface 112 and determine whether patient motions under consideration are indicative of seizure activity.

[0037] In other embodiments, the sensing unit 180 and monitoring interface 112 may comprise one or more types of neural imaging systems, such as a functional Magnetic Resonance Imaging (fMRI) system, a Positron Emission Tomography (PET) system, and/or a Magnetoencephalography (MEG) system. In general, the sensing unit 180 and/or the monitoring interface 112 may be configured to receive, detect, monitor, measure, and/or analyze one or more types of signals useful of indicating the presence of collateral neural activity.

[0038] The stimulation interface 110 and the monitoring interface 112 may be implemented as devices and/or modules that reside upon physically separate substrates or carriers positioned within and/or upon the patient 190. Alternatively or additionally, one or more portions of such interfaces 110, 112 may be implemented together upon a single implantable carrier or substrate.

[0039] Figure 3B is a plan view of an implantable stimulation and monitoring interface 130 configured for stimulating a target neural population and detecting signals corresponding to neural activity according to an embodiment of the invention. In one embodiment, the stimulation and monitoring interface 130 comprises a support member 132 carrying a stimulating element 134 and a monitoring element 136. The stimulating element 134 may comprise one or more electrodes organized in accordance with a particular pattern, and the

monitoring element 126 may comprise a set of electrodes and/or a CBF monitoring device positioned proximate or adjacent to the stimulating element 134. A set of leads 138 may couple the stimulating element 134 and the monitoring element 136 to the stimulus unit 140 and the sensing unit 180, respectively. A stimulation and monitoring interface 120 may be positioned or oriented within a patient 190 such that a stimulating element 124 can deliver or apply stimulation signals to one or more particular target neural populations, and the monitoring element 126 can detect signals indicative of neural activity associated with the targeted neural populations.

[0040] As previously indicated, one or more portions of the monitoring interface 112 may comprise an electrode arrangement, which may include a grid electrode 120 of the type shown in Figure 3A, a deep brain electrode, and/or one or more other electrode types. As a result, a stimulation and monitoring interface 130 may comprise a grid electrode 120 of the type shown in Figure 3A. In such an embodiment, particular contacts 124 within the grid electrode 120 may be designated for neural activity monitoring and other contacts 124 may be configured to deliver treatment and/or response signals.

[0041] Depending upon the nature of the monitoring interface 112, the delivery of stimulation signals to a target neural population may interfere with the detection of signals corresponding to neural activity. As a result, the controller 150 and/or the pulse system 160 may periodically interrupt a neural stimulation procedure, such that during stimulation procedure interruptions, the sensing unit 180 may analyze signals received from the monitoring interface 112 relative to collateral neural activity. Outside of such interruptions, the sensing unit 180 may be prevented from receiving or processing signals received from the monitoring interface 112. Alternatively, the sensing unit 180 may compensate for the presence of stimulation signals, for example, through signal subtraction and/or other compensation operations, to facilitate detection of collateral neural activity or evidence of collateral neural activity simultaneous with the delivery of stimulation signals to a target neural population.

[0042] In embodiments in which a neural stimulation procedure is periodically interrupted to facilitate detection of collateral neural activity or evidence of such

activity, the stimulation and monitoring interface 120 may be implemented using a single electrode arrangement or configuration in which any given electrode element used to deliver stimulation signals during the neural stimulation procedure may also be used to detect neural activity during a neural stimulation procedure interruption. Thus, the stimulation interface 110 and the monitoring interface 112 may physically be one and the same.

[0043] One or more portions of the controller 150, the pulse system 160, the stimulation interface 110, monitoring interface 112, and/or the sensing unit 180 can be integrated into a single implantable stimulation delivery, monitoring, and/or management apparatus in a manner identical analogous or similar to the devices described in U.S. Application No. 09/802,808. Such an integrated apparatus may be configured for implantation into a patient's skull so that the stimulation interface 110 and/or the monitoring interface 112 can contact the patient's dura matter or pia matter in one or more cortical regions. An integrated apparatus of this type can have an internal power source that can be implanted into the patient 190, and/or an external power source coupled to the pulse system 160 via electromagnetic coupling or a direct connection.

[0044] Figure 4 is a flowchart of a neural stimulation process 400 responsive to collateral neural activity according to an embodiment of the invention. In one embodiment, the process 400 begins with a stimulation operation 402 by initiating or continuing a neural stimulation procedure in which stimulation signals are delivered to one or more target neural populations within a patient 190 in accordance with a given set of stimulation signal parameters. After initiating the stimulation operation 402, the process 400 also includes a detection query 404 that determines whether collateral neural activity or evidence of such activity exists. The detection query 404 may be performed in a simultaneous or sequential manner relative to the stimulation operation 402. If collateral neural activity or evidence thereof does not exist, the process 400 continues with a termination query 406 that decides whether the neural stimulation procedure is complete. If the process is not complete, the process 400 returns to the stimulation operation 402; otherwise, if the process 400 is complete, it is terminated. If the detection query 404 the process 400

determines that collateral neural activity exists, the process 400 halts the neural stimulation procedure in a termination operation 410, and generates and/or issues a notification signal indicative of such activity in a notification procedure 412. Following the notification procedure 412, the process 400 ends.

[0045] Figure 5 is a flowchart of a neural stimulation process 500 responsive to collateral neural activity according to another embodiment of the invention. In one embodiment, the process 500 begins with a stimulation operation 502 by initiating or continuing a neural stimulation procedure in which stimulation signals are delivered to one or more target neural populations within a patient 190 in accordance with a first set of stimulation signal parameters. Next, the process 500 includes a detection query 504 that determines whether collateral neural activity or evidence thereof exists. If not, the process 500 proceeds to a termination query 506 to determine whether the neural stimulation procedure is complete. If the neural stimulation procedure is not complete, the process 500 returns to the stimulation procedure 502; otherwise, the stimulation process 500 is terminated.

[0046] If collateral neural activity or evidence of such activity exists, the process 500 includes a termination operation 510 that halts the neural stimulation procedure and a notification procedure 512 that generates and/or issues a notification signal indicative of such activity. The stimulation process 500 proceeds to a collateral activity query 520 that subsequently determines whether the collateral neural activity has been abated or eliminated. If so, the process 500 proceeds to a query 530 that determines whether to resume the neural stimulation procedure. Such a determination may be based upon, for example, an elapsed time between initiation of a neural stimulation procedure and detection of collateral neural activity; stored information characterizing and/or specifying frequency and/or history information associated with detection of collateral neural activity in the patient 190 undergoing the neural stimulation procedure; an authorization signal received from a doctor or therapist through the controls/indicators 170; and/or other information.

[0047] If resumption of the neural stimulation procedure is to occur, the process 500 continues with a modification operation 532 in which one or more stimulation signal parameters may be modified. Such a modification may involve changing (e.g., decreasing) a stimulation current level or intensity; changing (*e.g.*, increasing) a stimulation signal pulse repetition frequency; and/or modifying one or more other parameters shown in Figure 2. Following the modification operation 532, the process 500 includes time query 534 to determine whether a minimum time interval has elapsed. The time query 534 may provide a quiescent period during which the patient's neural activity becomes predominantly normal and/or representative of an acceptable baseline condition. If a minimum time interval has not elapsed, the process 500 remains at the time query 534; otherwise, the process 500 returns to the stimulation operation 502.

[0048] If the collateral activity query 520 determines that collateral neural activity has not been abated, the process 500 proceeds with a response query 540 that determines whether to apply to the patient 190 one or more response signals directed toward abating or terminating the collateral neural activity. If not, the process 500 ends. Otherwise, the process 500 proceeds with a signal selection procedure 542 that determines one or more appropriate response signal types and corresponding signal parameters, and a response procedure 544 that applies one or more response signals to the patient 190. Response signals may include one or more neural stimulation and/or other types of signals applied to the patient 190 through the stimulation interface 110. Following the response procedure 544, the process 500 returns to the stimulation operation 520.

[0049] As previously indicated, a neural stimulation procedure in accordance with the present invention may facilitate and/or effectuate neuroplastic change or reorganization within a patient 190, which in turn may rehabilitate, restore, and/or enhance one or more patient neural functions and/or behaviors. To facilitate and/or effectuate neuroplasticity, a neural stimulation procedure may be performed cooperatively with a behavioral therapy, such as described in U.S. Application No. 90/802,808. A behavioral therapy may encompass, for

example, physical therapy, cognitive therapy, and/or a variety of behavioral tasks.

[0050] Figure 6 is a flowchart of a neural stimulation process 600 responsive to collateral neural activity according to another embodiment of the invention. Relative to Figure 5, like reference numbers indicate like steps. In one embodiment, the process 600 begins with a stimulation operation 602 by initiating or continuing a neural stimulation procedure in conjunction or association with a behavioral therapy. During the stimulation operation 602, stimulation signals are delivered to one or more target neural populations within a patient 190 in accordance with a first set of stimulation signal parameters. Following the stimulation operation 602, other steps within the process 600 may proceed in manners described above with reference to Figure 5.

[0051] From the foregoing, it will be appreciated that specific embodiments of the invention have been described herein for purposes of illustration, but that various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

I/We claim:

[c1] 1. A neural stimulation method comprising:

applying a first stimulation signal to a target neural population within a patient, the first stimulation signal being selected to affect a patient perception of pain, rehabilitate a functional deficit exhibited by the patient, and/or enhance a functional capability of the patient;

monitoring a parameter associated with a collateral neural activity using a sensing unit and a monitoring interface; and

responding to a state of the parameter indicative of collateral neural activity.

[c2] 2. The method of claim 1, wherein applying the first stimulation signal induces the collateral neural activity.

[c3] 3. The method of claim 1, wherein responding to an indication of collateral neural activity comprises discontinuing application of the first stimulation signal.

[c4] 4. The method of claim 1, wherein responding to an indication of collateral neural activity comprises applying a second stimulation signal to the patient.

[c5] 5. The method of claim 4, wherein the second stimulation signal is applied to the target neural population and/or a neural population adjacent to a portion of the target neural population.

[c6] 6. The method of claim 1, wherein monitoring a parameter associated with the collateral neural activity comprises monitoring an electrophysiological signal of the patient.

[c7] 7. The method of claim 1, wherein monitoring a parameter associated with the collateral neural activity comprises monitoring an EEG signal, a cerebral bloodflow signal, an EMG signal, an accelerometer signal, a motion sensor signal, and/or a neural imaging signal.

[c8] 8. The method of claim 1, wherein applying the first stimulation signal occurs while a behavioral therapy is being performed on the patient.

[c9] 9. The method of claim 1, further comprising:

interrupting application of the first stimulation signal; and

resuming application of the first stimulation signal when the monitored parameter indicates that the collateral neural activity is absent.

[c10] 10. A neural stimulation method comprising:

applying a first stimulation signal to a target neural population within a patient, the first stimulation signal directed toward altering a neural condition that exists within the patient on at least an essentially continuous basis in the absence of the first stimulation signal;

automatically determining whether collateral neural activity exists; and

responding to collateral neural activity when it is determined to exist.

[c11] 11. The method of claim 10, wherein applying the first stimulation induces the collateral neural activity.

[c12] 12. The method of claim 10, wherein responding to the collateral neural activity comprises discontinuing application of the first stimulation signal.

[c13] 13. The method of claim 10, wherein responding to the collateral neural activity comprises applying a second stimulation signal to the patient.

[c14] 14. The method of claim 13, wherein the second stimulation signal is applied to the target neural population and/or a neural population adjacent to a portion of the target neural population.

[c15] 15. The method of claim 10, wherein the determining whether collateral neural activity exists comprises monitoring an electrophysiological signal and/or a patient behavior.

[c16] 16. The method of claim 10, wherein the determining whether collateral neural activity exists comprises monitoring an EEG signal, a cerebral bloodflow signal, an EMG signal, an accelerometer signal, a motion sensor signal, and/or a neural imaging signal.

[c17] 17. The method of claim 10, wherein applying the first stimulation signal occurs while the patient is performing a behavioral therapy.

[c18] 18. The method of claim 10, further comprising:

interrupting application of the first stimulation signal; and

resuming application of the first stimulation signal in the event that evidence of the collateral neural activity is absent.

[c19] 19. A neural stimulation method comprising:

applying a first stimulation signal to a target neural population within a patient while the patient performs a behavioral therapy;

monitoring a parameter indicative of whether collateral neural activity exists; and

attempting to abate the collateral neural activity in the event that evidence of the collateral neural activity exists.

[c20] 20. The method of claim 19, wherein the first stimulation signal is directed toward one from the group of rehabilitating a functional deficit exhibited by the patient and enhancing a functional capability of the patient.

[c21] 21. The method of claim 19, wherein the collateral neural activity arises in association with application of the first stimulation signal to the patient.

[c22] 22. The method of claim 19, wherein attempting to abate the collateral neural activity comprises discontinuing application of the first stimulation signal.

[c23] 23. The method of claim 19, wherein attempting to abate the collateral neural activity comprises applying a second stimulation signal to the patient.

[c24] 24. The method of claim 23, wherein the second stimulation signal is applied to at least one of the target neural population and a neural population adjacent to a portion of the target neural population.

[c25] 25. The method of claim 19, wherein monitoring the parameter comprises monitoring at least one of an electrophysiological signal and a patient behavior.

[c26] 26. The method of claim 19, wherein monitoring the parameter comprises monitoring at least one of an EEG signal, a cerebral bloodflow signal, an EMG signal, an accelerometer signal, a motion sensor signal, and a neural imaging signal.

[c27] 27. The method of claim 19, further comprising:

interrupting application of the first stimulation signal; and

resuming application of the first stimulation signal in the event that evidence of the collateral neural activity is absent.

[c28] 28. A neural stimulation system comprising:

a first set of electrodes configured to be positioned upon a target neural population corresponding to a site at which neuroplasticity is occurring, a site at which neuroplasticity is expected to occur, and/or a site associated with neuropathic pain;

a monitoring device to receive signals corresponding to a neural activity within a portion of the target neural population;

a stimulus unit coupled to deliver stimuli to the first set of electrodes; and

a sensing unit coupled receive signals from the monitoring device.

[c29] 29. The neural stimulation system of claim 28, wherein the sensing unit is further coupled to the stimulus unit.

[c30] 30. The neural stimulation system of claim 28, wherein the first set of electrodes and a portion of the stimulus unit are configured for implantation into the patient.

[c31] 31. The neural stimulation system of claim 28, wherein the first set of electrodes, the monitoring device, and a portion of the stimulus unit are configured for implantation into a patient.

[c32] 32. The neural stimulation system of claim 28, wherein the first set of electrodes, the monitoring device, a portion of the stimulus unit, and a portion of the sensing unit are configured for implantation into a patient.

[c33] 33. The neural stimulation system of claim 28, further comprising a substrate that carries the first set of electrodes and the monitoring device.

[c34] 34. The neural stimulation system of claim 28, wherein the monitoring device comprises one from the group of a second set of electrodes and a cerebral bloodflow monitor.

[c35] 35. An implantable stimulation and monitoring device comprising:

a substrate;

an electrode carried by the substrate; and

a cerebral bloodflow monitor carried by the substrate.

[c36] 36. A neural stimulation system comprising:

an electrode configuration positioned to deliver a stimulation signal to a target neural population corresponding to one from the group of a site at which neuroplasticity is occurring, a site at which neuroplasticity is expected to occur, and a site associated with a neurological disorder that is present on an essentially continuous basis in the absence of the stimulation signal;

a monitoring device positioned to receive signals corresponding to a neural activity within a portion of the target neural population;

a pulse system coupled to the electrode configuration, the pulse system delivering the stimulation signal to the electrode configuration;

a controller coupled to the pulse system, the controller including a computer operable medium containing instructions that generate command signals that define a set of parameters corresponding to the stimulation signal and selectively enable operation of the pulse system; and

a sensing unit coupled to the monitoring device, the sensing unit including a computer operable medium containing instructions that detect evidence of an collateral neural activity and generate a notification signal in the event that evidence of the collateral neural activity exists.

[c37] 37. The neural stimulation system of claim 36, wherein the controller is further coupled to the sensing unit and the computer operable medium within the controller further contains instructions for attempting to abate the collateral neural activity in response to the notification signal.

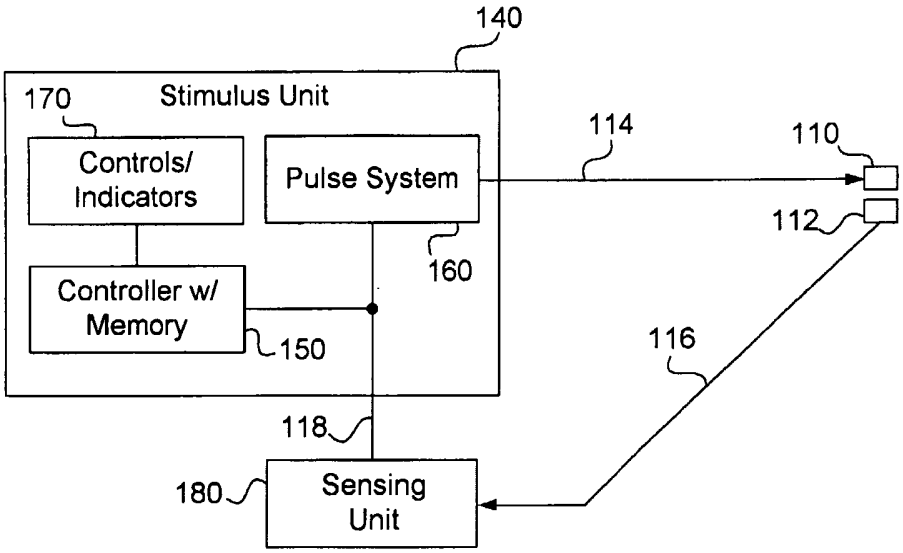
140
170
Stimulus Unit
Controls/
Indicators
Pulse System
114
110
112
160
Controller w/
Memory
150
116
118
180
Sensing
Unit
100

FIG. 1

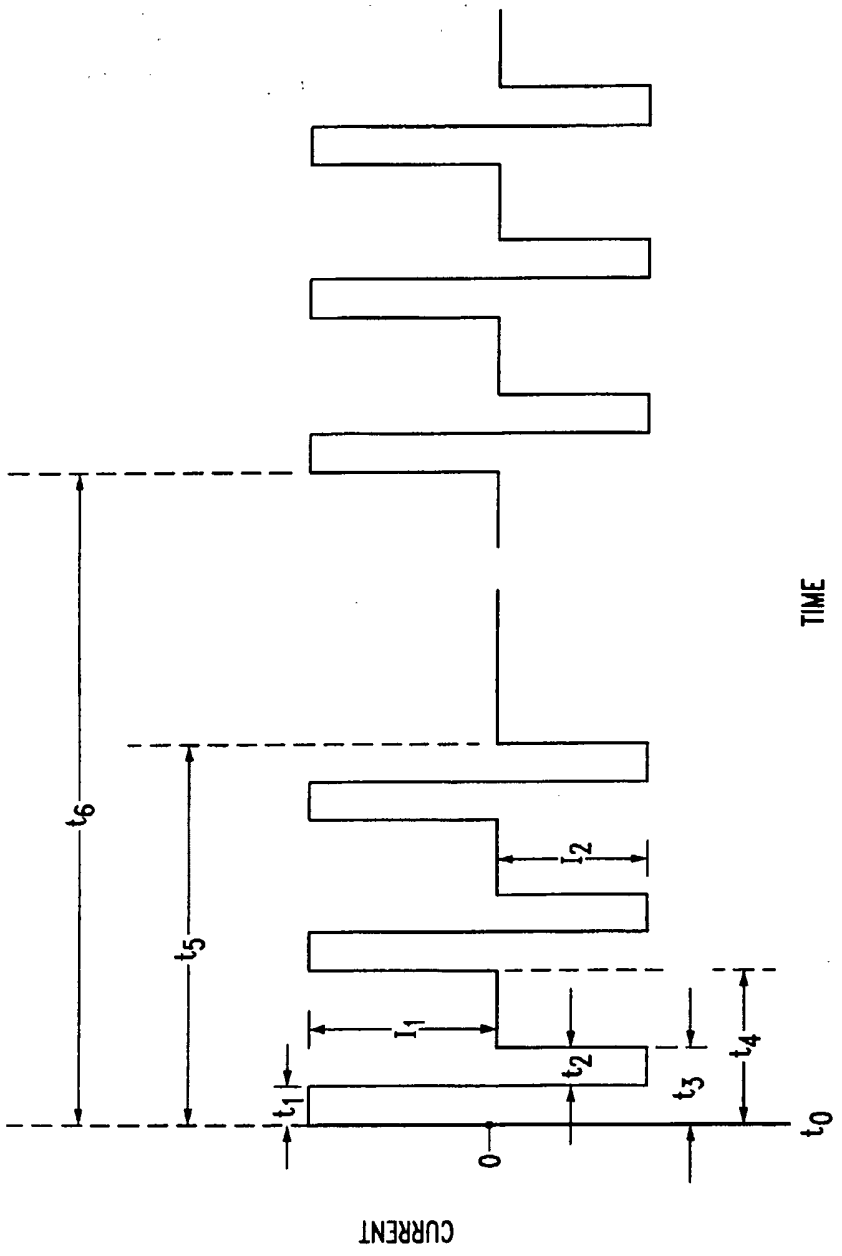

Fig. 2

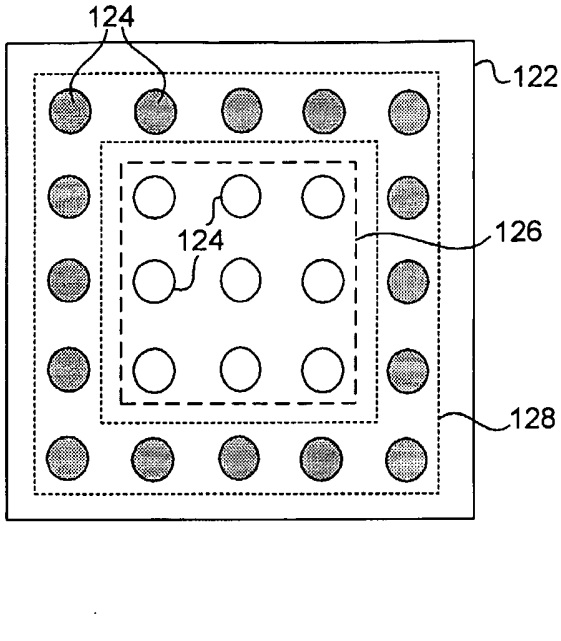

FIG. 3A

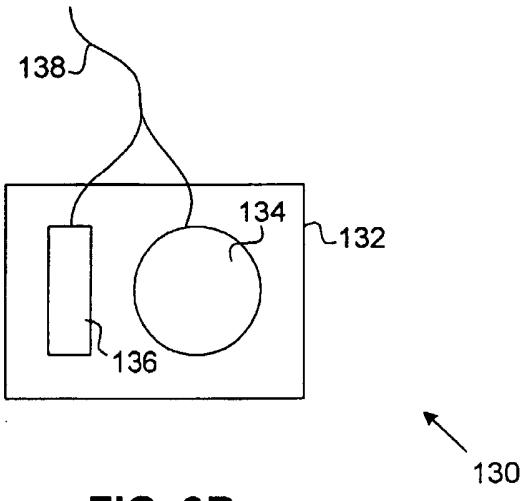

FIG. 3B

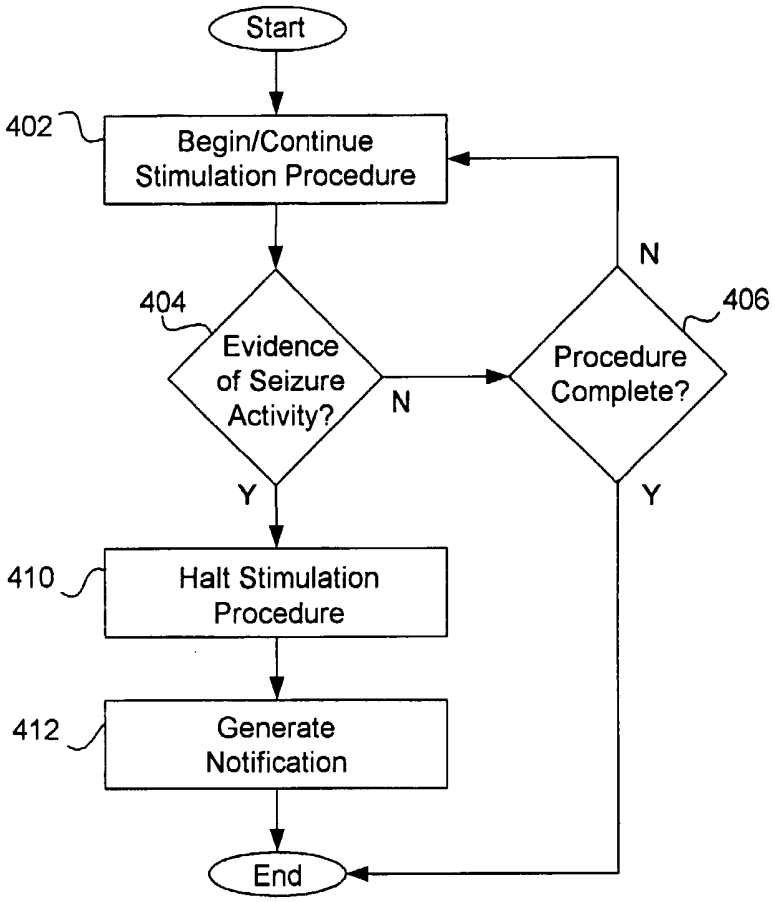
Start
402
Begin/Continue Stimulation Procedure
404
Evidence of Seizure Activity?
N
406
Procedure Complete?
N
Y
Y
410
Halt Stimulation Procedure
412
Generate Notification
End
400

FIG. 4

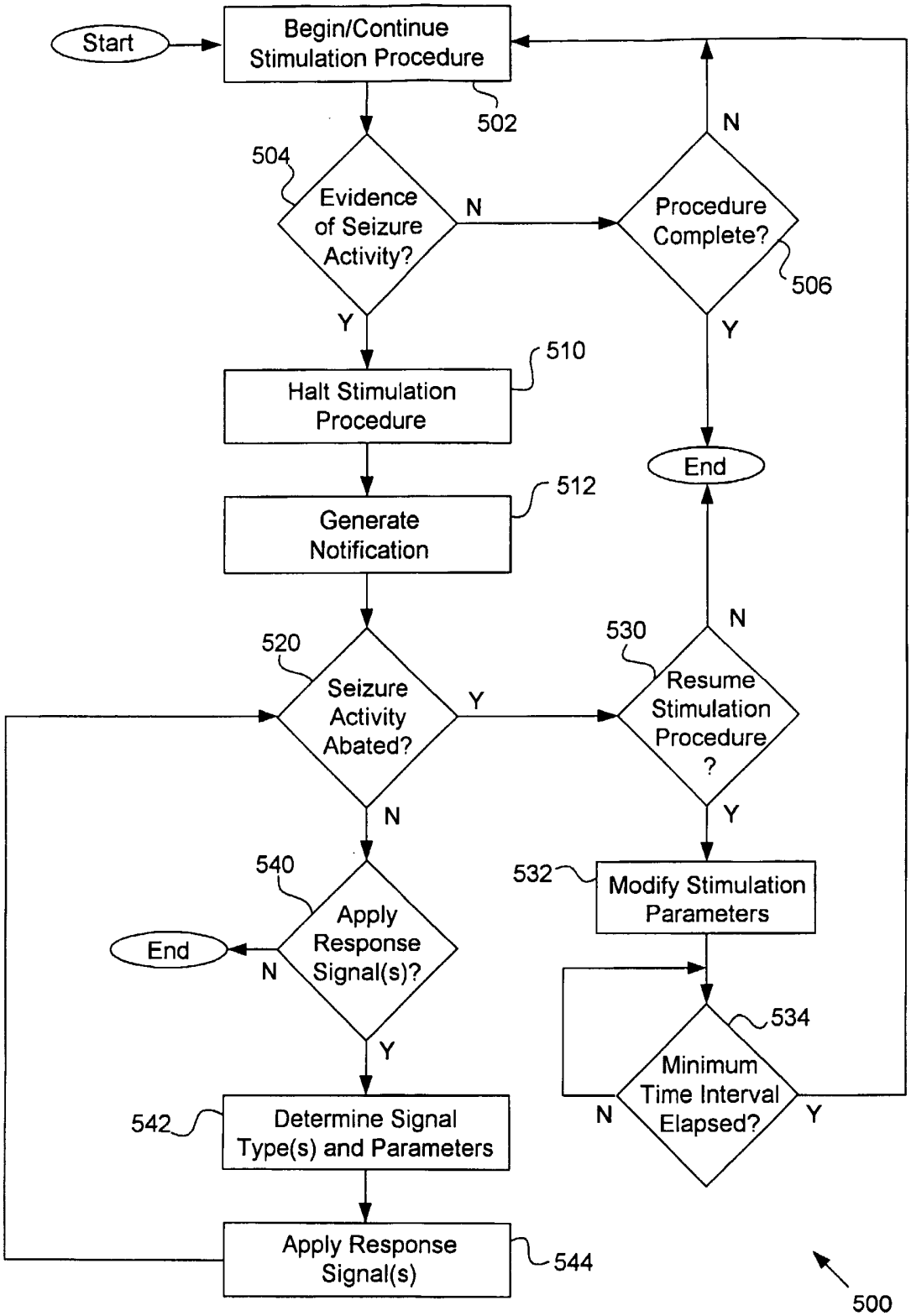
Start
Begin/Continue Stimulation Procedure
502
504
Evidence of Seizure Activity?
N
Procedure Complete?
506
N
Y
Y
510
Halt Stimulation Procedure
End
512
Generate Notification
520
Seizure Activity Abated?
Y
530
Resume Stimulation Procedure ?
N
N
Y
540
Apply Response Signal(s)?
End
N
532
Modify Stimulation Parameters
534
Minimum Time Interval Elapsed?
N
Y
Y
542
Determine Signal Type(s) and Parameters
Apply Response Signal(s)
544
500

FIG. 5

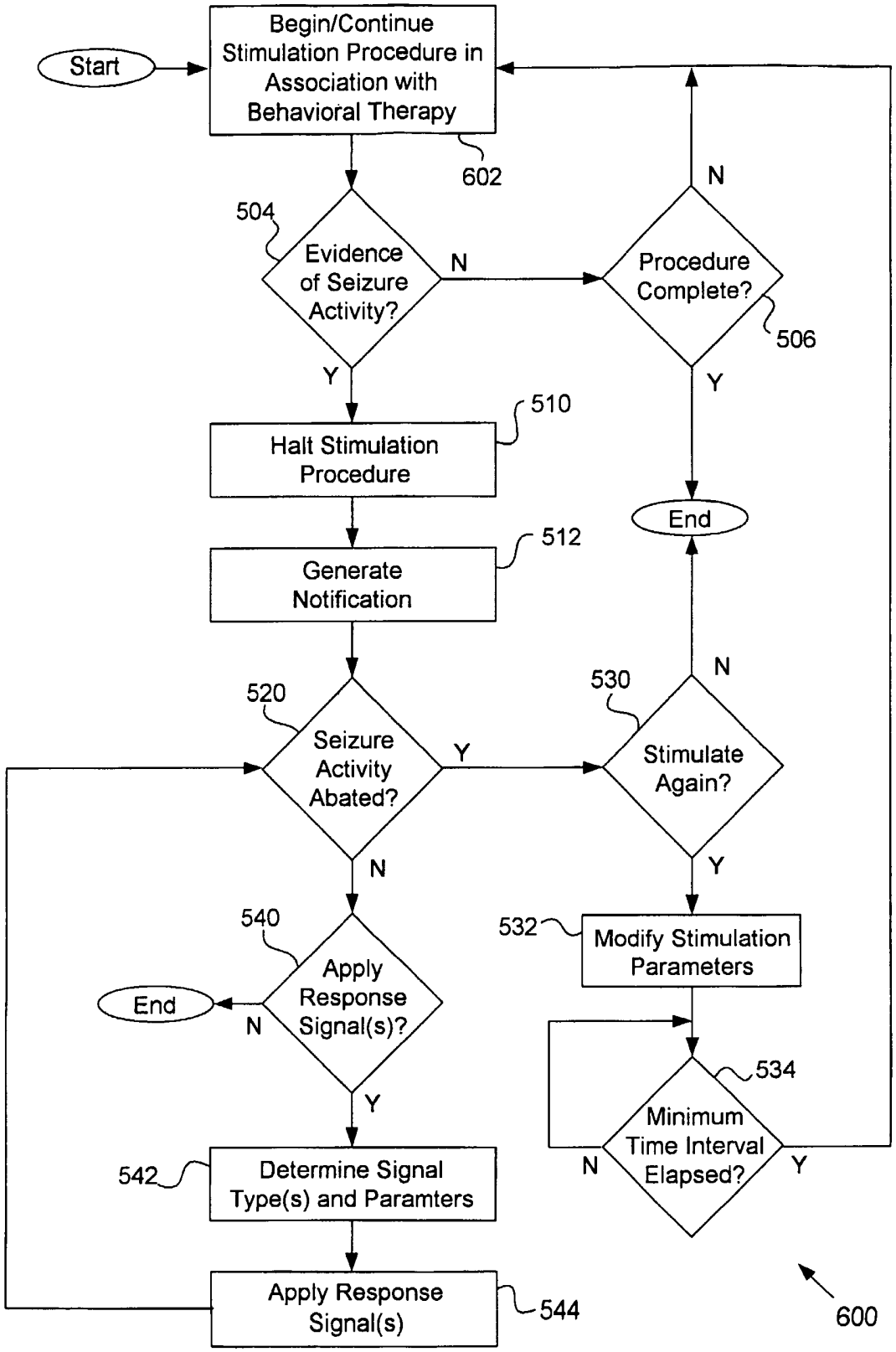
Start
Begin/Continue Stimulation Procedure in Association with Behavioral Therapy
602
504
Evidence of Seizure Activity?
N
Procedure Complete?
506
N
Y
Y
510
Halt Stimulation Procedure
End
512
Generate Notification
520
Seizure Activity Abated?
Y
530
Stimulate Again?
N
N
Y
540
Apply Response Signal(s)?
End
N
532
Modify Stimulation Parameters
534
Minimum Time Interval Elapsed?
N
Y
Y
542
Determine Signal Type(s) and Paramters
Apply Response Signal(s)
544
600

FIG. 6