



US008852100B2

(12) **United States Patent**  
**Osorio**

(10) **Patent No.:** **US 8,852,100 B2**  
(45) **Date of Patent:** **Oct. 7, 2014**

(54) **DETECTING, QUANTIFYING, AND/OR CLASSIFYING SEIZURES USING MULTIMODAL DATA**

(58) **Field of Classification Search**  
None  
See application file for complete search history.

(71) Applicant: **Flint Hills Scientific, LLC**, Lawrence, KS (US)

(56) **References Cited**

(72) Inventor: **Ivan Osorio**, Leawood, KS (US)

U.S. PATENT DOCUMENTS

(73) Assignee: **Flint Hills Scientific, LLC**, Lawrence, KS (US)

4,172,459 A 10/1979 Hepp  
4,197,856 A 4/1980 Northrop  
(Continued)

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 34 days.

FOREIGN PATENT DOCUMENTS

(21) Appl. No.: **13/776,176**

EP 1145736 10/2001  
EP 1486232 12/2004  
(Continued)

(22) Filed: **Feb. 25, 2013**

OTHER PUBLICATIONS

(65) **Prior Publication Data**  
US 2013/0225992 A1 Aug. 29, 2013

Bachman, D.,S. et al.; "Effects of Vagal Volleys and Serotonin on Units of Cingulate Cortex in Monkeys;" Brain Research , vol. 130 (1977). pp. 253-269.

**Related U.S. Application Data**

(Continued)

(63) Continuation of application No. 13/098,262, filed on Apr. 29, 2011, now Pat. No. 8,382,667, which is a continuation-in-part of application No. 12/896,525, filed on Oct. 1, 2010, now Pat. No. 8,337,404.

*Primary Examiner* — Brian T Gedeon

(51) **Int. Cl.**  
*A61B 5/00* (2006.01)  
*A61B 5/0205* (2006.01)  
*A61B 5/11* (2006.01)  
*A61N 1/36* (2006.01)  
*A61B 5/0245* (2006.01)  
*A61N 1/365* (2006.01)

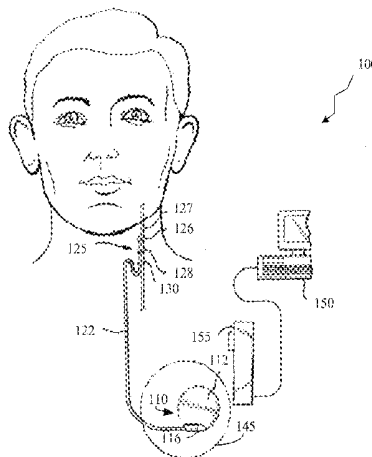
(57) **ABSTRACT**

A method, comprising receiving at least one of a signal relating to a first cardiac activity and a signal relating to a first body movement from a patient; triggering at least one of a test of the patient's responsiveness, awareness, a second cardiac activity, a second body movement, a spectral analysis test of the second cardiac activity, and a spectral analysis test of the second body movement, based on at least one of the signal relating to the first cardiac activity and the signal relating to the first body movement; determining an occurrence of an epileptic event based at least in part on said one or more triggered tests; and performing a further action in response to said determination of said occurrence of said epileptic event. Further methods allow classification of epileptic events. Apparatus and systems capable of implementing the method.

(52) **U.S. Cl.**  
CPC ..... *A61B 5/0205* (2013.01); *A61N 1/36064* (2013.01); *A61N 1/36135* (2013.01); *A61B 5/0245* (2013.01); *A61B 5/4094* (2013.01); *A61B 5/7264* (2013.01); *A61B 5/686* (2013.01); *A61N 1/36585* (2013.01); *A61B 5/1117* (2013.01)

USPC ..... **600/301**

**16 Claims, 14 Drawing Sheets**



(56)

## References Cited

## U.S. PATENT DOCUMENTS

4,291,699 A	9/1981	Geddes et al.	5,941,906 A	8/1999	Barreras, Sr. et al.
4,320,766 A	3/1982	Alihanka et al.	5,942,979 A	8/1999	Luppino
4,541,432 A	9/1985	Molina-Negro et al.	5,978,702 A	11/1999	Ward et al.
4,573,481 A	3/1986	Bullara	5,978,972 A	11/1999	Stewart et al.
4,702,254 A	10/1987	Zabara	5,987,352 A	11/1999	Klein et al.
4,867,164 A	9/1989	Zabara	5,995,868 A	11/1999	Osorio et al.
4,920,979 A	5/1990	Bullara	6,016,449 A	1/2000	Fischell et al.
4,949,721 A	8/1990	Toriu et al.	6,018,682 A	1/2000	Rise
4,979,511 A	12/1990	Terry, Jr.	6,048,324 A	4/2000	Socci et al.
5,025,807 A	6/1991	Zabara	6,061,593 A	5/2000	Fischell et al.
5,062,169 A	11/1991	Kennedy et al.	6,073,048 A	6/2000	Kieval et al.
5,113,869 A	5/1992	Nappholz et al.	6,083,249 A	7/2000	Familoni
5,137,020 A	8/1992	Wayne et al.	6,091,992 A	7/2000	Bourgeois et al.
5,154,172 A	10/1992	Terry, Jr. et al.	6,095,991 A	8/2000	Krausman et al.
5,179,950 A	1/1993	Stanislaw	6,104,956 A	8/2000	Naritoku et al.
5,186,170 A	2/1993	Varrichio et al.	6,115,628 A	9/2000	Stadler et al.
5,188,104 A	2/1993	Wernicke et al.	6,115,630 A	9/2000	Stadler et al.
5,194,847 A	3/1993	Taylor et al.	6,128,538 A	10/2000	Fischell et al.
5,203,326 A	4/1993	Collins	6,134,474 A	10/2000	Fischell et al.
5,205,285 A	4/1993	Baker, Jr.	6,162,191 A	12/2000	Foxlin
5,213,568 A	5/1993	Lattin et al.	6,163,281 A	12/2000	Torch
5,215,086 A	6/1993	Terry, Jr. et al.	6,167,311 A	12/2000	Rezai
5,215,089 A	6/1993	Baker, Jr.	6,171,239 B1	1/2001	Humphrey
5,222,494 A	6/1993	Baker, Jr.	6,175,764 B1	1/2001	Loeb et al.
5,231,988 A	8/1993	Wernicke et al.	6,205,359 B1	3/2001	Boveja
5,235,980 A	8/1993	Varrichio et al.	6,208,894 B1	3/2001	Schulman et al.
5,237,991 A	8/1993	Baker, Jr. et al.	6,208,902 B1	3/2001	Boveja
5,243,980 A	9/1993	Mehra	6,221,908 B1	4/2001	Kilgard et al.
5,251,634 A	10/1993	Weinberg	6,246,344 B1	6/2001	Torch
5,263,480 A	11/1993	Wernicke et al.	6,248,080 B1	6/2001	Miesel et al.
5,269,302 A	12/1993	Swartz et al.	6,253,109 B1	6/2001	Gielen
5,269,303 A	12/1993	Wernicke et al.	6,269,270 B1	7/2001	Boveja
5,299,569 A	4/1994	Wernicke et al.	6,272,379 B1	8/2001	Fischell et al.
5,304,206 A	4/1994	Baker, Jr. et al.	6,304,775 B1	10/2001	Iasemidis et al.
5,311,876 A	5/1994	Olsen et al.	6,315,740 B1	11/2001	Singh
5,313,953 A	5/1994	Yomtov et al.	6,324,421 B1	11/2001	Stadler et al.
5,330,507 A	7/1994	Schwartz	6,337,997 B1	1/2002	Rise
5,330,515 A	7/1994	Rutecki et al.	6,339,725 B1	1/2002	Naritoku et al.
5,334,221 A	8/1994	Bardy	6,341,236 B1	1/2002	Osorio et al.
5,335,657 A	8/1994	Terry, Jr. et al.	6,356,784 B1	3/2002	Lozano et al.
5,404,877 A	4/1995	Nolan et al.	6,356,788 B2	3/2002	Boveja
5,425,373 A	6/1995	Causey, III	6,361,507 B1	3/2002	Foxlin
5,513,649 A	5/1996	Gevens et al.	6,361,508 B1	3/2002	Johnson et al.
5,522,862 A	6/1996	Testerman et al.	6,366,813 B1	4/2002	DiLorenzo
5,523,742 A	6/1996	Simkins et al.	6,366,814 B1	4/2002	Boveja
5,540,730 A	7/1996	Terry, Jr. et al.	6,374,140 B1	4/2002	Rise
5,540,734 A	7/1996	Zabara	6,397,100 B2	5/2002	Stadler et al.
5,571,150 A	11/1996	Wernicke et al.	6,427,086 B1	7/2002	Fischell et al.
5,610,590 A	3/1997	Johnson et al.	6,429,217 B1	8/2002	Puskas
5,611,350 A	3/1997	John	6,441,731 B1	8/2002	Hess
5,645,077 A	7/1997	Foxlin	6,449,512 B1	9/2002	Boveja
5,645,570 A	7/1997	Corbucci	6,459,936 B2	10/2002	Fischell et al.
5,651,378 A	7/1997	Matheny et al.	6,463,328 B1	10/2002	John
5,658,318 A	8/1997	Stroetmann et al.	6,466,822 B1	10/2002	Pless
5,683,422 A	11/1997	Rise et al.	6,473,639 B1	10/2002	Fischell et al.
5,690,681 A	11/1997	Geddes et al.	6,473,644 B1	10/2002	Terry, Jr. et al.
5,690,688 A	11/1997	Noren et al.	6,477,418 B2	11/2002	Plicchi et al.
5,700,282 A	12/1997	Zabara	6,480,743 B1	11/2002	Kirkpatrick et al.
5,707,400 A	1/1998	Terry, Jr. et al.	6,484,132 B1	11/2002	Hively et al.
5,716,377 A	2/1998	Rise et al.	6,501,983 B1	12/2002	Natarajan et al.
5,720,771 A	2/1998	Snell	6,505,074 B2	1/2003	Boveja et al.
5,743,860 A	4/1998	Hively et al.	6,532,388 B1	3/2003	Hill et al.
5,748,113 A	5/1998	Torch	6,539,263 B1	3/2003	Schiff et al.
5,792,186 A	8/1998	Rise	6,542,081 B2	4/2003	Torch
5,800,474 A	9/1998	Benabid et al.	6,542,774 B2	4/2003	Hill et al.
5,807,284 A	9/1998	Foxlin	6,549,804 B1	4/2003	Osorio et al.
5,808,552 A	9/1998	Wiley et al.	6,556,868 B2	4/2003	Naritoku et al.
5,833,709 A	11/1998	Rise et al.	6,560,486 B1	5/2003	Osorio et al.
5,853,005 A	12/1998	Scanlon et al.	6,564,102 B1	5/2003	Boveja
5,879,309 A	3/1999	Johnson et al.	6,587,719 B1	7/2003	Barrett et al.
5,905,436 A	5/1999	Dwight et al.	6,587,727 B2	7/2003	Osorio et al.
5,913,876 A	6/1999	Taylor et al.	6,594,524 B2	7/2003	Esteller et al.
5,916,181 A	6/1999	Socci et al.	6,599,250 B2	7/2003	Webb et al.
5,916,239 A	6/1999	Geddes et al.	6,609,025 B2	8/2003	Barrett et al.
5,928,272 A	7/1999	Adkins et al.	6,610,713 B2	8/2003	Tracey
			6,611,715 B1	8/2003	Boveja
			6,611,783 B2	8/2003	Kelly, Jr. et al.
			6,615,081 B1	9/2003	Boveja
			6,615,085 B1	9/2003	Boveja

(56)

## References Cited

## U.S. PATENT DOCUMENTS

6,622,038	B2	9/2003	Barrett et al.	7,231,254	B2	6/2007	DiLorenzo
6,622,041	B2	9/2003	Terry, Jr. et al.	7,236,830	B2	6/2007	Gliner
6,622,047	B2	9/2003	Barrett et al.	7,236,831	B2	6/2007	Firlik et al.
6,628,985	B2	9/2003	Sweeney et al.	7,242,983	B2	7/2007	Frei et al.
6,628,987	B1	9/2003	Hill et al.	7,242,984	B2	7/2007	DiLorenzo
6,629,990	B2	10/2003	Putz et al.	7,254,439	B2	8/2007	Miszczynski et al.
6,647,296	B2	11/2003	Fischell et al.	7,263,467	B2	8/2007	Sackellares et al.
6,656,125	B2	12/2003	Miszczynski et al.	7,274,298	B2	9/2007	Frank
6,656,960	B2	12/2003	Puskas	7,277,758	B2	10/2007	DiLorenzo
6,668,191	B1	12/2003	Boveja	7,280,867	B2	10/2007	Frei et al.
6,671,555	B2	12/2003	Gielen et al.	7,282,030	B2	10/2007	Frei et al.
6,671,556	B2	12/2003	Osorio et al.	7,289,844	B2	10/2007	Miszczynski et al.
6,684,105	B2	1/2004	Cohen et al.	7,292,890	B2	11/2007	Whitehurst et al.
6,721,603	B2	4/2004	Zabara et al.	7,295,881	B2	11/2007	Cohen et al.
6,730,047	B2	5/2004	Socci et al.	7,299,096	B2	11/2007	Balzer et al.
6,735,474	B1	5/2004	Loeb et al.	7,302,298	B2	11/2007	Lowry et al.
6,738,671	B2	5/2004	Christopherson et al.	7,304,580	B2	12/2007	Sullivan et al.
6,760,626	B1	7/2004	Boveja	7,305,268	B2	12/2007	Gliner et al.
6,763,256	B2	7/2004	Kimball et al.	7,313,440	B2	12/2007	Miesel
6,768,969	B1	7/2004	Nikitin et al.	7,314,451	B2	1/2008	Halperin et al.
6,786,877	B2	9/2004	Foxlin	7,321,837	B2	1/2008	Osorio et al.
6,788,975	B1	9/2004	Whitehurst et al.	7,324,850	B2	1/2008	Persen et al.
6,793,670	B2	9/2004	Osorio et al.	7,324,851	B1	1/2008	DiLorenzo
6,819,953	B2	11/2004	Yonce et al.	7,330,760	B2	2/2008	Heruth et al.
6,819,956	B2	11/2004	DiLorenzo	7,346,391	B1	3/2008	Osorio et al.
6,832,114	B1	12/2004	Whitehurst et al.	7,353,063	B2	4/2008	Simms, Jr.
6,836,685	B1	12/2004	Fitz	7,353,064	B2	4/2008	Gliner et al.
6,850,601	B2	2/2005	Jones et al.	7,373,199	B2	5/2008	Sackellares et al.
6,879,850	B2	4/2005	Kimball	7,385,443	B1	6/2008	Denison
6,885,888	B2	4/2005	Rezai	7,389,144	B1	6/2008	Osorio et al.
6,904,390	B2	6/2005	Nikitin et al.	7,389,147	B2	6/2008	Wahlstrand et al.
6,920,357	B2	7/2005	Osorio et al.	7,395,113	B2	7/2008	Heruth et al.
6,923,784	B2	8/2005	Stein	7,401,008	B2	7/2008	Frei et al.
6,931,274	B2	8/2005	Williams et al.	7,403,820	B2	7/2008	DiLorenzo
6,934,580	B1	8/2005	Osorio et al.	7,420,472	B2	9/2008	Tran
6,934,585	B1	8/2005	Schloss	7,433,732	B1	10/2008	Carney et al.
6,944,501	B1	9/2005	Pless	7,447,545	B2	11/2008	Heruth et al.
6,957,107	B2	10/2005	Rogers	7,454,245	B2	11/2008	Armstrong et al.
6,961,618	B2	11/2005	Osorio et al.	7,488,293	B2	2/2009	Marcovecchio et al.
6,984,993	B2	1/2006	Ariav	7,488,294	B2	2/2009	Torch
6,985,771	B2	1/2006	Fischell et al.	7,491,181	B2	2/2009	Heruth et al.
6,990,377	B2	1/2006	Gliner et al.	7,494,464	B2	2/2009	Rzesnitzeck et al.
7,006,859	B1	2/2006	Osorio et al.	7,502,643	B2	3/2009	Farringdon et al.
7,006,872	B2	2/2006	Gielen et al.	7,515,054	B2	4/2009	Torch
7,010,351	B2	3/2006	Firlik et al.	7,539,532	B2	5/2009	Tran
7,024,247	B2	4/2006	Gliner et al.	7,539,533	B2	5/2009	Tran
7,035,684	B2	4/2006	Lee	7,539,543	B2	5/2009	Schiff et al.
7,054,792	B2	5/2006	Frei et al.	7,558,622	B2	7/2009	Tran
7,058,453	B2	6/2006	Nelson et al.	7,565,132	B2	7/2009	Ben Ayed
7,068,842	B2	6/2006	Liang et al.	7,590,453	B2	9/2009	Heruth et al.
7,076,288	B2	7/2006	Skinner	7,620,456	B2	11/2009	Gliner et al.
7,077,810	B2	7/2006	Lange et al.	7,629,890	B2	12/2009	Sullivan et al.
7,079,977	B2	7/2006	Osorio et al.	7,643,655	B2	1/2010	Liang et al.
7,104,947	B2	9/2006	Riehl et al.	7,647,121	B2	1/2010	Wahlstrand et al.
7,110,820	B2	9/2006	Tcheng et al.	7,658,112	B2	2/2010	Nakamura
7,112,319	B2	9/2006	Broderick et al.	7,666,151	B2	2/2010	Sullivan et al.
7,127,370	B2	10/2006	Kelly et al.	7,714,757	B2	5/2010	Denison et al.
7,134,996	B2	11/2006	Bardy	7,717,848	B2	5/2010	Heruth et al.
7,139,677	B2	11/2006	Hively et al.	RE41,376	E	6/2010	Torch
7,146,211	B2	12/2006	Frei et al.	7,733,224	B2	6/2010	Tran
7,146,217	B2	12/2006	Firlik et al.	7,747,318	B2	6/2010	John et al.
7,146,218	B2	12/2006	Esteller et al.	7,769,464	B2	8/2010	Gerber et al.
7,149,572	B2	12/2006	Frei et al.	7,775,993	B2	8/2010	Heruth et al.
7,164,941	B2	1/2007	Miszczynski et al.	7,792,583	B2	9/2010	Miesel et al.
7,167,743	B2	1/2007	Heruth et al.	7,801,603	B2	9/2010	Westlund et al.
7,167,750	B2	1/2007	Knudson et al.	7,801,618	B2	9/2010	Pless
7,174,206	B2	2/2007	Frei et al.	7,801,743	B2	9/2010	Graves et al.
7,177,678	B1	2/2007	Osorio et al.	7,813,802	B2	10/2010	Tcheng et al.
7,188,053	B2	3/2007	Nikitin et al.	7,822,481	B2	10/2010	Gerber et al.
RE39,539	E	4/2007	Torch	7,827,011	B2	11/2010	DeVaul et al.
7,204,833	B1	4/2007	Osorio et al.	7,831,305	B2	11/2010	Gliner
7,209,786	B2	4/2007	Brockway	7,847,628	B2	12/2010	Denison
7,209,787	B2	4/2007	DiLorenzo	7,866,212	B2	1/2011	Ariav et al.
7,221,981	B2	5/2007	Gliner	7,899,545	B2	3/2011	John
7,228,167	B2	6/2007	Kara	7,935,076	B2	5/2011	Estes et al.
				RE42,471	E	6/2011	Torch
				7,957,809	B2	6/2011	Bourget et al.
				7,965,833	B2	6/2011	Meir et al.
				7,974,671	B2	7/2011	Fujiwara et al.

(56)

## References Cited

## U.S. PATENT DOCUMENTS

7,996,076 B2	8/2011	Burns et al.	2005/0070971 A1	3/2005	Fowler et al.
7,999,857 B2	8/2011	Bunn et al.	2005/0075701 A1	4/2005	Shafer
8,000,789 B2	8/2011	Denison et al.	2005/0075702 A1	4/2005	Shafer
8,000,794 B2	8/2011	Lozano	2005/0101873 A1	5/2005	Misczynski et al.
8,021,299 B2	9/2011	Miesel et al.	2005/0107716 A1	5/2005	Eaton et al.
8,027,730 B2	9/2011	John et al.	2005/0119703 A1	6/2005	DiLorenzo
8,027,737 B2	9/2011	Kokones et al.	2005/0124901 A1	6/2005	Misczynski et al.
8,075,499 B2	12/2011	Nathan et al.	2005/0131467 A1	6/2005	Boveja et al.
8,109,891 B2	2/2012	Kramer et al.	2005/0131485 A1	6/2005	Knudson et al.
2001/0032059 A1	10/2001	Kelly et al.	2005/0131486 A1	6/2005	Boveja et al.
2002/0072782 A1	6/2002	Osorio et al.	2005/0131493 A1	6/2005	Boveja et al.
2002/0099417 A1	7/2002	Naritoku et al.	2005/0143786 A1	6/2005	Boveja et al.
2002/0116030 A1	8/2002	Rezai	2005/0148893 A1	7/2005	Misczynski et al.
2002/0151939 A1	10/2002	Rezai	2005/0148894 A1	7/2005	Misczynski et al.
2002/0188214 A1	12/2002	Misczynski et al.	2005/0148895 A1	7/2005	Misczynski et al.
2003/0040680 A1	2/2003	Hassert et al.	2005/0153885 A1	7/2005	Yun et al.
2003/0074032 A1	4/2003	Gliner	2005/0154425 A1	7/2005	Boveja et al.
2003/0083716 A1	5/2003	Nicolelis et al.	2005/0154426 A1	7/2005	Boveja et al.
2003/0083726 A1	5/2003	Zeijlemaker et al.	2005/0165458 A1	7/2005	Boveja et al.
2003/0125786 A1	7/2003	Gliner et al.	2005/0187590 A1	8/2005	Boveja et al.
2003/0130706 A1	7/2003	Sheffield et al.	2005/0192644 A1	9/2005	Boveja et al.
2003/0144829 A1	7/2003	Geatz et al.	2005/0197590 A1	9/2005	Osorio et al.
2003/0181954 A1	9/2003	Rezai	2005/0203366 A1	9/2005	Donoghue et al.
2003/0181958 A1	9/2003	Dobak	2005/0245971 A1	11/2005	Brockway et al.
2003/0195588 A1	10/2003	Upton et al.	2005/0261542 A1	11/2005	Riehl
2003/0208212 A1	11/2003	Cigaina	2005/0277998 A1	12/2005	Tracey et al.
2003/0210147 A1	11/2003	Humbar	2005/0283200 A1	12/2005	Rezai et al.
2003/0212440 A1	11/2003	Boveja	2005/0283201 A1	12/2005	Machado et al.
2003/0236474 A1	12/2003	Singh	2005/0288600 A1	12/2005	Zhang et al.
2003/0236558 A1	12/2003	Whitehurst et al.	2005/0288760 A1	12/2005	Machado et al.
2004/0006278 A1	1/2004	Webb et al.	2006/0009815 A1	1/2006	Boveja
2004/0030365 A1	2/2004	Rubin et al.	2006/0018833 A1	1/2006	Murphy et al.
2004/0088024 A1	5/2004	Firlik et al.	2006/0074450 A1	4/2006	Boveja
2004/0111045 A1	6/2004	Sullivan et al.	2006/0079936 A1	4/2006	Boveja
2004/0122484 A1	6/2004	Hatlestad et al.	2006/0094971 A1	5/2006	Drew
2004/0122485 A1	6/2004	Stahmann et al.	2006/0095081 A1	5/2006	Zhou et al.
2004/0133119 A1	7/2004	Osorio et al.	2006/0106430 A1	5/2006	Fowler et al.
2004/0138516 A1	7/2004	Osorio et al.	2006/0135877 A1	6/2006	Giftakis et al.
2004/0138517 A1	7/2004	Osorio et al.	2006/0135881 A1	6/2006	Giftakis et al.
2004/0138647 A1	7/2004	Osorio et al.	2006/0149139 A1	7/2006	Bonmassar et al.
2004/0138711 A1	7/2004	Osorio et al.	2006/0155495 A1	7/2006	Osorio et al.
2004/0153129 A1	8/2004	Pless et al.	2006/0167497 A1	7/2006	Armstrong et al.
2004/0158119 A1	8/2004	Osorio et al.	2006/0173493 A1	8/2006	Armstrong et al.
2004/0158165 A1	8/2004	Yonce et al.	2006/0173522 A1	8/2006	Osorio
2004/0172085 A1	9/2004	Knudson et al.	2006/0190056 A1	8/2006	Fowler et al.
2004/0172091 A1	9/2004	Rezai	2006/0195163 A1	8/2006	KenKnight et al.
2004/0172094 A1	9/2004	Cohen et al.	2006/0200206 A1	9/2006	Firlik et al.
2004/0176812 A1	9/2004	Knudson et al.	2006/0212091 A1	9/2006	Lozano et al.
2004/0176831 A1	9/2004	Gliner et al.	2006/0212097 A1	9/2006	Varadan et al.
2004/0199212 A1	10/2004	Fischell et al.	2006/0224067 A1	10/2006	Giftakis et al.
2004/0225335 A1	11/2004	Whitehurst et al.	2006/0224191 A1	10/2006	DiLorenzo
2004/0249302 A1	12/2004	Donoghue et al.	2006/0241697 A1	10/2006	Libbus et al.
2004/0249416 A1	12/2004	Yun et al.	2006/0241725 A1	10/2006	Libbus et al.
2004/0267152 A1	12/2004	Pineda	2006/0293720 A1	12/2006	DiLorenzo
2005/0004621 A1	1/2005	Boveja et al.	2007/0027486 A1	2/2007	Armstrong et al.
2005/0020887 A1	1/2005	Goldberg	2007/0027497 A1	2/2007	Parnis
2005/0021092 A1	1/2005	Yun et al.	2007/0027498 A1	2/2007	Maschino et al.
2005/0021103 A1	1/2005	DiLorenzo	2007/0027500 A1	2/2007	Maschino et al.
2005/0021104 A1	1/2005	DiLorenzo	2007/0032834 A1	2/2007	Gliner et al.
2005/0021105 A1	1/2005	Firlik et al.	2007/0043392 A1	2/2007	Gliner et al.
2005/0021106 A1	1/2005	Firlik et al.	2007/0055320 A1	3/2007	Weinand et al.
2005/0021107 A1	1/2005	Firlik et al.	2007/0073150 A1	3/2007	Gopalsami et al.
2005/0021118 A1	1/2005	Genau et al.	2007/0073355 A1	3/2007	DiLorenzo
2005/0022606 A1	2/2005	Partin et al.	2007/0088403 A1	4/2007	Wyler et al.
2005/0027284 A1	2/2005	Lozano et al.	2007/0100278 A1	5/2007	Frei et al.
2005/0033378 A1	2/2005	Sheffield et al.	2007/0100392 A1	5/2007	Maschino et al.
2005/0033379 A1	2/2005	Lozano et al.	2007/0142862 A1	6/2007	DiLorenzo
2005/0038484 A1	2/2005	Knudson et al.	2007/0142873 A1	6/2007	Esteller et al.
2005/0049515 A1	3/2005	Misczynski et al.	2007/0150024 A1	6/2007	Leyde et al.
2005/0049655 A1	3/2005	Boveja et al.	2007/0150025 A1	6/2007	DiLorenzo et al.
2005/0060001 A1	3/2005	Singhal et al.	2007/0161919 A1	7/2007	DiLorenzo
2005/0065562 A1	3/2005	Rezai	2007/0162086 A1	7/2007	DiLorenzo
2005/0065573 A1	3/2005	Rezai	2007/0167991 A1	7/2007	DiLorenzo
2005/0065574 A1	3/2005	Rezai	2007/0173901 A1	7/2007	Reeve
2005/0065575 A1	3/2005	Dobak	2007/0173902 A1	7/2007	Maschino et al.
			2007/0179534 A1	8/2007	Firlik et al.
			2007/0179557 A1	8/2007	Maschino et al.
			2007/0179558 A1	8/2007	Gliner et al.
			2007/0208212 A1	9/2007	DiLorenzo

(56)

## References Cited

## U.S. PATENT DOCUMENTS

2007/0213785 A1 9/2007 Osorio et al.  
 2007/0233192 A1 10/2007 Craig  
 2007/0239210 A1 10/2007 Libbus et al.  
 2007/0242661 A1 10/2007 Tran et al.  
 2007/0244407 A1 10/2007 Osorio  
 2007/0249953 A1 10/2007 Osorio et al.  
 2007/0249954 A1 10/2007 Virag et al.  
 2007/0255147 A1 11/2007 Drew et al.  
 2007/0255155 A1 11/2007 Drew et al.  
 2007/0260147 A1 11/2007 Giftakis et al.  
 2007/0260289 A1 11/2007 Giftakis et al.  
 2007/0265536 A1 11/2007 Giftakis et al.  
 2007/0272260 A1 11/2007 Nikitin et al.  
 2007/0282177 A1 12/2007 Pilz  
 2008/0004904 A1 1/2008 Tran et al.  
 2008/0033503 A1 2/2008 Fowler et al.  
 2008/0033508 A1 2/2008 Frei et al.  
 2008/0046035 A1 2/2008 Fowler et al.  
 2008/0064934 A1 3/2008 Frei et al.  
 2008/0071323 A1 3/2008 Lowry et al.  
 2008/0077028 A1 3/2008 Schaldach et al.  
 2008/0081958 A1 4/2008 Denison et al.  
 2008/0103548 A1 5/2008 Fowler et al.  
 2008/0114417 A1 5/2008 Leyde  
 2008/0119900 A1 5/2008 DiLorenzo  
 2008/0125820 A1 5/2008 Stahmann et al.  
 2008/0139870 A1 6/2008 Gliner et al.  
 2008/0146890 A1 6/2008 LeBoeuf et al.  
 2008/0146959 A1 6/2008 Sheffield et al.  
 2008/0161712 A1 7/2008 Leyde  
 2008/0161713 A1 7/2008 Leyde et al.  
 2008/0161879 A1 7/2008 Firlik et al.  
 2008/0161880 A1 7/2008 Firlik et al.  
 2008/0161881 A1 7/2008 Firlik et al.  
 2008/0161882 A1 7/2008 Firlik et al.  
 2008/0183096 A1 7/2008 Snyder et al.  
 2008/0183097 A1 7/2008 Leyde et al.  
 2008/0208013 A1 8/2008 Zhang et al.  
 2008/0208284 A1 8/2008 Rezaei et al.  
 2008/0258907 A1 10/2008 Kalpaxis et al.  
 2008/0269579 A1 10/2008 Schiebler et al.  
 2008/0275327 A1 11/2008 Faarbaek et al.  
 2008/0275328 A1 11/2008 Jones et al.  
 2008/0275349 A1 11/2008 Halperin et al.  
 2008/0281376 A1 11/2008 Gerber et al.  
 2008/0281381 A1 11/2008 Gerber et al.  
 2008/0281550 A1 11/2008 Hogle et al.  
 2008/0319281 A1 12/2008 Aarts  
 2009/0030345 A1 1/2009 Bonnet et al.  
 2009/0040052 A1 2/2009 Cameron et al.  
 2009/0054737 A1 2/2009 Magar et al.  
 2009/0054742 A1 2/2009 Kaminska et al.  
 2009/0060287 A1 3/2009 Hyde et al.  
 2009/0076350 A1 3/2009 Bly et al.  
 2009/0099624 A1 4/2009 Kokones et al.  
 2009/0099627 A1 4/2009 Molnar et al.  
 2009/0105785 A1 4/2009 Wei et al.  
 2009/0137921 A1 5/2009 Kramer  
 2009/0227882 A1 9/2009 Foo  
 2009/0227888 A1 9/2009 Salmi  
 2009/0322540 A1 12/2009 Richardson et al.  
 2010/0010382 A1 1/2010 Panken  
 2010/0010392 A1 1/2010 Skelton et al.  
 2010/0010583 A1 1/2010 Panken et al.  
 2010/0023348 A1 1/2010 Hardee et al.  
 2010/0056878 A1 3/2010 Partin et al.  
 2010/0106217 A1 4/2010 Colborn  
 2010/0109875 A1 5/2010 Ayon et al.  
 2010/0121214 A1 5/2010 Giftakis et al.  
 2010/0217533 A1 8/2010 Nadkarni et al.  
 2010/0223020 A1 9/2010 Goetz  
 2010/0228103 A1 9/2010 Schectter  
 2010/0228314 A1 9/2010 Goetz  
 2010/0268056 A1 10/2010 Picard et al.  
 2010/0280336 A1 11/2010 Giftakis et al.

2010/0280578 A1 11/2010 Skelton et al.  
 2010/0280579 A1 11/2010 Denison et al.  
 2010/0286567 A1 11/2010 Wolfe et al.  
 2010/0298661 A1 11/2010 McCombie et al.  
 2010/0298742 A1 11/2010 Perlman et al.  
 2010/0305665 A1 12/2010 Miesel et al.  
 2010/0312188 A1 12/2010 Robertson et al.  
 2011/0029044 A1 2/2011 Hyde et al.  
 2011/0040204 A1 2/2011 Ivorra et al.  
 2011/0040546 A1 2/2011 Gerber et al.  
 2011/0060252 A1 3/2011 Simonsen et al.  
 2011/0066062 A1 3/2011 Banet et al.  
 2011/0066081 A1 3/2011 Goto et al.  
 2011/0137372 A1 6/2011 Makous et al.  
 2011/0172545 A1 7/2011 Grudic et al.  
 2011/0230730 A1 9/2011 Quigg et al.  
 2011/0245629 A1 10/2011 Giftakis et al.  
 2011/0251469 A1 10/2011 Varadan  
 2011/0270117 A1 11/2011 Warwick et al.  
 2011/0270134 A1 11/2011 Skelton et al.  
 2011/0295127 A1 12/2011 Sandler et al.  
 2011/0306846 A1 12/2011 Osorio  
 2011/0313484 A1 12/2011 Hincapie Ordenez et al.

## FOREIGN PATENT DOCUMENTS

GB 2026870 2/1980  
 GB 2079610 1/1982  
 WO 00/64336 11/2000  
 WO 2004/036377 4/2004  
 WO 2005/007120 1/2005  
 WO 2005/053788 6/2005  
 WO 2005/067599 7/2005  
 WO 2006/050144 5/2006  
 WO 2006/122148 11/2006  
 WO 2006/134359 12/2006  
 WO 2007/066343 6/2007  
 WO 2007/072425 6/2007  
 WO 2007/124126 11/2007  
 WO 2007/124190 11/2007  
 WO 2007/124192 11/2007  
 WO 2007/142523 12/2007  
 WO 2008/045597 4/2008  
 WO 2011/126931 10/2011

## OTHER PUBLICATIONS

Baevskii, R.M. "Analysis of Heart Rate Variability in Space Medicine," Human Physiology, vol. 28, No. 2, (2002); pp. 202-213.  
 Baevsky, R.M., et al.; "Autonomic Cardiovascular and Respiratory Control During Prolonged Spaceflights Aboard the International Space Station," J. Applied Physiological, vol. 103, (2007) pp. 156-161.  
 Boon, P., et al.; "Vagus Nerve Stimulation for Epilepsy, Clinical Efficacy of Programmed and Magnet Stimulation;" (2001); pp. 93-98.  
 Boon, Paul, et al.; "Programmed and Magnet-Induced Vagus Nerve Stimulation for Refractory Epilepsy;" Journal of Clinical Neurophysiology vol. 18 No. 5; (2001); pp. 402-407.  
 Borovikova, L.V., et al.; "Vagus Nerve Stimulation Attenuates the Systemic Inflammatory Response to Endotoxin;" Letters to Nature; vol. 405; (May 2000); pp. 458-462.  
 Brack, Kieran E., et al.; "Interaction Between Direct Sympathetic and Vagus Nerve Stimulation on Heart Rate in the Isolated Rabbit Heart;" Experimental Physiology vol. 89, No. 1; pp. 128-139.  
 Chakravarthy, N., et al.; "Controlling Synchronization in a Neuron-Level Population Model;" International Journal of Neural Systems, vol. 17, No. 2 (2007) pp. 123-138.  
 Clark, K.B., et al.; "Posttraining Electrical Stimulation of Vagal Afferents with Concomitant Vagal Efferent Inactivation Enhances Memory Storage Processes in the Rat;" Neurobiology of Learning and Memory, vol. 70, 364-373 (1998) Art. No. NL983863.  
 Elmpt, W.J.C., et al.; "A Model of Heart Rate Changes to Detect Seizures in Severe Epilepsy" Seizure vol. 15, (2006) pp. 366-375.  
 Frei, M.G., et al.; "Left Vagus Nerve Stimulation with the Neurocybernetic Prosthesis Has Complex Effects on Heart Rate and on Its Variability in Humans ." Epilepsia, vol. 42, No. 8 (2001); pp. 1007-1016.

(56)

## References Cited

## OTHER PUBLICATIONS

- George, M.S., et al.; "Vagus Nerve Stimulation: A New Tool for Brain Research and Therapy;" Society of Biological Psychiatry vol. 47 (2000) pp. 287-295.
- "Heart Rate Variability—Standards of Measurement, Physiological Interpretation, and Clinical Use" Circulation—Electrophysiology vol. 93, No. 5; <http://circ.ahajournals.org/cgi/content-nw/full/93/5/1043/F3>.
- Henry, Thomas R.; "Therapeutic Mechanisms of Vague Name Stimulation;" Neurology, vol. 59 (Supp 4) (Sep. 2002), pp. S3-S14.
- Hallowitz et al., "Effects of Vagal Volleys on Units of Intralaminar and Juxtalaminar Thalamic Nuclei in Monkeys;" Brain Research, vol. 130 (1977), pp. 271-286.
- Iasemidis, L.D., et al.; "Dynamical Resetting of the Human Brain at Epileptic Seizures: Application of Nonlinear Dynamics and Global Optimization Techniques;" IEEE Transactions on Biomedical Engineering, vol. 51, No. 3 (Mar. 2004); pp. 493-506.
- Iasemidis, L.D., et al.; "Spatiotemporal Transition to Epileptic Seizures: A Nonlinear Dynamical Analysis of Scalp and Intracranial EEG Recordings;" Spatiotemporal Models in Biological and Artificial Systems; F.L. Silva et al. (Eds.) IOS Press, 1997; pp. 81-88.
- Iasemidis, L.D.; "Epileptic Seizure Prediction and Control" IEEE Transactions on Biomedical Engineering, vol. 50, No. 5 (May 2003); pp. 549-558.
- Kautzner, J., et al.; "Utility of Short-Term Heart Rate Variability for Prediction of Sudden Cardiac Death After Acute Myocardial Infarction" Acta Univ. Palacki. Olomuc., Fac. Med., vol. 141 (1998) pp. 69-73.
- Koenig, S.A., et al.; "Vagus Nerve Stimulation Improves Severely Impaired Heart Rate Variability in a Patient with Lennox-Gastaut Syndrome" Seizure (2007) Article in Press—YSEIZ-1305; pp. 1-4.
- Koo, B., "EEG Changes With Vagus Nerve Stimulation" Journal of Clinical Neurophysiology, vol. 18 No. 5 (Sep. 2001); pp. 434-441.
- Krittayaphong, M.D., et al.; "Heart Rate Variability in Patients with Coronary Artery Disease: Differences in Patients with Higher and Lower Depression Scores" Psychosomatic Medicine vol. 59 (1997) pp. 231-235.
- Leutmezer, F., et al.; "Electrocardiographic Changes at the Onset of Epileptic Seizures;" Epilepsia, vol. 44, No. 3; (2003); pp. 348-354.
- Lewis, M.E., et al.; "Vagus Nerve Stimulation Decreases Left Ventricular Contractility in Vivo in the Human and Pig Heart" The Journal of Physiology vol. 534, No. 2, (2001) pp. 547-552.
- Li, M., et al.; "Vagal Nerve Stimulation Markedly Improves Long-Term Survival After Chronic Heart Failure in Rats;" Circulation (Jan. 2004) pp. 120-124.
- Licht, C.M.M.; Association Between Major Depressive Disorder and Heart Rate Variability in the Netherlands Study of Depression and Anxiety (NESDA); Arch. Gen Psychiatry, vol. 65, No. 12 (Dec. 2008); pp. 1358-1367.
- Lockard et al., "Feasibility and Safety of Vagal Stimulation in Monkey Model;" Epilepsia, vol. 31 (Supp. 2) (1990), pp. S20-S26.
- McClintock, P., "Can Noise Actually Boost Brain Power" Physics World Jul. 2002; pp. 20-21.
- Mori, T., et al.; "Noise-Induced Entrainment and Stochastic Resonance in Human Brain Waves" Physical Review Letters vol. 88, No. 21 (2002); pp. 218101-1-218101-4.
- Mormann, F., "Seizure prediction: the long and winding road," Brain 130 (2007), 314-333.
- Nouri, M.D.; "Epilepsy and the Autonomic Nervous System" emedicine (updated May 5, 2006); pp. 1-14; <http://www.emedicine.com/neuro/topic658.htm>.
- O'Regan, M.E., et al.; "Abnormalities in Cardiac and Respiratory Function Observed During Seizures in Childhood" Developmental Medicine & Child Neurology, vol. 47 (2005) pp. 4-9.
- Pathwardhan, R.V., et al., Control of Refractory status epilepticus precipitated by anticonvulsant withdrawal using left vagal nerve stimulation: a case report, Surgical Neurology 64 (2005) 170-73.
- Poddubnaya, E.P., "Complex Estimation of Adaptation Abilities of the Organism in Children Using the Indices of Responsiveness of the Cardiovascular System and Characteristics of EEG" Neurophysiology vol. 38, No. 1 (2006); pp. 63-74.
- Rugg-Gunn, F.J., et al.; "Cardiac Arrhythmias in Focal Epilepsy: a Prospective Long-Term Study" www.thelancet.com vol. 364 (2004) pp. 2212-2219.
- Sajadieh, A., et al.; "Increased Heart Rate and Reduced Heart-Rate Variability are Associated with Subclinical Inflammation in Middle-Aged and Elderly Subjects with No Apparent Heart Disease" European Heart Journal vol. 25, (2004); pp. 363-370.
- Scherthaner, C., et al.; "Autonomic Epilepsy—The Influence of Epileptic Discharges on Heart Rate and Rhythm" The Middle European Journal of Medicine vol. 111, No. 10 (1999) pp. 392-401.
- Terry et al.; "The Implantable Neurocybernetic Prosthesis System", Pacing and Clinical Electrophysiology, vol. 14, No. 1 (Jan. 1991), pp. 86-93.
- Tubbs, R.S., et al.; "Left-Sided Vagus Nerve Stimulation Decreases Intracranial Pressure Without Resultant Bradycardia in the Pig: A Potential Therapeutic Modality for Humans" Child's Nervous System Original Paper; Springer-Verlag 2004.
- Umetani, M.D., et al.; "Twenty-Four Hour Time Domain Heart Rate Variability and Heart Rate: Relations to Age and Gender Over Nineteen Decades" JACC vol. 31, No. 3; (Mar. 1998); pp. 593-601.
- Vonck, K., et al. "The Mechanism of Action of Vagus Nerve Stimulation for Refractory Epilepsy—The Current Status", Journal of Neurophysiology, vol. 18 No. 5 (2001), pp. 394-401.
- Woodbury, et al., "Vagal Stimulation Reduces the Severity of Maximal Electroshock Seizures in Intact Rats. Use of a Cuff Electrode for Stimulating and Recording"; Pacing and Clinical Electrophysiology, vol. 14 (Jan. 1991), pp. 94-107.
- Zabara, J.; "Neuroinhibition of Xylazine Induced Emesis" Pharmacology & Toxicology, vol. 63 (1988) pp. 70-74.
- Zabara, J. "Inhibition of Experimental Seizures in Canines by Repetitive Vagal Stimulation" Epilepsia vol. 33, No. 6 (1992); pp. 1005-1012.
- Zabara, J., et al.; "Neural Control of Circulation I" The Physiologist, vol. 28 No. 4 (1985); 1 page.
- Zabara, J., et al.; "Neuroinhibition in the Regulation of Emesis" Space Life Sciences, vol. 3 (1972) pp. 282-292.
- Osorio, Ivan et al., "An Introduction to Contingent (Closed-Loop) Brain Electrical Stimulation for Seizure Blockage, to Ultra-Short-Term Clinical Trials, and to Multidimensional Statistical Analysis of Therapeutic Efficacy;" Journal of Clinical Neurophysiology, vol. 18, No. 6, pp. 533-544, 2001.
- Osorio, Ivan et al., "Automated Seizure Abatement in Humans Using Electrical Stimulation," Annals of Neurology, vol. 57, No. 2, pp. 258-268, 2005.
- Sunderam, Sridhar et al., "Vagal and Sciatic Nerve Stimulation Have Complex, Time-Dependent Effects on Chemically-Induced Seizures: A Controlled Study," Brain Research, vol. 918, pp. 60-66, 2001.
- Weil, Sabine et al., "Heart Rate Increase in Otherwise Subclinical Seizures Is Different in Temporal Versus Extratemporal Seizure Onset: Support for Temporal Lobe Automatic Influence," Epileptic Disord., vol. 7, No. 3, Sep. 2005, pp. 199-2043.
- Digenarro, Giancarlo et al., "Ictal Heart Rate Increase Precedes EEG Discharge in Drug-Resistant Mesial Temporal Lobe Seizures," Clinical Neurophysiology, No. 115, 2004, pp. 1169-1177.
- Zijlmans, Maeike et al., "Heart Rate Changes and ECG Abnormalities During Epileptic Seizures: Prevalence and Definition of an Objective Clinical Sign," Epilepsia, vol. 43, No. 8, 2002, pp. 847-854.
- O'Donovan, Cormac A. et al., "Computerized Seizure Detection Based on Heart Rate Changes," abstract of AES Proceedings, Epilepsia, vol. 36, Suppl. 4, 1995, p. 7.
- Robinson, Stephen E et al., "Heart Rate Variability Changes as Predictor of Response to Vagal Nerve Stimulation Therapy for Epilepsy;" abstract of AES Proceedings, Epilepsia, vol. 40, Suppl. 7, 1999, p. 147.
- Long, Teresa J. et al., "Effectiveness of Heart Rate Seizure Detection Compared to EEG in an Epilepsy Monitoring Unit (EMU)," abstract of AES Proceedings, Epilepsia, vol. 40, Suppl. 7, 1999, p. 174. PCT Search Report and Written Opinion for International Application No. PCT/US2011/054287, dated Mar. 12, 2012, 18 pages.

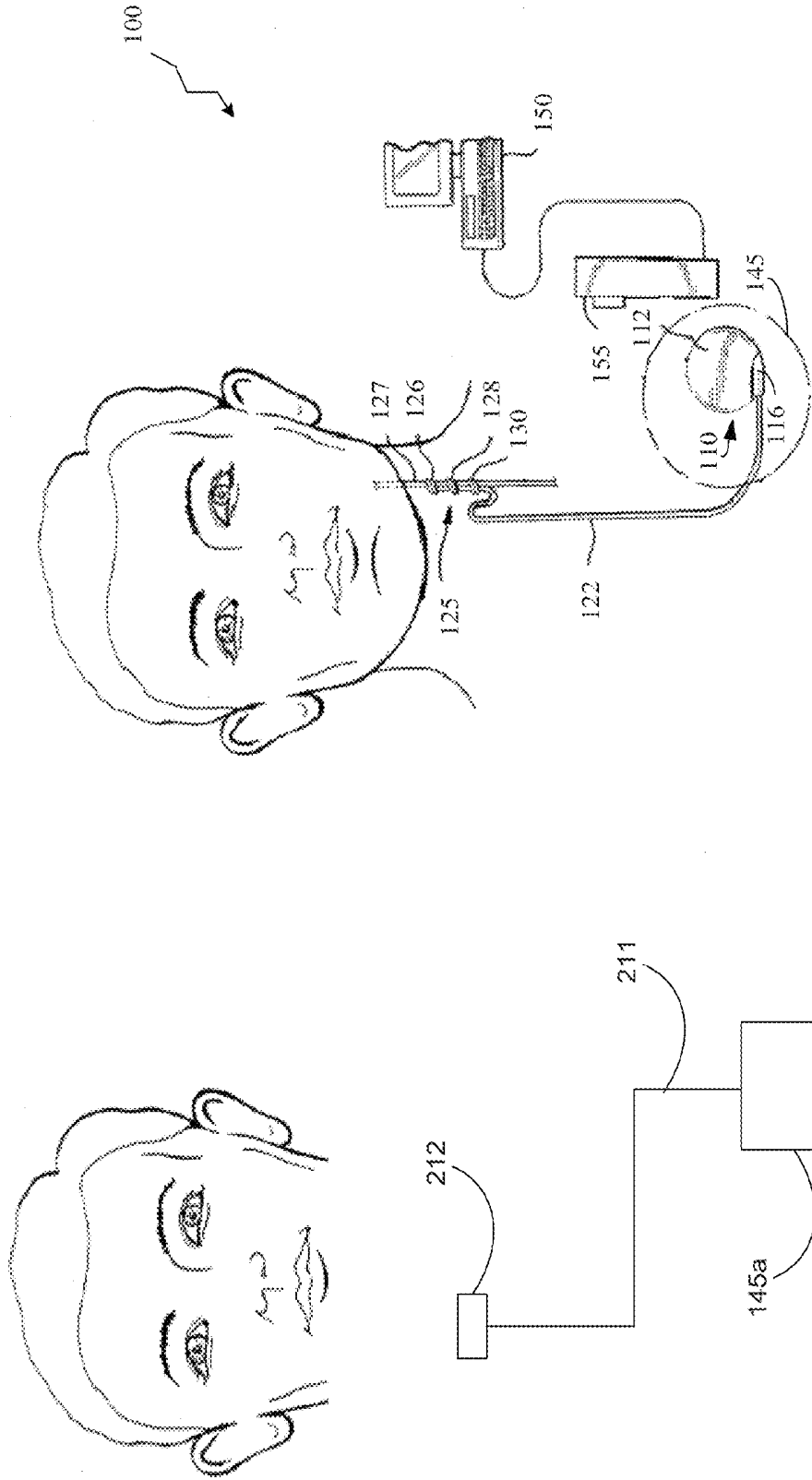


FIG. 1B

FIG. 1A

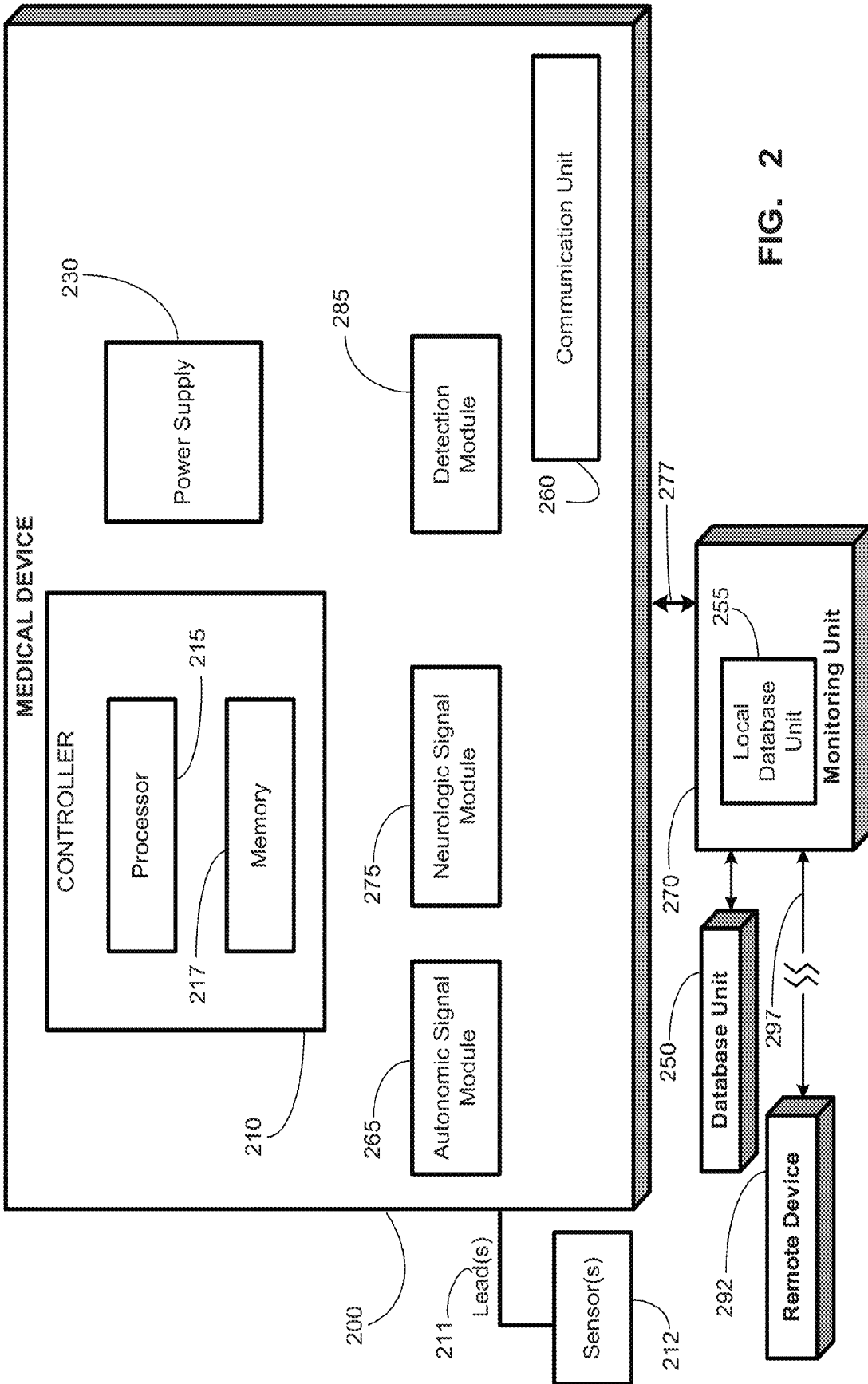


FIG. 2

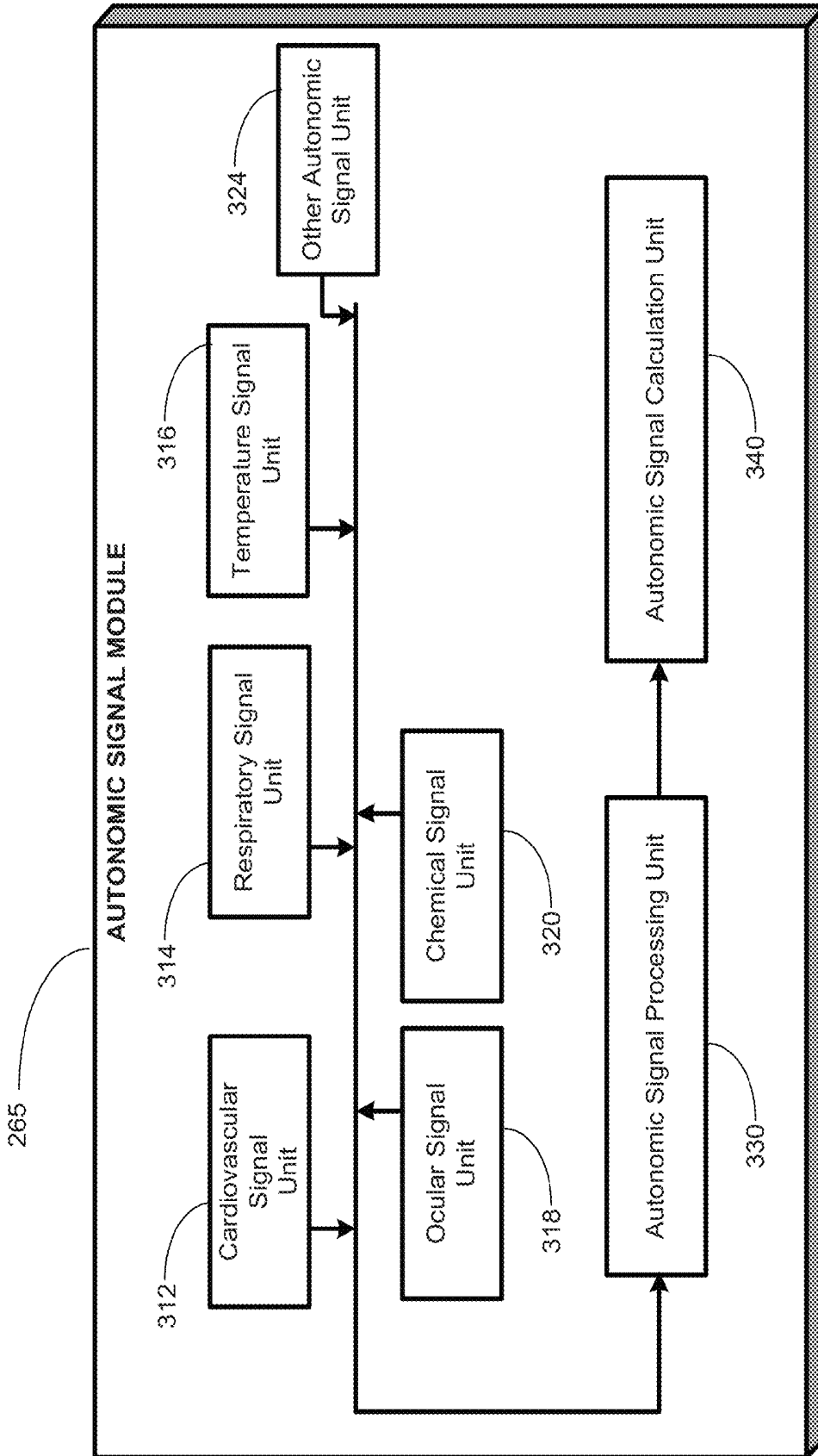


FIG. 3A

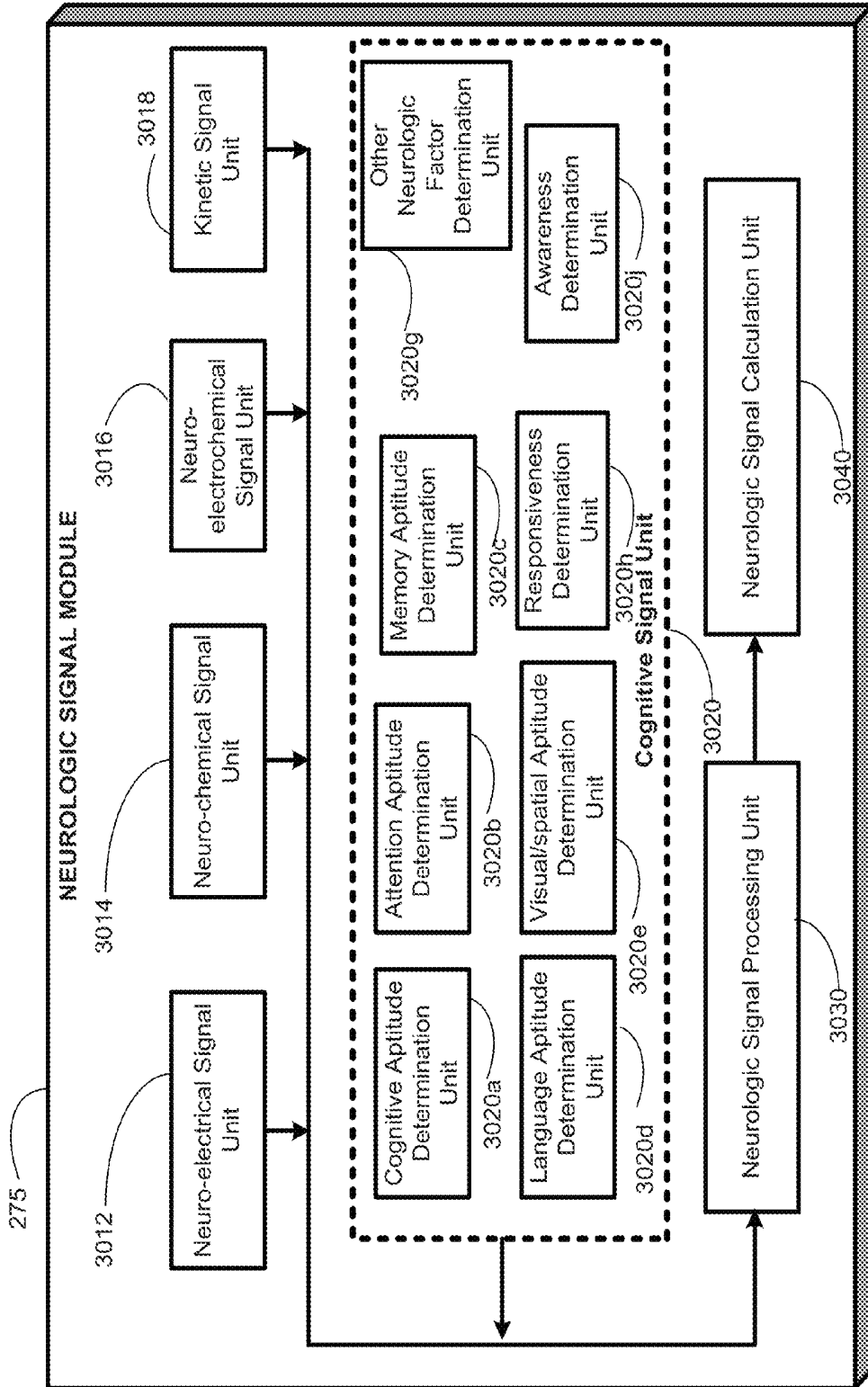


FIG. 3B

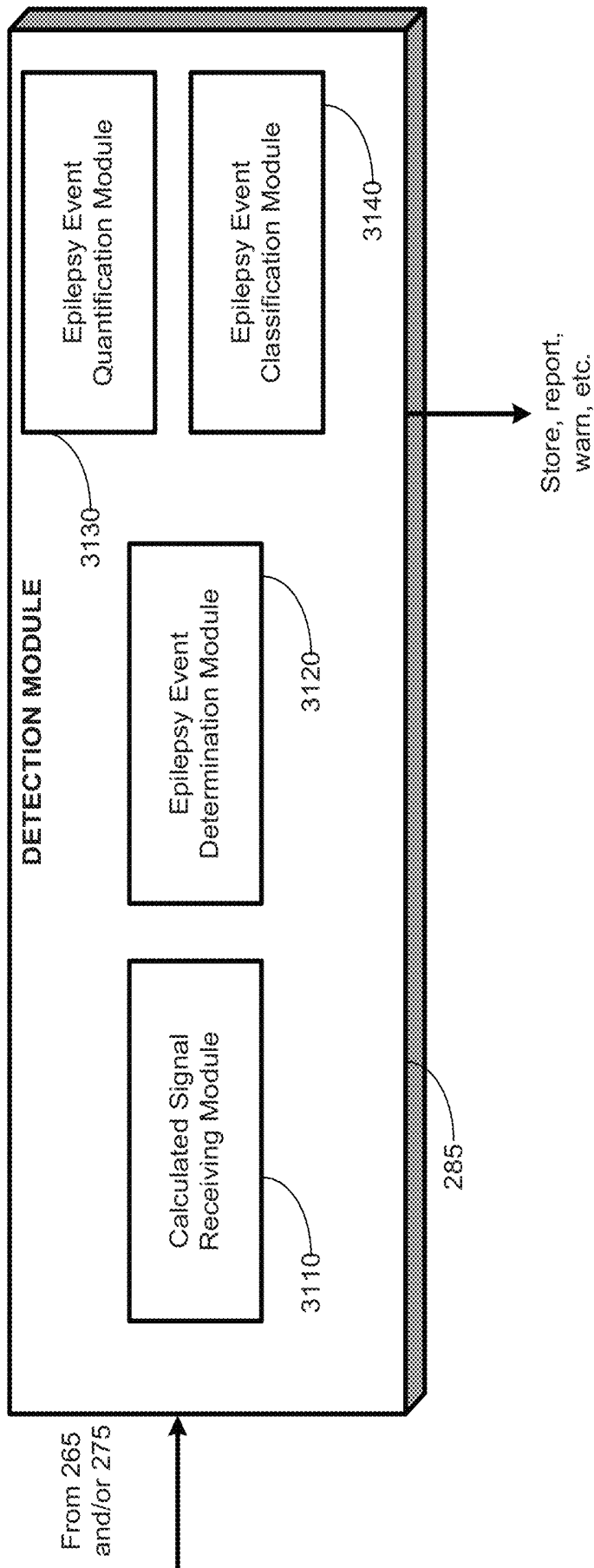
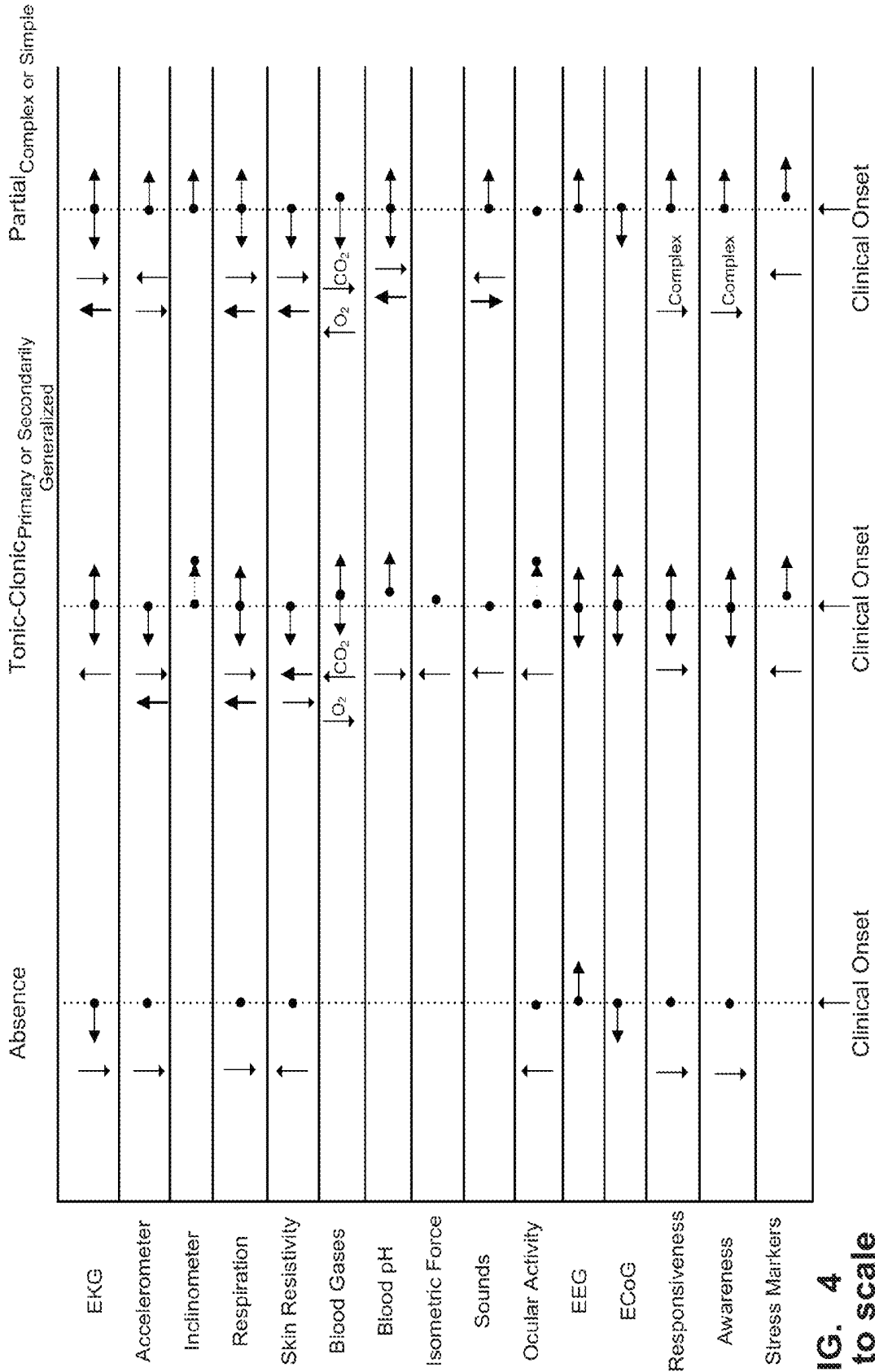
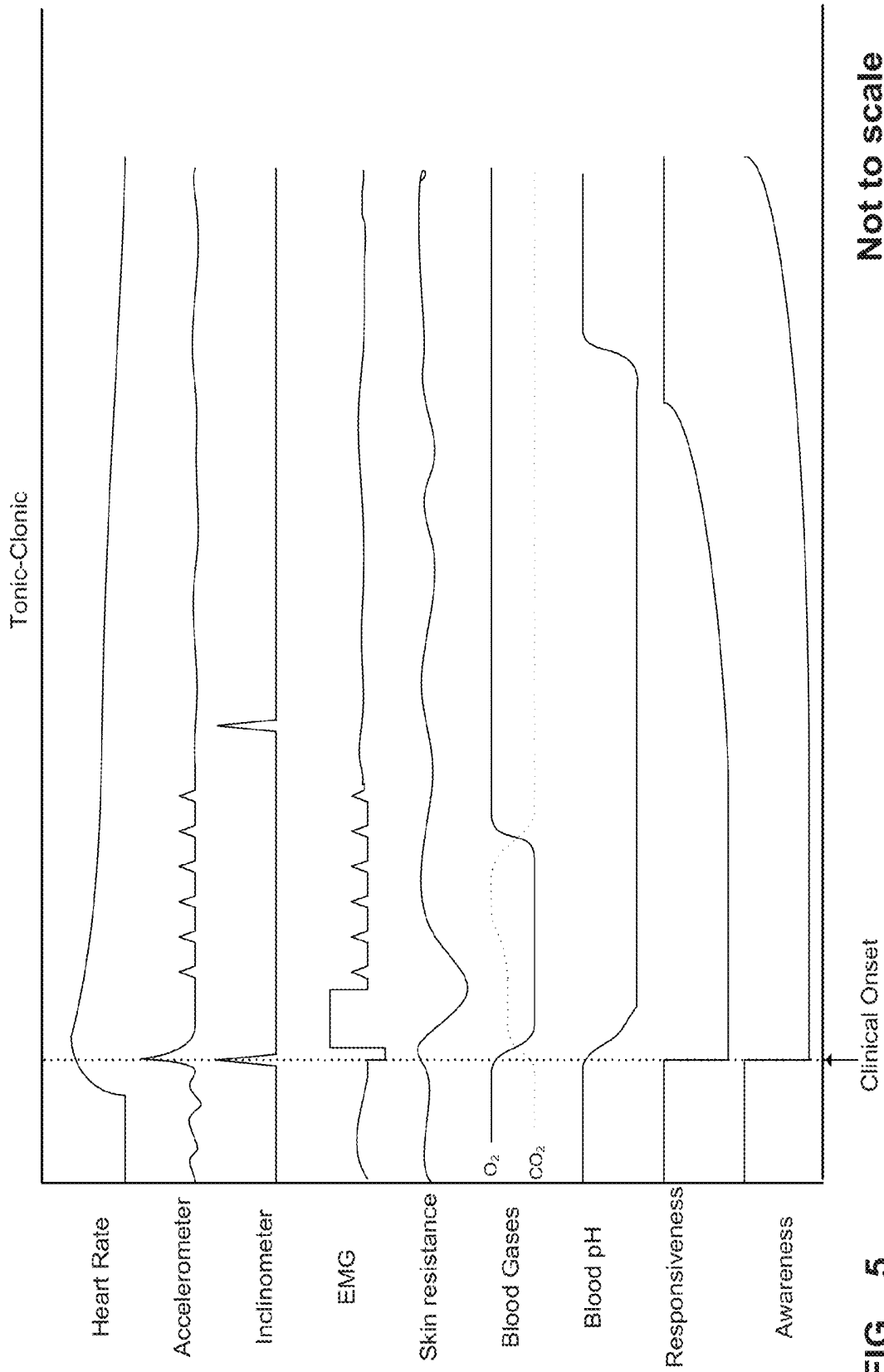


FIG. 3C

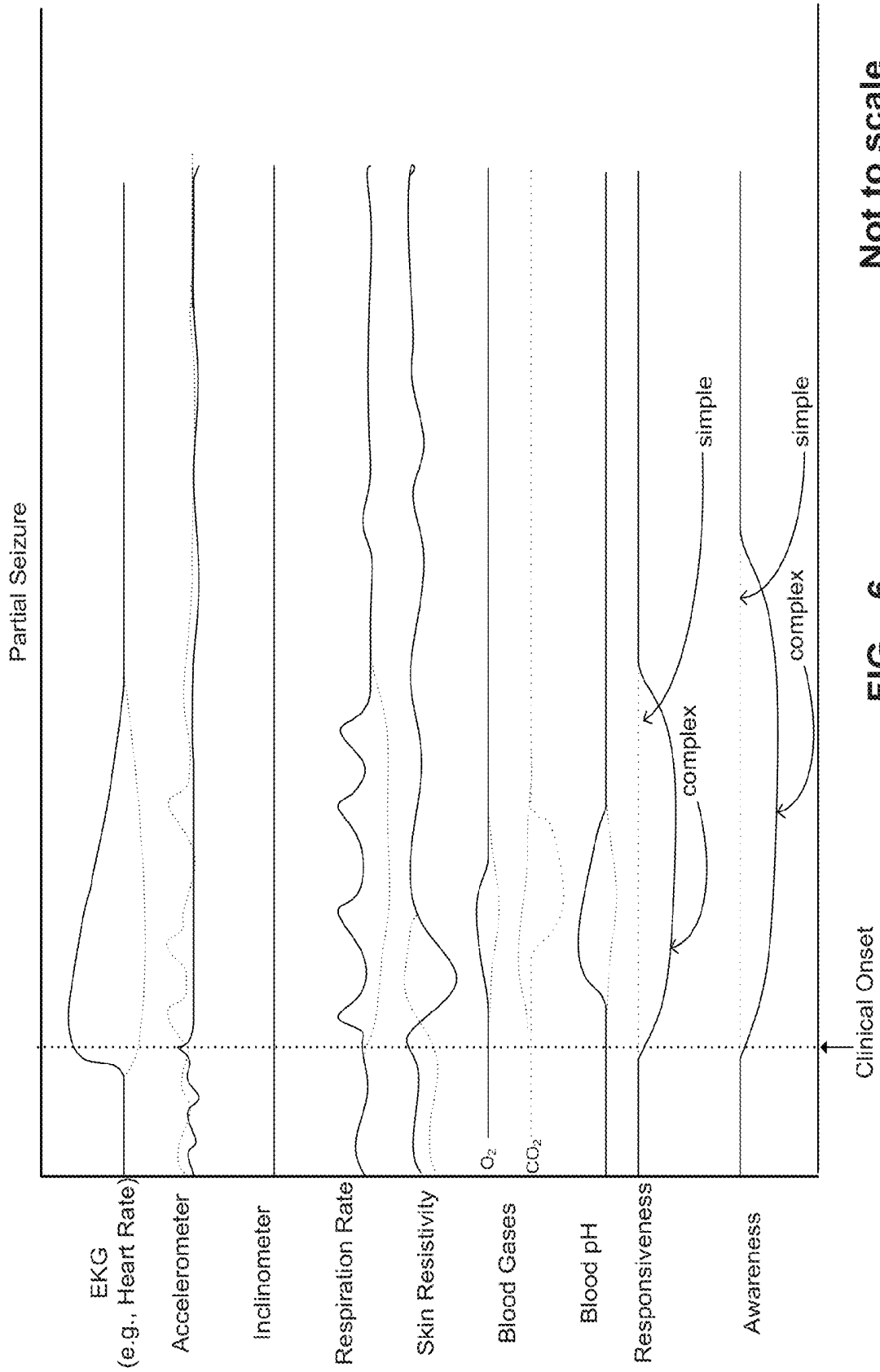


**FIG. 4**  
Not to scale



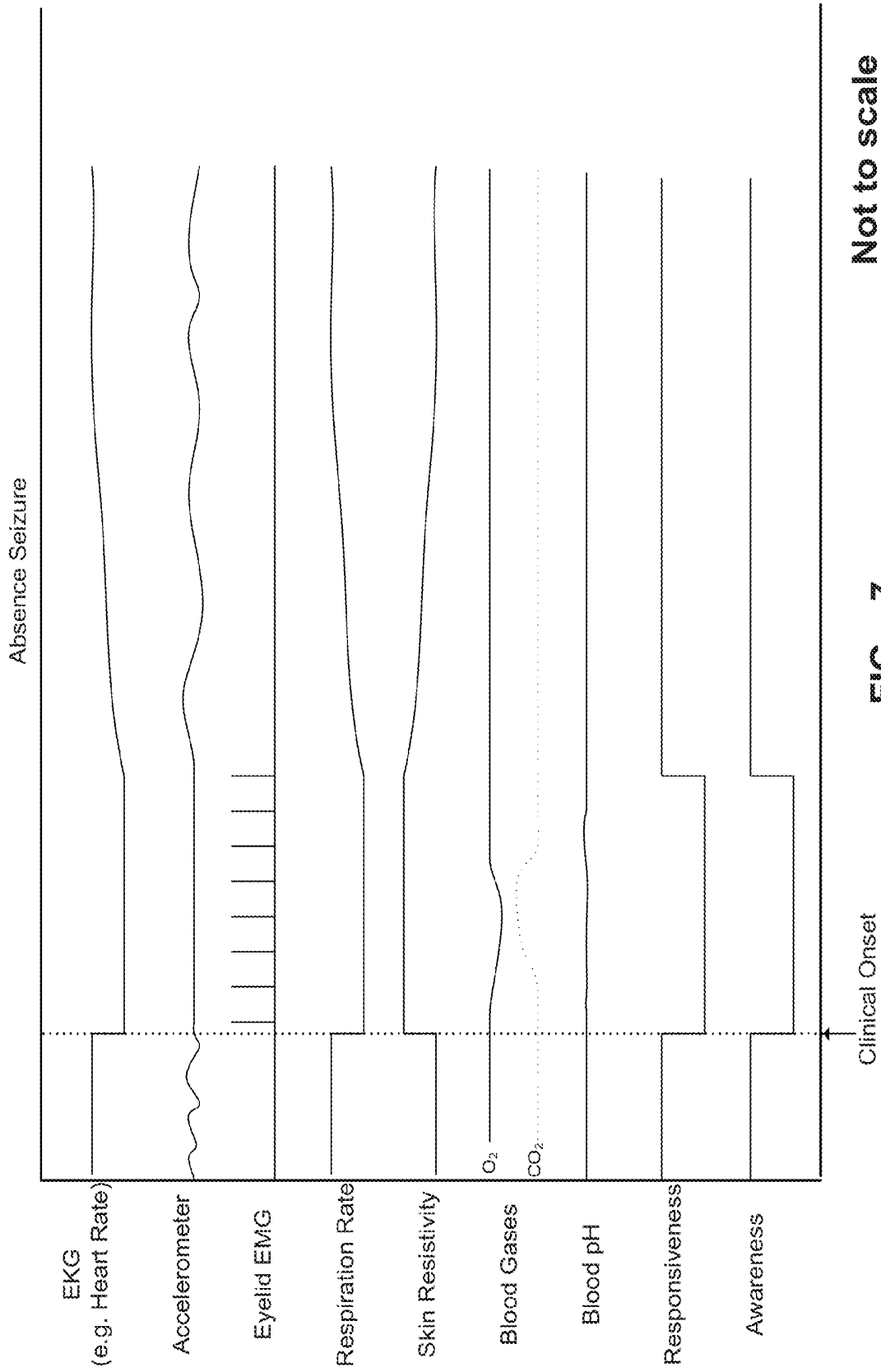
Not to scale

FIG. 5



Not to scale

FIG. 6



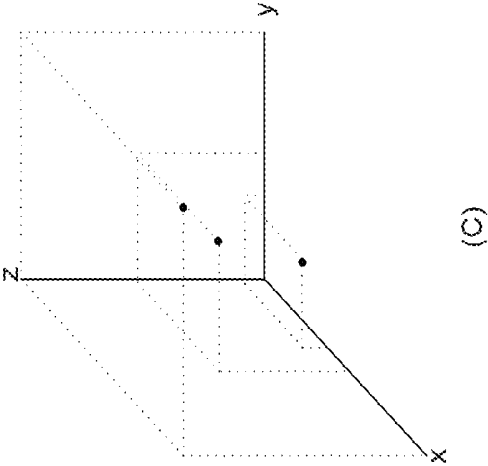
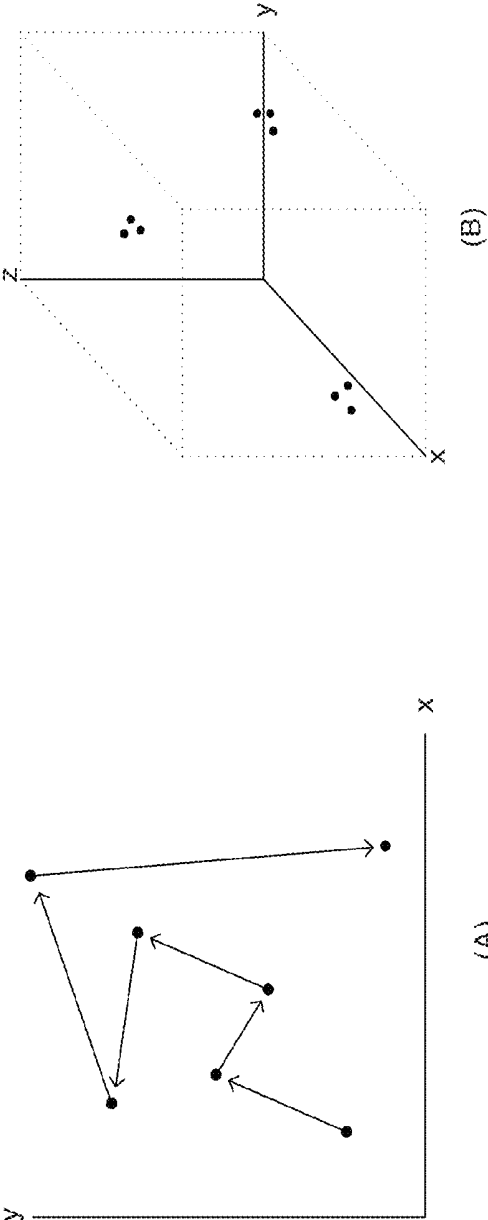


FIG. 8

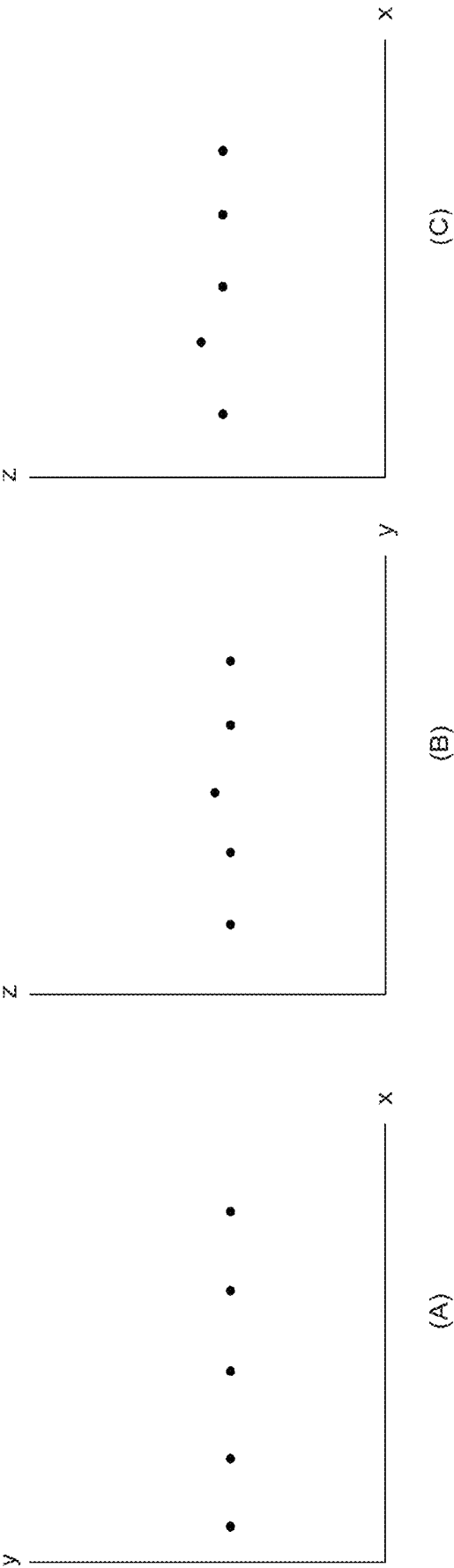


FIG. 9

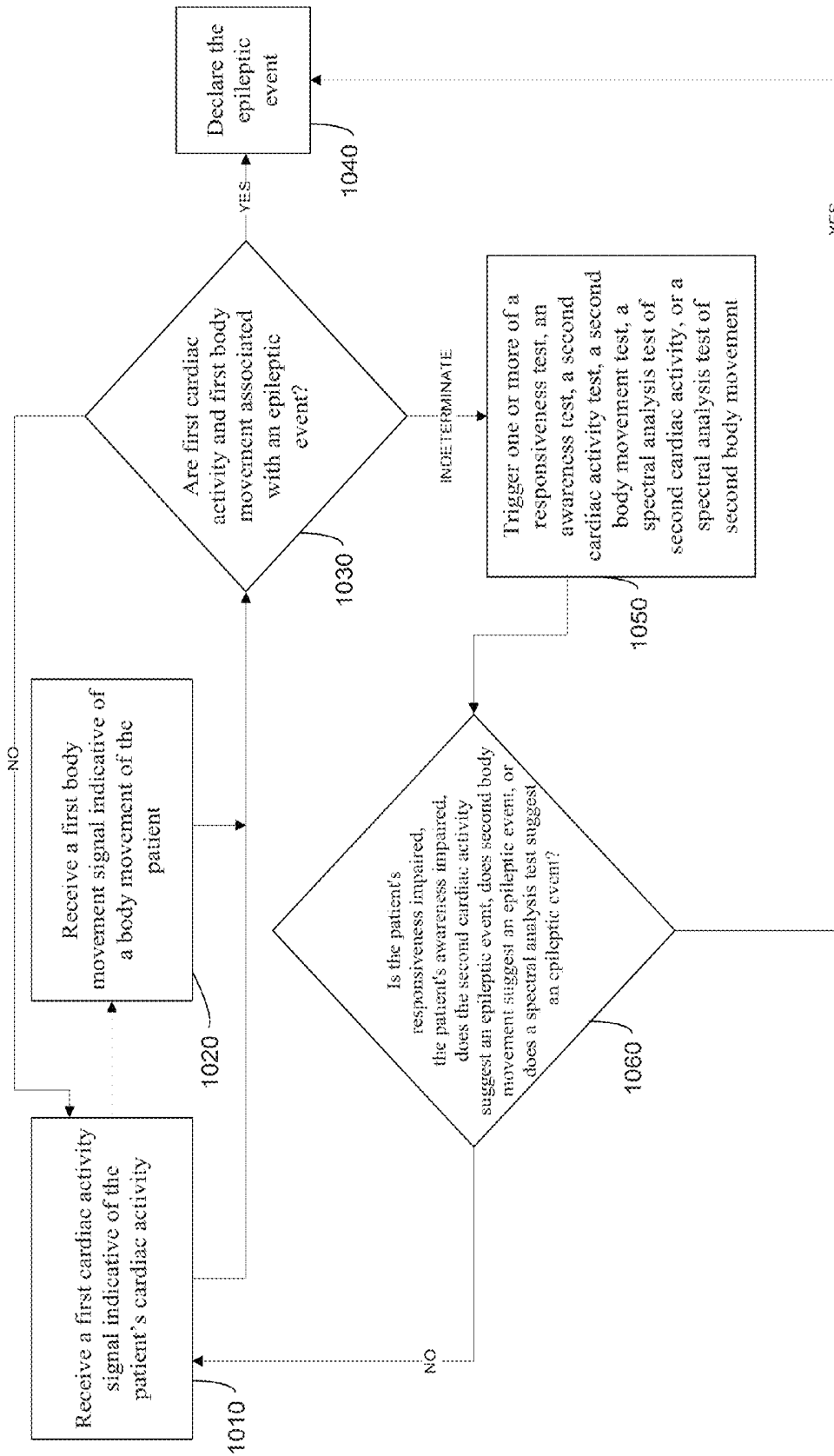


FIG. 10

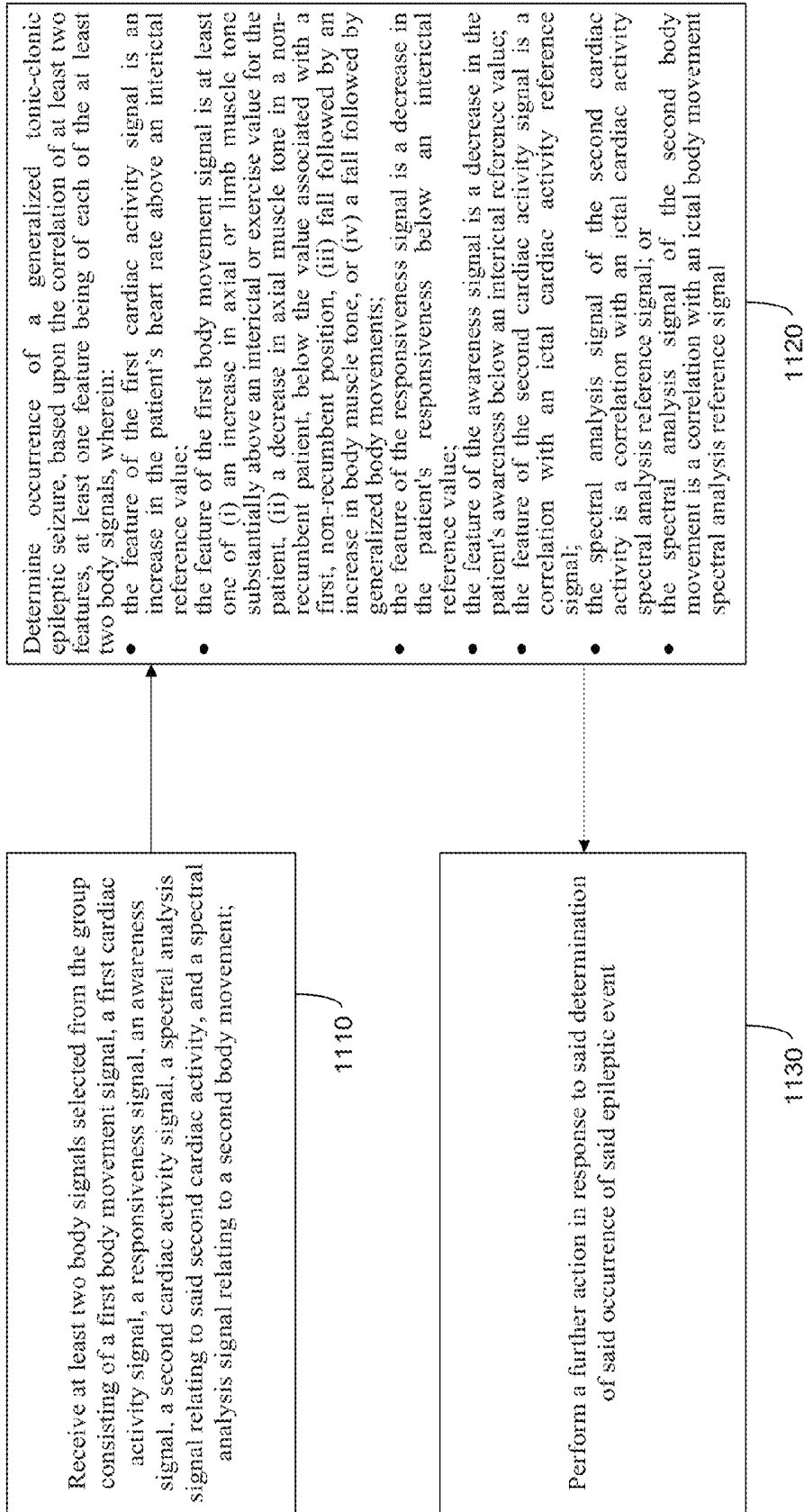


FIG. 11

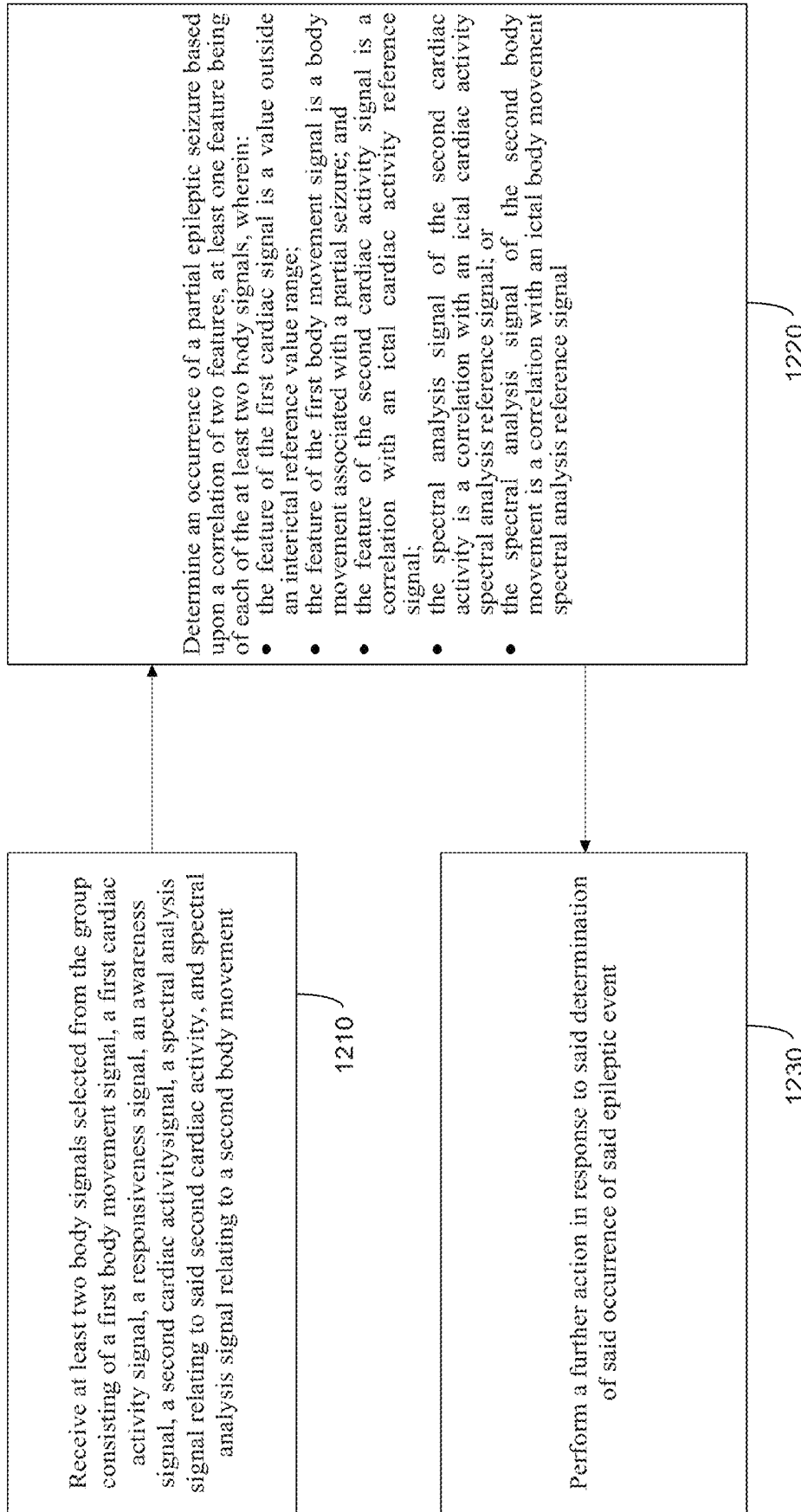


FIG. 12

# DETECTING, QUANTIFYING, AND/OR CLASSIFYING SEIZURES USING MULTIMODAL DATA

## BACKGROUND OF THE INVENTION

This application is a continuation application of U.S. patent application Ser. No. 13/098,262, filed Apr. 29, 2011 and issued as U.S. Pat. No. 8,382,667 on Feb. 26, 2013. U.S. patent application Ser. No. 13/098,262 is hereby incorporated herein by reference in its entirety.

## FIELD OF THE INVENTION

This invention relates to medical device systems and methods capable of detecting and, in some embodiments, treating an occurring or impending seizure using multimodal body data.

## INCORPORATION BY REFERENCE

The following United States patents or patent applications are incorporated by reference:

U.S. patent application Ser. No. 12/756,065, filed Apr. 7, 2010.

U.S. patent application Ser. No. 12/770,562, filed Apr. 29, 2010.

U.S. patent application Ser. No. 12/884,051, filed Sep. 16, 2010.

U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

U.S. patent application Ser. No. 13/040,996, filed Mar. 4, 2011.

## DESCRIPTION OF THE RELATED ART

Of the approximately 60 million people worldwide affected with epilepsy, roughly 23 million people suffer from epilepsy resistant to multiple medications. In the USA alone, the annual cost of epilepsy care is USD 12 billion (in 1995 dollars), most of which is attributable to subjects with pharmaco-resistant seizures. Pharmaco-resistant seizures are associated with an increase mortality and morbidity (e.g., compared to the general population and to epileptics whose seizures are controlled by medications) and with markedly degraded quality of life for patients. Seizures may impair motor control, responsiveness to a wide class of stimuli, and other cognitive functions. The sudden onset of a patient's impairment of motor control, responsiveness, and other cognitive functions precludes the performance of necessary and even simple daily life tasks such as driving a vehicle, cooking, or operating machinery, as well as more complex tasks such as acquiring knowledge and socializing.

Therapies using electrical currents or fields to provide a therapy to a patient (electrotherapy) are beneficial for certain neurological disorders, such as epilepsy. Implantable medical devices have been effectively used to deliver therapeutic electrical stimulation to various portions of the human body (e.g., the vagus nerve) for treating epilepsy. As used herein, "stimulation," "neurostimulation," "stimulation signal," "therapeutic signal," or "neurostimulation signal" refers to the direct or indirect application of an electrical, mechanical, magnetic, electro-magnetic, photonic, acoustic, cognitive, and/or chemical signal to an organ or a neural structure in the patient's body. The signal is an exogenous signal that is distinct from the endogenous electro-chemical activity inherent to the patient's body and also from that found in the

environment. In other words, the stimulation signal (whether electrical, mechanical, magnetic, electro-magnetic, photonic, acoustic, cognitive, and/or chemical in nature) applied to a cranial nerve or to other nervous tissue structure in the present invention is a signal applied from a medical device, e.g., a neurostimulator.

A "therapeutic signal" refers to a stimulation signal delivered to a patient's body with the intent of treating a medical condition through a suppressing (e.g., blocking) or modulating effect to neural tissue. The effect of a stimulation signal on neuronal activity may be suppressing or modulating; however, for simplicity, the terms "stimulating", suppressing, and modulating, and variants thereof, are sometimes used interchangeably herein. In general, however, the delivery of an exogenous signal itself refers to "stimulation" of an organ or a neural structure, while the effects of that signal, if any, on the electrical activity of the neural structure are properly referred to as suppression or modulation.

Depending upon myriad factors such as the history (recent and distant) of a patient's brain activity (e.g., electro-chemical, mental, emotional), stimulation parameters and time of day, to name a few, the effects of stimulation upon the neural tissue may be excitatory or inhibitory, facilitatory or disfacilitatory and may suppress, enhance, or leave unaltered neuronal activity. For example, the suppressing effect of a stimulation signal on neural tissue would manifest as the blockage of abnormal activity (e.g., epileptic seizures) see Osorio et al., *Ann Neurol* 2005; Osorio & Frei *IJNS* 2009) The mechanisms thorough which this suppressing effect takes place are described in the foregoing articles. Suppression of abnormal neural activity is generally a threshold or suprathreshold process and the temporal scale over which it occurs is usually in the order of tens or hundreds of milliseconds. Modulation of abnormal or undesirable neural activity is typically a "sub-threshold" process in the spatio-temporal domain that may summate and result under certain conditions, in threshold or suprathreshold neural events. The temporal scale of modulation is usually longer than that of suppression, encompassing seconds to hours, even months. In addition to inhibition or dysfacilitation, modification of neural activity (e.g., wave annihilation) may be exerted through collision with identical, similar or dissimilar waves, a concept borrowed from wave mechanics, or through phase resetting (Winfree).

In some cases, electrotherapy may be provided by implanting an electrical device, e.g., an implantable medical device (IMD), inside a patient's body for stimulation of a nervous tissue, such as a cranial nerve. Generally, electrotherapy signals that suppress or modulate neural activity are delivered by the IMD via one or more leads. When applicable, the leads generally terminate at their distal ends in one or more electrodes, and the electrodes, in turn, are coupled to a target tissue in the patient's body. For example, a number of electrodes may be attached to various points of a nerve or other tissue inside a human body for delivery of a neurostimulation signal.

While contingent (also referred to as "closed-loop," "active," or "feedback" stimulation; i.e., electrotherapy applied in response to sensed information, such as heart rate) stimulation schemes have been proposed, non-contingent, programmed periodic stimulation is the prevailing modality. For example, vagus nerve stimulation for the treatment of epilepsy usually involves a series of grouped electrical pulses defined by an "on-time" (such as 30 sec.) and an "off-time" (such as 5 min.). This type of stimulation is also referred to as "open-loop," "passive," or "non-feedback" stimulation. Each sequence of pulses during an on-time may be referred to as a "pulse burst." The burst is followed by the off-time period in

which no signals are applied to the nerve. During the on-time, electrical pulses of a defined electrical current (e.g., 0.5-3.5 milliamps) and pulse width (e.g., 0.25-1.0 milliseconds) are delivered at a defined frequency (e.g., 20-30 Hz) for a certain duration (e.g., 10-60 seconds). The on-time and off-time parameters together define a duty cycle, which is the ratio of the on-time to the sum of the on-time and off-time, and which describes the fraction of time that the electrical signal is applied to the nerve.

In VNS, the on-time and off-time may be programmed to define an intermittent pattern in which a repeating series of electrical pulse bursts are generated and applied to a cranial nerve such as the vagus nerve. The off-time is provided to minimize adverse effects and conserve power. If the off-time is set at zero, the electrical signal in conventional VNS may provide continuous stimulation to the vagus nerve. Alternatively, the off time may be as long as one day or more, in which case the pulse bursts are provided only once per day or at even longer intervals. Typically, however, the ratio of "off-time" to "on-time" may range from about 0.5 to about 10.

In addition to the on-time and off-time, the other parameters defining the electrical signal in VNS may be programmed over a range of values. The pulse width for the pulses in a pulse burst of conventional VNS may be set to a value not greater than about 1 msec, such as about 250-500  $\mu$ sec, and the number of pulses in a pulse burst is typically set by programming a frequency in a range of about 20-300 Hz (i.e., 20 pulses per second to 300 pulses per second). A non-uniform frequency may also be used. Frequency may be altered during a pulse burst by either a frequency sweep from a low frequency to a high frequency, or vice versa. Alternatively, the timing between adjacent individual signals within a burst may be randomly changed such that two adjacent signals may be generated at any frequency within a range of frequencies.

Although neurostimulation has proven effective in the treatment of a number of medical conditions, it would be desirable to further enhance and optimize neurostimulation-based therapy for this purpose. For example, it may be desirable to detect an occurring or impending seizure. Such detection may be useful in triggering a therapy, monitoring the course of a patient's disease, or the progress of his or her treatment thereof. Alternatively or in addition, such detection may be useful in issuing a warning of an impending or ongoing seizure. Such a warning may, for example, minimize the risk of injury or death. Said warning may be perceived by the patient, a physician, a caregiver, or a suitably programmed computer and allow that person or computer program to take action intended to reduce the likelihood, duration, or severity of the seizure or impending seizure, or to facilitate further medical treatment or intervention for the patient. In particular, detection of an occurring or impending seizure enables the use of contingent neurostimulation. The state of the art does not provide an efficient and effective means for performing such detection and/or warning. Conventional VNS stimulation as described above does not detect occurring or impending seizures.

Closed-loop neurostimulation therapies for treating epilepsy have been proposed in which stimulation is triggered based upon factors including EEG activity (see, e.g., U.S. Pat. Nos. 5,995,868 and 7,280,867) as well as cardiac-based activity (see, e.g., U.S. Pat. Nos. 6,961,618 and 5,928,272). EEG- or ECoG-based approaches involving recording of neural electrical activity at any spatio-temporal scale involve determination of one or more parameters from brain electrical activity that indicate a seizure. Such approaches have met with limited success and have a number of drawbacks, includ-

ing highly invasive and technically demanding and costly surgery for implanted systems. Approaches that do not invade the brain have marked limitations due mainly to the extremely low/unreliable S/N, and poor patient compliance with, e.g., the patient wearing electrodes on the scalp for extended periods.

#### SUMMARY OF THE INVENTION

In one embodiment, the present invention provides a method. In one embodiment, the method comprises receiving at least one of signal relating to a first cardiac activity from a patient and a signal relating to a first body movement from the patient; deriving at least one patient index from said at least one received signal; triggering at least one of a test of the patient's responsiveness, a test of the patient's awareness, a test of a second cardiac activity of the patient, a test of a second body movement of the patient, a spectral analysis test of a second cardiac activity of the patient, and a spectral analysis test of the second body movement of the patient, based on said at least one patient index; determining an occurrence of an epileptic event based at least in part on the one or more triggered tests; and performing a further action in response to the determination of the occurrence of the epileptic event.

In one embodiment, the present invention provides a method. In one embodiment, the method comprises receiving at least two body signals selected from the group consisting of a signal relating to a first body movement, a signal relating to a first cardiac activity, a responsiveness signal, an awareness signal, a signal relating to a second cardiac activity, a signal relating to a second body movement, a spectral analysis signal relating to the second cardiac activity, and a spectral analysis signal relating to the second body movement; determining an occurrence of a generalized tonic-clonic epileptic seizure, the determination being based upon the correlation of at least two features, at least one feature being of each of the at least two body signals, wherein: the feature of the first cardiac activity signal is an increase in the patient's heart rate above an interictal reference value; the feature of the first body movement signal is at least one of (i) an increase in axial or limb muscle tone substantially above an interictal or exercise value for the patient, (ii) a decrease in axial muscle tone in a non-recumbent patient, below the value associated with a first, non-recumbent position, (iii) fall followed by an increase in body muscle tone, or (iv) a fall followed by generalized body movements; the feature of the responsiveness signal is a decrease in the patient's responsiveness below an interictal reference value; the feature of the awareness signal is a decrease in the patient's awareness below an interictal reference value; the feature of the second cardiac activity signal is a correlation with an ictal cardiac activity reference signal; the feature of the second body movement signal is a correlation with an ictal body movement reference signal; the feature of the spectral analysis signal of the second cardiac activity is a correlation with an ictal cardiac activity spectral analysis reference signal; or the feature of the spectral analysis signal of the second body movement is a correlation with an ictal body movement spectral analysis reference signal; and performing a further action in response to the determination of the occurrence of the epileptic event.

In one embodiment, the present invention provides a method. In one embodiment, the method comprises receiving at least two body signals selected from the group consisting of a signal relating to a first body movement, a signal relating to a first cardiac activity, a responsiveness signal, an awareness signal, a signal relating to a second cardiac activity, a signal

relating to a second body movement, a spectral analysis signal relating to the second cardiac activity, and spectral analysis signal relating to the second body movement; and determining an occurrence of a partial epileptic seizure based upon a correlation of two features, at least one feature being of each of the at least two body signals, wherein: the feature of the first cardiac signal is a value outside an interictal reference value range; the feature of the first body movement signal is a body movement associated with a partial seizure; the feature of the second cardiac activity signal is a correlation with an ictal cardiac activity reference signal; the feature of the second body movement signal is a correlation with an ictal body movement reference signal; the feature of the spectral analysis signal of the second cardiac activity is a correlation with an ictal cardiac activity spectral analysis reference signal; or the feature of the spectral analysis signal of the second body movement is a correlation with an ictal body movement spectral analysis reference signal; and performing a further action in response to the determination of the occurrence of the epileptic event.

In other embodiments, a computer readable program storage device is provided that is encoded with instructions that, when executed by a computer, perform a method described above.

In one embodiment, a medical device is provided comprising an autonomic signal module, a kinetic signal module, a detection module, and a processor adapted to perform a method as described above.

#### BRIEF DESCRIPTION OF THE DRAWINGS

The invention may be understood by reference to the following description taken in conjunction with the accompanying drawings, in which like reference numerals identify like elements, and in which:

FIG. 1A shows a stylized diagram of an external Medical device in communication with a sensor, in accordance with one illustrative embodiment of the present invention;

FIG. 1B shows a stylized diagram of an implanted medical device providing a therapeutic signal to a structure of the patient's body, in accordance with one illustrative embodiment of the present invention;

FIG. 2 provides a block diagram of a medical device system that includes a medical device and an external unit, in accordance with one illustrative embodiment of the present invention;

FIG. 3A provides a block diagram of a cardiac signal module of a medical device, in accordance with one illustrative embodiment of the present invention;

FIG. 3B provides a block diagram of a kinetic signal module of a medical device, in accordance with one illustrative embodiment of the present invention;

FIG. 3C provides a block diagram of a detection module of a medical device, in accordance with one illustrative embodiment of the present invention;

FIG. 4 shows the time of appearance (relative to clinical onset, dashed vertical line) and direction of deviations from reference activity of a plurality of body signals for four seizure types, specifically, absence seizures, tonic-clonic seizures, and simple or complex partial seizures;

FIG. 5 shows time courses (relative to clinical onset, dashed vertical line) of activity of a plurality of body signals for tonic-clonic seizures;

FIG. 6 shows time courses (relative to clinical onset, dashed vertical line) of activity of a plurality of body signals for partial (simple or complex) seizures;

FIG. 7 shows time courses (relative to clinical onset, dashed vertical line) of activity of a plurality of body signals for idiopathic absence seizures;

FIG. 8 shows (A) an exemplary two-dimensional plot of a trajectory of epileptic movements, (B) an exemplary three-dimensional plot of epileptic movements, and (C) an additional exemplary three-dimensional plot of epileptic movements;

FIG. 9 shows three two-dimensional, temporally cumulative plots of discrete movements during the clonic phase of a primarily or secondarily generalized tonic-clonic seizure;

FIG. 10 shows a flowchart of an implementation of a method according to one embodiment of the present invention;

FIG. 11 shows a flowchart of an implementation of a method according to one embodiment of the present invention; and

FIG. 12 shows a flowchart of an implementation of a method according to one embodiment of the present invention.

While the invention is susceptible to various modifications and alternative forms, specific embodiments thereof have been shown by way of example in the drawings and are herein described in detail. It should be understood, however, that the description herein of specific embodiments is not intended to limit the invention to the particular forms disclosed, but on the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

#### DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

Illustrative embodiments of the invention are described herein. In the interest of clarity, not all features of an actual implementation are described in this specification. In the development of any such actual embodiment, numerous implementation-specific decisions must be made to achieve the design-specific goals, which will vary from one implementation to another. It will be appreciated that such a development effort, while possibly complex and time-consuming, would nevertheless be a routine undertaking for persons of ordinary skill in the art having the benefit of this disclosure.

This document does not intend to distinguish between components that differ in name but not function. In the following discussion and in the claims, the terms "including" and "includes" are used in an open-ended fashion, and thus should be interpreted to mean "including, but not limited to." Also, the term "couple" or "couples" is intended to mean either a direct or an indirect electrical connection. "Direct contact," "direct attachment," or providing a "direct coupling" indicates that a surface of a first element contacts the surface of a second element with no substantial attenuating medium there between. The presence of small quantities of substances, such as bodily fluids, that do not substantially attenuate electrical connections does not vitiate direct contact. The word "or" is used in the inclusive sense (i.e., "and/or") unless a specific use to the contrary is explicitly stated.

The term "electrode" or "electrodes" described herein may refer to one or more stimulation electrodes (i.e., electrodes for delivering a therapeutic signal generated by an IMD to a tissue), sensing electrodes (i.e., electrodes for sensing a physiological indication of a state of a patient's body), and/or electrodes that are capable of delivering a therapeutic signal, as well as performing a sensing function.

Identification of changes in brain state are generally described in U.S. patent application Ser. No. 12/896,525,

filed Oct. 1, 2010, incorporated herein by reference. As stated therein, implanted sensors or electrodes beneath the scalp but above the outer skull table or intra-cranial (epidural, subdural or depth) have been used to overcome the limitations of scalp recordings. However, the quality of data is limited; there are risks (e.g., infection, bleeding, brain damage) associated with these devices; and in addition, at this time, there are at most about 300 neurosurgeons capable of implanting intracranial electrodes, far too few to perform such implantation for the roughly 900,000 pharmaco-resistant epileptics in the United States.

The basis for our work in using multimodal signals for detection of state changes in the brain is as generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. Various multimodal signals that may be used in the invention are set forth in the following table:

TABLE 1

Multimodal Signals
Autonomic
<p>Cardiac: EKG, PKG, Echocardiography, Apexcardiography (ApKG), Intra-cardiac pressure, Cardiac blood flow, cardiac thermography; from which can be derived, e.g., heart rate (HR), change of HR, rate of change of HR, heart rhythm, changes in heart rhythm, heart rate variability (HRV), change of HRV, rate of change of HRV, HRV vs. HR. Also, heart morphology (e.g., size) blood pressure (arterial and venous), heart sounds, , heartbeat wave morphology, heartbeat complex morphology, and magnitude and shape of thoracic wall deflection.</p> <p>Vascular: Arterial Pressure, Arterial and venous blood wave pressure morphology; Arterial and venous blood flow velocity and degree of turbulence, arterial and venous blood flow sounds, arterial and venous temperature</p> <p>Respiratory: Frequency, tidal volume, minute volume, respiratory wave morphology, respiratory sounds, end-tidal CO<sub>2</sub>, Intercostal EMG, Diaphragmatic EMG, chest wall and abdominal wall motion, from which can be derived, e.g.,, respiration rate (RR), change of RR, rate of change of RR, respiratory rhythm, morphology of breaths. Also, arterial gas concentrations, including oxygen saturation, as well as blood pH can be considered respiratory signals.</p> <p>Dermal: Skin resistance, skin temperature, skin blood flow, sweat gland activity</p> <p>Concentrations of catecholamines (and their metabolites) and acetylcholine or acetylcholinesterase activity in blood, saliva and other body fluids concentrations and its rate of change.</p>
Neurologic
<p>Cognitive/behavioral: Level of consciousness, attention, reaction time, memory, visuospatial, language, reasoning, judgment, mathematical calculations, auditory and/or visual discrimination</p> <p>Kinetic: Direction, speed/acceleration, trajectory (1D to 3D), pattern, and quality of movements, force of contraction, body posture, body orientation/position, body part orientation/position in reference to each other and to imaginary axes, muscle tone, agonist-to-antagonist muscle tone relation, from which can be derived, e.g., information about gait, posture, accessory movements, falls</p> <p>Vocalizations: Formed, unformed</p> <p>EEG/ECoG, Evoked potentials, field potentials, single unit activity</p> <p>Endocrine: Prolactin, luteinizing hormone, follicle stimulation hormone, growth hormone, ACTH, cortisol, vasopressin, beta-endorphin, beta, lipotropin-, corticotropin-releasing factor (CRF)</p> <p>Stress Markers: CK, troponin, reactive oxygen and nitrogen species including but not limited to iso- and neuro-prostanes and nitrite/nitrate ratio, glutathione, glutathione disulfide and glutathione peroxidase activity, citrulline, protein carbonyls, thiobarbituric acid, the heat shock protein family, catecholamines, lactic acid, N-acetylaspartate, and metabolites of any of the foregoing.</p> <p>Metabolic: arterial pH and gases, lactate/pyruvate ratio, electrolytes, glucose</p>

Terms such as “epileptic event” and “reference value,” among others, have been defined in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. “Interictal” refers to a period after a post-ictal period and before a pre-ictal period.

FIGS. 4-7 have been substantially fully described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

Various features of signals for various types of seizures are also generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010 also discusses methods capable of distinguishing epileptic generalized from non-epileptic generalized or “convulsive” seizures whose kinetic activity, but not patho-physiology, resembles that of epileptic seizures.

The selectivity (SI), sensitivity (Se) and specificity (Sp) of various signal features are generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. U.S. patent application Ser. No. 12/896,525 also discusses consideration of these and other signal features in determining optimal signal(s) for use in detection of epileptic events in a particular patient, of a particular type, or the like.

A Positive Predictive Value (PPV) of a signal or combination of signals is generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. The person of ordinary skill in the art will also understand a Negative Predictive Value (NPV) of a signal, defined as:

$(\text{number of True Negatives}) / (\text{number of True Negatives} + \text{number of False Negatives})$

In one embodiment, the present invention relates to a method, comprising receiving at least one of a signal relating to a first cardiac activity from a patient and a signal relating to a first body movement from the patient; deriving at least one patient index from said at least one received signal; triggering at least one of a test of the patient’s responsiveness, a test of the patient’s awareness, a test of a second cardiac activity of the patient, a test of a second body movement of the patient, a spectral analysis test of a second cardiac activity of the patient, and a spectral analysis test of a second body movement of the patient, based on said at least one patient index; determining an occurrence of an epileptic event based at least in part on the one or more triggered tests; and performing a further action in response to the determination of the occurrence of the epileptic event.

Cardiac activity signals, as well as techniques for determining them, are generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

Body movement (a.k.a. kinetic) signals, as well as techniques for determining them, are generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. It should be borne in mind that the terms “body movement” and “kinetic,” as used herein, also encompass the absence of specific body movements (motionless).

The term, and concept of, “responsiveness” as used in reference to the embodiments described herein, has a motor and a cognitive component which may be strongly correlated or dissociated; further the motor component may be in the form of a simple response (e.g., withdrawal of a limb from a pain source) or complex (e.g., drawing a triangle in response to a command). Consequently, responsiveness may be tested using simple stimuli (e.g., acoustic in the form of a loud noise or sensory in the form of a pinprick) or complex (e.g., complex reaction time tests; questions probing knowledge, judgment, abstraction, memory, etc.). In this invention, when “responsiveness” is tested using complex stimuli, “awareness” is being probed and therefore in that case these terms/concepts are used interchangeably. The meaning of “responsiveness” is thus, context dependent: if the objective is to determine if a patient generates simple motor responses or movements, the term “responsiveness” may be used and if it is to test the presence and quality of complex responses, “awareness” may replace responsiveness.

As used herein, “spectral analysis” encompasses spectral analyses using at least one of the known methods (e.g., Fou-

rier-based, wavelet based; multifractal spectral, etc) of cardiac activity or body movements. Spectral analysis techniques are known to the person of ordinary skill in the art and can be implemented by such a person having the benefit of the present disclosure. Spectral analysis may be discrete or continuous. Spectral analysis of a cardiac activity can comprise spectral analysis of heart rate or individual beats' EKG complexes, among others.

The patient index can be a value derived directly from the signal relating to the first cardiac activity or the signal relating to the first body movement. For example, one or more heart rate values can be derived from a cardiac activity signal over one or more periods of time. For example, as described in U.S. patent application Ser. No. 12/770,562, filed Apr. 29, 2010, a foreground heart rate over a relatively short time period (e.g., 5-30 sec) and a background heart rate over a longer time period (e.g., 30-600 sec) can both be derived from a cardiac activity signal. For another example, an accelerometer or inclinometer mounted on a patient's body can give information about the patient's (and/or parts of his body) movements and body position, such as are described in more detail in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

The patient index can also be a determination of an epileptic event. For example, the cardiac activity and/or body movement can be analyzed to determine an occurrence of an epileptic event, a non-occurrence of an epileptic event, or a probable occurrence of an epileptic event.

In one embodiment, triggering the test(s) can be based on at least one of a patient's cardiac activity and the patient's body movement upon a finding that the cardiac activity and/or body movement are indicative of a possible epileptic event. For example, if the cardiac activity and/or body movement clearly indicate an epileptic event with high confidence, triggering the test(s) need not be performed; but if the cardiac activity and/or body movement are outside their interictal reference value ranges but have values that give only low confidence of an epileptic event, triggering can be performed to provide additional information about the patient's condition to indicate whether he or she is suffering an epileptic event or not.

For another example, the patient's cardiac activity at a first time may indicate an epileptic event, and the patient's body movement at a second time and in a particular region of the body may indicate an epileptic event, but if the two times differ, or the body movement is in a different region of the body, or changes in their characteristics (e.g., rate, morphology, pattern, etc.) are discordant with declaring the epileptic event, consideration of cardiac activity and body movement may lead to low confidence of an indication of an epileptic event, and in response thereto, triggering of additional test(s) and/or consideration of additional body signals may be desirable. In other words, there may be a low absolute value of correlation (e.g., a correlation between about -0.4 and 0.4) between the patient's cardiac activity and the patient's body movement that would prevent highly confident determination of an epileptic event. The triggered test(s) may provide enough additional information to make a highly confident determination of an epileptic event (or the non-occurrence of an epileptic event).

Generally, two parameters can be considered highly correlated if the coefficient of correlation is greater than about 0.7, and lowly correlated if the coefficient of correlation is less than about 0.4. Two parameters can be considered highly anticorrelated if the coefficient of correlation is less than about -0.7, and lowly anticorrelated if the coefficient of correlation is greater than about -0.4. One example of parameters/situations that can be considered to be anticorrelated includes an appearance of tachycardia with a disappearance

of body movement. Other examples that can be considered to be anticorrelated are a strong body movement with either a substantially unchanged heart rate or a decreased heart rate. The example with the substantially unchanged heart rate can be considered a low anticorrelation, and the example with the decreased heart rate can be considered a high anticorrelation.

Another pair of examples to consider are the correlations between body movement and first derivative of heart rate in an epileptic event vs. in exercise. Generally, the first derivative of heart rate is greater in an epileptic event than in exercise, i.e., body movement and the first derivative of heart rate can be considered more highly correlated in epileptic events than in exercise.

The presence of either high or low correlation or anticorrelations may be used in this invention to determine the occurrence of an epileptic event and trigger an action(s) or to determine that an epileptic event is not occurring or did not occur. The first and second cardiac activity may be the same (in other words, triggering can be of a second iteration of a test that reported the first cardiac activity as a result of a first iteration, giving a more current value of the cardiac activity), or they may be different. In one embodiment, the first cardiac activity is heart rate or heart rate variability, and the second cardiac activity is heart beat morphology.

Similarly, the first and second body movement may be the same, or they may be different.

A "test" is used herein to refer to any assay of the patient's cardiac activity, body movement, responsiveness, awareness, or a spectral analysis thereof. The product of a test can be considered a signal, and a signal can be considered as resulting from a test. A test of the second cardiac activity may use substantially the same data source, data processing, and/or related techniques as are used in receiving the signal relating to the first cardiac activity. In another embodiment, the techniques may differ. For example, the first cardiac activity can be heart beat morphology determined by electrocardiography (EKG), and the second cardiac activity can be heart beat morphology determined by phonocardiography (PKG).

Similarly, a test of the second body movement may, but need not, use substantially the same data source, data processing, and/or related techniques as are used in receiving the signal relating to the first body movement.

The concept of first and second cardiac activity or first and second body movement is also applicable to responsiveness and awareness. For example responsiveness activity may be a reflex movement such as withdrawal from a source of painful stimuli and a second responsiveness activity may be a complex movement such as that required to draw a triangle. Different tests of varying levels of complexity may be administered to test responsiveness as defined in this invention.

The particular triggered test(s) may be selected based at least in part on the first cardiac activity, the first body movement, or both.

In one embodiment, determining is based on at least one of a finding the patient's awareness differs from a reference responsiveness level, a finding the patient's awareness differs from a reference awareness level, a finding the patient's second cardiac activity includes a characteristic suggestive of an epileptic event, a finding the spectral analysis of the patient's second cardiac activity includes a characteristic suggestive of an epileptic event, and a finding the spectral analysis of the patient's second body movement includes a characteristic suggestive of an epileptic event.

FIG. 10 shows a flowchart depicting one embodiment of a method according to the present invention. A cardiac activity signal indicative of the patient's cardiac activity is received at

block 1010 and/or a body movement signal indicative of a body movement of the patient is received at block 1020.

Thereafter, a determination is made in block 1030 whether cardiac activity and body movement are associated with an epileptic event. If no, flow returns to the receiving blocks 1010-1020. If yes, an epileptic event is declared at block 1040. However, if no determination can be made, flow moves to block 1050, where one or more of a responsiveness test, an awareness test, a second cardiac activity test, a second body movement test, a spectral analysis test of the second cardiac activity, or a spectral analysis test of the second body movement, are triggered.

Thereafter, a determination is made in block 1060 whether the patient's responsiveness, awareness, second cardiac activity, second body movement, and/or spectral analysis of second cardiac activity or second body movement are indicative of an epileptic event. If no, flow returns to the receiving blocks 1010-1020. If yes, an epileptic event is declared at block 1040.

Alternatively or in addition to declaring an epileptic event, further actions can be performed. In one embodiment, the method further comprises classifying the epileptic event based upon at least one of the first cardiac activity, the first body movement, the responsiveness, the awareness, the second cardiac activity, the second body movement, the spectral properties of the second cardiac activity, the spectral properties of the second body movement, and two or more thereof.

Classifications of epileptic events can be generally based on the information shown in FIGS. 4-7 and the discussion herein and in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. Classifications can also be based in part on observations of stereotypical seizures of a particular patient. Not all seizures that a clinician would recognize as being of a particular type may exhibit all the properties discussed herein, and thus, not all may be amenable to classification by the methods described herein, but a substantial majority are expected to be amenable to classification by the methods described herein.

In one embodiment, the epileptic event is classified as a generalized tonic-clonic seizure when the following occur in a patient in a first, non-recumbent position: the first body movement comprises a fall from the first, non-recumbent position, wherein (i) the fall is associated with a loss of responsiveness, a loss of awareness, or both; and (ii) the fall is followed by generalized body movements.

Falls to the ground associated with a primarily or secondarily generalized tonic-clonic, generalized tonic, generalized clonic-tonic-clonic seizure or generalized atonic seizure are distinguishable from those caused by tripping or slipping by the absence of protective/defensive actions (e.g., breaking the fall with the arms) and other features such which body part(s) is(are) first on contact with the ground.

Primarily generalized seizures usually result in synchronous bilateral movements of equal amplitude, with maintenance of head and eyes on the midline. Secondarily generalized seizures usually manifest at onset with unilateral movements of limbs, head, eyes, or trunk.

In one embodiment, the generalized body movement comprises a rhythmic body movement. Alternatively or additionally, the generalized body movements can comprise flexion and extension of joints and/or can have a frequency of about 3 Hz at some time during the epileptic event. In another embodiment, the rhythmic movement is temporally associated with an epileptiform discharge.

Body movement can allow classification of an epileptic event as to primarily generalized or secondarily generalized. Specifically, the epileptic event can be classified as primarily

generalized if body movements are synchronous and of equal amplitude on both sides of the body, and as secondarily generalized if not.

In a further embodiment, the epileptic event is classified as a generalized tonic-clonic seizure when recovery of awareness follows recovery of responsiveness, provided at least one of the key identifiers (e.g., loss of postural tone or diffuse increase in muscle tone or rhythmical body movements) have occurred.

In one embodiment, the epileptic event is classified as an atonic seizure when the following occur in a patient in a first, non-recumbent position:

i) a body movement comprises a fall from the first, non-recumbent position, wherein the fall is associated with a loss of responsiveness, a loss of awareness, or both; and

(ii) the patient shows a significant reduction in body movements below a reference value after the fall, a significant reduction in muscle tone below a reference value after the fall, or both.

Typically, the significant reductions in body movements and/or muscle tone commonly seen in atonic seizures are not caused by changes in heart or respiratory activity.

In one embodiment, the epileptic event is classified as tonic when the following occur to a patient in a first, non-recumbent position: an increase in muscle tone above a reference value, a loss of responsiveness, and an absence of generalized movements.

In a further embodiment, the epileptic event is classified as tonic when recovery of awareness follows recovery of responsiveness, provided it has been associated with loss of responsiveness or awareness.

In one embodiment, the epileptic event is classified as a complex partial seizure based upon a finding the patient's cardiac activity is associated with impaired awareness and is not associated with a fall or at some point in time with generalized rhythmical body movements; and the epileptic event is classified as a simple partial seizure based upon a finding the patient's cardiac activity is not associated with impaired awareness and is not associated with generalized rhythmical body movements.

In one embodiment, the event is classified as syncope, when at least one of the following occur: the body movement comprises a fall from a non-recumbent position and the fall is associated with a loss of responsiveness or a loss of awareness, and recovery of responsiveness or recovery of awareness occurs immediately after the fall, or when the body movement comprises a fall from a recumbent position, there is marked decrease in heart rate or a brief transient cessation of heart beats (asystole).

Epileptic events can be determined or classified in view of the patient's body position. For example, an epileptic event when the patient is in a decubitus position (lying down) may be determined from an observation of transient loss of muscle tone in antigravitatory muscles (e.g., paraspinal; quadriceps), followed by transient increase in muscle tone in agonist and antagonist muscle groups (e.g., paraspinal and abdominal recti; quadriceps and hamstrings), which in turn is followed by generalized rhythmical muscle contractions (typically with a frequency of 3 Hz and/or 10-12 Hz at some time during the event).

For another example, an epileptic event when the patient is in a seated position may be determined using both electromyography (EMG) signals and accelerometer signals.

The one or more of the first cardiac activity, the second cardiac activity, the first body movement, the second body movement, the responsiveness, and the awareness can be provided by any known technique. In one embodiment, at

least one of the first cardiac activity and the second cardiac activity is sensed by at least one of an electrocardiogram (EKG), phonocardiogram (PKG), apexcardiography, blood pressure monitor, and echocardiography. The body movement can be sensed by any known technique. In one embodiment, at least one of the first body movement and the second body movement is sensed by an accelerometer, an inclinometer, an actigraph, an imaging system, a dynamometer, a gyroscope, electromyography (EMG), or two or more thereof.

In certain circumstances, the method can make a false positive determination of an epileptic event, i.e., determine an epileptic event based on the signals and tests described above when no epileptic event (as may be determined using direct/invasive recording of electrical activity at/near the epileptogenic zone, observation by a skilled practitioner, or other techniques known to the person of ordinary skill in the art) occurred. In one embodiment, the method further comprises receiving an indication that the determined epileptic event was not an actual epileptic event. Such indications may include, but are not limited to, the first body movement is a fall but the fall is not characteristic of an epileptic fall; the generalized body movements are not rhythmical and bilaterally synchronous; the generalized body movement have a frequency substantially different from 3 Hz or a variable frequency; the generalized body movements change direction, pairs of agonist-antagonist muscles, and/or movements in different directions occur simultaneously in two or more joints; the change in cardiac activity, cardiac activity morphology, cardiac spectral analysis, apexcardiography, or echocardiography is not characteristic of epileptic seizures.

Similarly, in one embodiment, the method further comprises receiving an indication of a false negative, i.e., an indication an epileptic event occurred but no determination thereof was made.

The indication may be based at least in part on input from the patient, a caregiver, or a medical professional, and/or on quantification or characterization of one or more body signals. The indication may be provided at the time of the false determination or later.

A false determination (whether positive or negative) may render it appropriate to modify the body signals or analyses used in making future determinations. In one embodiment, the method further comprises reducing a likelihood of a future determination of a false positive epileptic event based at least in part on one or more of the first cardiac activity, the first body movement, the responsiveness, the awareness, the second cardiac activity, the second body movement, the spectral analysis of the second cardiac activity, or the spectral analysis of the second body movement, in response to the indication. In another embodiment, the method further comprises reducing a likelihood of a future determination of a false negative epileptic event based at least in part on one or more of the first cardiac activity, the first body movement, the responsiveness, the awareness, the second cardiac activity, the second body movement, the spectral analysis of the second cardiac activity, or the spectral analysis of the second body movement, in response to the indication.

When an epileptic event is determined, the method can further comprise one or more of logging the occurrence and/or time of occurrence of the seizure; providing a warning, alarm or alert to the patient, a caregiver or a health care provider; providing a therapy to prevent, abort, and/or reduce the severity of the seizure; assessing one or more patient parameters such as awareness or responsiveness during the seizure; assessing the severity of the seizure; identifying the end of the seizure; and assessing the patient's post-ictal

impairment or recovery from the seizure. "Recovery" is used herein to encompass a time after seizure onset and/or seizure end when the patient's parameters are returning to baseline. Other examples include, but are not limited to, logging one or more of a time of onset of the epileptic event, a time of termination of the epileptic event, a severity of the epileptic event, an impact of the epileptic event, an interval between the epileptic event and the most recent preceding epileptic event, an epileptic event frequency over a time window, an epileptic event burden over a time window, time spent in epileptic events over a time window, or a type of epileptic event.

To reduce the rate of false positive detections or for other reasons, in one embodiment, the method further comprises recording one or more of the patient's reference body movement or movements, reference cardiac activity, reference responsiveness level, reference awareness level, reference cardiac activity, reference spectral analysis of the cardiac activity, or reference spectral analysis of the body movement during one or more interictal activities at one or more times when the patient is not suffering an epileptic event, to yield recorded data not associated with an epileptic event; defining one or more interictal activity reference characteristics from the recorded data; and overruling the determination of the epileptic event based at least in part on finding the patient's first body movement, first cardiac activity, responsiveness level, awareness level, second cardiac activity, second body movement, spectral analysis of the second cardiac activity, and spectral analysis of the second body movement matches the one or more interictal event reference characteristics.

The interictal activities at one or more times when the patient is not suffering an epileptic event can include different activities (e.g., walking vs. running vs. swimming, etc.), and can alternatively or in addition include the same activity at different times of day, week, month, or year, or under different external circumstances (e.g., walking at sea level vs. walking at higher altitude, etc.).

The overruling of a determination of an epileptic event may be made with some probability between zero and one. The overruling may be made according to a permanent or semi-permanent rule or on a case-by-case basis. The references may be stored in a library on a per-patient, per-seizure type, or per-population basis.

In one embodiment, the overruling may involve the triggering of one or more additional test(s). Such further triggering may allow more accurate determination of epileptic events.

Recording one or more of the patient's reference body movement or movements, reference cardiac activity, reference responsiveness level, reference awareness level, reference cardiac activity, reference spectral analysis of the cardiac activity, or reference spectral analysis of the body movement during epileptic event may allow overruling of false negative or false positive determinations.

The body movement during one or more interictal activities can include at least one of a movement of a part of the body (e.g., the eyes or eyelids), a movement of a limb (e.g., an arm), a movement of a part of a limb (e.g., a wrist), a direction of a movement, a velocity of a movement, a force of a movement, an acceleration of a movement, a quality of a movement, an aiming precision of a movement, or a purpose or lack thereof of a movement.

The likelihood of a patient suffering an epileptic event may change at different times and/or under different conditions. In one embodiment, a plurality of interictal event reference characteristics are defined which differ from one another based on one or more of the time of day of the recording, the time of week of the recording, the time of month of the recording, the

time of year of the recording, the type of activity, changes in the patient's body weight or body mass index, changes in the patient's medication, changes in the patient's physical fitness or body integrity, state of physical or mental health, mood level or changes in the patient's mobility. Alternatively or in addition, a plurality of interictal event reference characteristics in a female patient can be defined in reference to the menstrual cycle and/or to pregnancy. Alternatively or in addition, changes in the patient's environment may change the likelihood of the patient suffering an epileptic event.

In a further embodiment, the overruling is based at least in part on one or more of the plurality of interictal event reference characteristics.

Any characteristic of the one or more interictal events may be considered. In one embodiment, the one or more characteristics are patterns or templates.

It may be desirable in certain embodiments to adapt at least one of a reference value on one or more of the body movement, the cardiac activity, the responsiveness level, the awareness level, the second cardiac activity, the second body movement, and the spectral analysis of cardiac activity or body movement, based upon one or more determinations that the specificity of past detections was above or below a specificity measure, the sensitivity of past detections was above or below a sensitivity measure, the speed of detection defined as the time elapsed between the occurrence of the first body signal change indicative of the onset of the seizure and the issuance of the detection, the cost of the therapy was below or above a cost measure, the patient's tolerance of the therapy was below an acceptable tolerance, the adverse effects were above an acceptable level, or the patient's disease state was below or above a first disease state threshold. Positive predictive value or negative predictive value may be used in addition to or instead of specificity or sensitivity.

As should be apparent, a single "threshold" can be mathematically defined in a number of ways that may be above or below a particular value of a particular parameter. For example, an elevated heart rate can be defined, with equal validity, as a heart rate above a threshold in units of beats/unit time or an interbeat interval below a threshold in units of time. More than one "threshold" may be used to optimize specificity, sensitivity or speed of detection.

For example, the method can further comprise determining one or more of a specificity of past detections, a sensitivity of past detections, a speed of past detections, a cost of a therapy for epileptic events, a patient's tolerance of a therapy for epileptic events, and a disease state of the patient; and loosening at least one constraint on one or more of the body movement, the cardiac activity, the responsiveness test, the awareness test, the second cardiac activity test, the second body movement test, and the spectral analysis of second cardiac activity or second body movement based upon one or more determinations that the specificity of past detections was above a first specificity threshold, the sensitivity of past detections was below a first sensitivity threshold, the speed of detection was below a first speed of detection threshold, the cost of the therapy was below a first cost threshold, the patient's tolerance of the therapy was below a first tolerance threshold (i.e., the patient can tolerate more detections or actions performed in response to detections), and the patient's disease state was below a first disease state threshold; or tightening the at least one constraint based upon one or more determinations that the specificity of past detections was below a second specificity threshold, the sensitivity of past detections was above a second sensitivity threshold, the speed of detection was above an acceptable threshold for efficacy of therapy and safety of the patient, the cost of the therapy was

above a second cost threshold, the patient's tolerance of the therapy was above a second tolerance threshold (i.e., the patient cannot tolerate more detections or actions performed in response to detections), and the patient's disease state was above a second disease state threshold.

In another embodiment, the invention can be used for the detection of generalized tonic-clonic seizures. A "generalized tonic-clonic seizure" is used herein to refer to a primarily or secondarily generalized seizure that features at least one tonic, clonic, or both tonic and clonic phase. Myoclonic seizures are included in this definition. At onset or at some point during the generalized tonic-clonic seizure, at least a majority of the body muscles or joints are involved. "Body muscle" is used herein to refer to those capable of moving joints, as well as muscles of the eyes, face, orolaryngeal, pharyngeal, abdominal, and respiratory systems.

In one embodiment, the present invention relates to a method, comprising:

receiving at least two body signals selected from the group consisting of a signal relating to a first body movement, a signal relating to a first cardiac activity, a responsiveness signal, an awareness signal, a signal relating to a second cardiac activity, a signal relating to a second body movement, a spectral analysis signal relating to the second cardiac activity, and a spectral analysis signal relating to the second body movement;

determining an occurrence of a generalized tonic-clonic epileptic seizure, the determination being based upon the correlation of at least two features, at least one feature being of each of the at least two body signals, wherein:

the feature of the first cardiac activity signal is an increase in the patient's heart rate above an interictal reference value;

the feature of the first body movement signal is at least one of (i) an increase in axial or limb muscle tone substantially above an interictal or exercise value for the patient, (ii) a decrease in axial muscle tone in a non-recumbent patient, below the value associated with a first, non-recumbent position, (iii) fall followed by an increase in body muscle tone, or (iv) a fall followed by generalized body movements;

the feature of the responsiveness signal is a decrease in the patient's responsiveness below an interictal reference value;

the feature of the awareness signal is a decrease in the patient's awareness below an interictal reference value;

the feature of the second cardiac activity signal is a correlation with an ictal cardiac activity reference signal;

the feature of the second body movement signal is a correlation with an ictal body movement reference signal;

the feature of the spectral analysis signal of the second cardiac activity is a correlation with an ictal cardiac activity spectral analysis reference signal; or

the feature of the spectral analysis signal of the second body movement is a correlation with an ictal body movement spectral analysis reference signal;

and

performing a further action in response to the determination of the occurrence of the epileptic event.

FIG. 11 depicts one embodiment of this method. FIG. 11 depicts a receiving step 1110, a determining step 1120, and a performing step 1130.

In one embodiment, the correlation has a high absolute value and is either positive or negative. E.g. the correlation may be positive, such as with a value greater than 0.7, 0.75, 0.8, 0.85, 0.9, or 0.95, or negative, such as with a value less than -0.7, -0.75, -0.8, -0.85, -0.9, or -0.95.

The further action may comprise one or more of logging the occurrence and/or time of occurrence of the seizure; providing a warning, alarm or alert to the patient, a caregiver or

a health care provider; providing a therapy to prevent, abort, and/or reduce the severity of the seizure; assessing one or more patient parameters such as awareness or responsiveness during the seizure; assessing the severity of the seizure, identifying the end of the seizure; and assessing the patient's post-ictal impairment or recovery from the seizure.

The various signals can be provided by any appropriate technique and their features referred to above can likewise be measured as a routine matter for the person of ordinary skill in the art having the benefit of the present disclosure. For example, in one embodiment, the correlation of the second cardiac activity signal with the ictal cardiac activity reference signal comprises a match to an ictal cardiac activity template; the correlation of the second body movement signal with the ictal body movement reference signal comprises a match to an ictal body movement template;

the correlation of the spectral analysis signal of the second cardiac activity with the ictal cardiac activity spectral analysis reference signal comprises a match to an ictal cardiac activity spectral analysis pattern or template; or the correlation of the spectral analysis signal of the second body movement with the ictal body movement spectral analysis reference signal comprises a match to an ictal body movement spectral analysis pattern or template. Aspects of the signals and their features may include, among others, a body movement signal further comprising an indication of a fall prior to the indication of the tonic or clonic activity.

In one embodiment, a tonic-clonic seizure can be further characterized as secondarily generalized if the first body movement signal does not comprise synchronous movement of all body muscles with equal amplitude or velocity prior to an indication of tonic or clonic activity.

In one embodiment, the end of the generalized tonic-clonic epileptic seizure can be indicated when at least one of the body signals trends toward an interictal reference value, range, or pattern of the body signal.

In one embodiment, the method further comprises indicating the beginning of a post-ictal period based upon the appearance of at least one post-ictal feature of at least one the body signal, wherein:

the post-ictal feature of the first cardiac signal or the second cardiac signal is a decrease in the patient's heart rate below an ictal reference value;

the post-ictal feature of the first body movement signal or the second body movement signal is a decrease in the patient's muscle tone or movement below an ictal reference value;

the post-ictal feature of the responsiveness signal is an increase in the patient's responsiveness above an ictal value and below an inter-ictal reference value; or

the post-ictal feature of the awareness signal is an increase in the patient's awareness above an ictal value and below an inter-ictal reference value.

The term "post-ictal," is not necessarily limited to the period of time immediately after the end of the primarily or secondarily generalized tonic-clonic epileptic seizure and is not limited to this type of seizure but also encompasses partial seizures (e.g., all complex and certain simple partial and absence seizures). Rather, it refers to the period of time during which at least one signal has one or more features that differs from the ictal and inter-ictal reference values that indicates one or more of the patient's body systems are not functioning normally (e.g., as a result of the seizure or of an injury suffered during the seizure) but are not exhibiting features indicative of a seizure.

In one embodiment, the end of the post-ictal period can be indicated when each of the post-ictal features is outside the range of values associated with the ictal and post-ictal states. In another embodiment, the end of the post-ictal period can be indicated when at least one of the post-ictal features is outside the range of values associated with the ictal and post-ictal states. In this embodiment, the onset and termination of the post-ictal period may be partial when all features have not returned to interictal reference values or complete when all features have. This distinction (partial vs. complete) has important therapeutic (the patient may require treatment until all body signals have fully recovered to inter-ictal values), safety (the patient's mortality and morbidity risks may remain increased until all body signal have fully recovered to inter-ictal values) and predictive implications (the probability of occurrence of the next seizure and time to it (inter-seizure interval) may depend on recovery of one more body signals to their interictal value.

It should also be borne in mind that different features are expected to return to their interictal reference values at different times. For example, from kinetic and brain electrical perspectives, a seizure can be defined as having ended when abnormal movements and abnormal EEG cease. These events typically take place before the patient's heart rate returns to baseline. Further, it may take a few minutes after abnormal movements and abnormal EEG end for cognition and responsiveness to return to baseline; up to about 30 min for awareness to return to baseline; and about 30-45 min for blood lactic acid concentration to return to baseline. Temporal relationships between changes in signal features, and transitions from one state to another, are generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. Transitions may have quantifiable differences in location as well, e.g., the number of either brain sites or body organs in which the transition has taken place may vary over time (e.g., an ictal change first occurring on the right mesiotemporal lobe, or a change in heart activity at or near seizure onset followed by changes in metabolic indices.

In another embodiment, the present invention relates to the detection of partial seizures. In one embodiment, the present invention relates to a method, comprising:

receiving at least two body signals selected from the group consisting of a signal relating to a first body movement, a signal relating to a first cardiac activity, a responsiveness signal, an awareness signal, a signal relating to a second cardiac activity, a signal relating to a second body movement, a spectral analysis signal relating to the second cardiac activity, and spectral analysis signal relating to the second body movement; and

determining an occurrence of a partial epileptic seizure based upon a correlation of two features, at least one feature being of each of the at least two body signals, wherein:

the feature of the first cardiac signal is a value outside an interictal reference value range;

the feature of the first body movement signal is a body movement associated with a partial seizure;

the feature of the second cardiac activity signal is a correlation with an ictal cardiac activity reference signal;

the feature of the second body movement signal is a correlation with an ictal body movement reference signal;

the feature of the spectral analysis signal of the second cardiac activity is a correlation with an ictal cardiac activity spectral analysis reference signal; or

the feature of the spectral analysis signal of the second body movement is a correlation with an ictal body movement spectral analysis reference signal; and

performing a further action in response to the determination of the occurrence of the epileptic event.

FIG. 12 depicts one embodiment of this method. FIG. 12 depicts a receiving step 1210, a determining step 1220, and a performing step 1230.

The various signals can be provided by any appropriate technique and their features referred to above can likewise be measured as a routine matter for the person of ordinary skill in the art having the benefit of the present disclosure. For example, in one embodiment, the correlation of the second cardiac activity signal with the ictal cardiac activity reference signal comprises a match to an ictal cardiac activity template;

the correlation of the second body movement signal with the ictal body movement reference signal comprises a match to an ictal body movement template;

the correlation of the spectral analysis signal of the second cardiac activity with the ictal cardiac activity spectral analysis reference signal comprises a match to an ictal cardiac activity spectral analysis pattern or template; or

the correlation of the spectral analysis signal of the second body movement with the ictal body movement spectral analysis reference signal comprises a match to an ictal body movement spectral analysis pattern or template.

Matches to patterns and templates are described in U.S. patent application Ser. No. 12/884,051, filed Sep. 16, 2010. A “match” should not be construed as requiring a complete or perfect fit to a pattern or template.

In one embodiment, the further action comprises one or more of logging the occurrence and/or time of occurrence of the seizure; providing a warning, alarm or alert to the patient, a caregiver or a health care provider; providing a therapy to prevent, abort, and/or reduce the severity of the seizure; assessing one or more patient parameters such as awareness or responsiveness during the seizure; assessing the severity of the seizure, identifying the end of the seizure; and assessing the patient’s post-ictal impairment or recovery from the seizure.

Partial seizures generally result in body movements that do not include falls.

The partial seizure can be classified as complex if at least one of the features of the awareness signal is a decrease in the patient’s awareness below its reference value, or as (ii) simple if there is no decrease in the patient’s awareness below its reference value, or if there is a decrease in the patient’s responsiveness but awareness remains at an interictal value.

In one embodiment, the end of the partial epileptic seizure can be indicated when at least one of the features of the respective body signals is outside the range of values associated with the ictal state for that body signal. In another embodiment, the end of the partial epileptic seizure can be indicated when each of the features of the respective body signals trends toward an interictal reference value, range, or pattern of the body signal.

In one embodiment, the method further comprises indicating the beginning of a post-ictal period when at least one of the body signals is outside the range of values associated with the ictal and inter-ictal states for that body signal, wherein:

the post-ictal feature of the cardiac signal is a heart rate outside the range of values associated with the ictal state;

the post-ictal feature of the body movement signal is a change in the patient’s movement outside the ictal range of values;

the post-ictal feature of the responsiveness signal is an increase in the patient’s responsiveness above an ictal reference value but remaining below an inter-ictal reference value; and

the post-ictal feature of the awareness signal is an increase in the patient’s awareness above an ictal reference value but remaining below an inter-ictal reference value.

In one embodiment, the end of the post-ictal period can be indicated when at least one of the post-ictal features is absent from its respective body signal.

In one embodiment, such responsive action(s) may be taken if the ictal or postictal state’s severity exceeds a threshold, e.g., the 90th percentile values for a patient.

Various responsive actions, such as warning, logging, and treating, among others, are generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. A warning may be graded, e.g., a yellow light for a mild seizure, a red light for a severe one. Treating can comprise providing supporting treatment (e.g., fluids, oxygen).

Seizure severity indices may be calculated and stored by appropriate techniques and apparatus. More information on seizure severity indices is available in U.S. patent application Ser. No. 13/040,996, filed Mar. 4, 2011.

In one embodiment, the present invention relates to a system, comprising:

at least one sensor configured to receive at least one of a signal relating to a first cardiac activity from a patient, a signal relating to a first body movement from the patient, a responsiveness signal from the patient, an awareness signal from the patient, a signal relating to a second cardiac activity of the patient, and a signal relating to a second body movement of the patient;

a detection unit configured to receive the at least one signal from the at least one sensor and determine an occurrence of an epileptic event; and

an action unit configured to receive an indication of the occurrence of the epileptic event from the detection unit and perform at least one of logging the occurrence and/or time of occurrence of the epileptic event; providing a warning, alarm or alert to the patient, a caregiver or a health care provider; providing a therapy to prevent, abort, and/or reduce the severity of the epileptic event; assessing one or more patient parameters such as awareness or responsiveness during the epileptic event; assessing the severity of the epileptic event, identifying the end of the epileptic event; and assessing the patient’s post-ictal impairment or recovery from the epileptic event.

The system can further comprise other units. For example, the system can comprise a spectral analysis unit configured to generate at least one spectral analysis signal from the signal relating to the second cardiac activity and/or the signal relating to the second body movement. In this embodiment, it may be desirable for the detection unit to be further configured to receive the at least one spectral analysis signal from the spectral analysis unit.

Although not limited to the following, exemplary systems capable of implementing embodiments of the present invention are generally discussed below and in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

FIG. 1A depicts a stylized system comprising an external unit 145a capable of receiving, storing, communicating, and/or calculating information relating a patient’s epileptic events. The system shown in FIG. 1A also includes at least one sensor 212. The sensor 212 may be configured to receive cardiac activity data, body movement data, responsiveness data, awareness data, or other data from the patient’s body. A lead 211 is shown allowing communication between the sensor 212 and the external unit 145a.

FIG. 1B depicts a stylized implantable medical system (IMD) 100, similar to that shown in FIG. 1 of U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010, and discussed therein.

FIG. 2 is shown and generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. As is apparent to the person of ordinary skill in the art, the neurological signal module 275 is capable of collecting neurological data and providing the collected neurological data to a detection module 285.

In other embodiments (not shown), other types of signals may be collected and provided to the detection module 285.

FIG. 3A and FIG. 3B are generally as shown and described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010. The ocular signal unit 318 is generally capable of providing at least one ocular signal (e.g., pupil dilation, pupillary hippus, blinking, etc.).

FIG. 3B herein also depicts an awareness determination unit 3020j.

In addition, a device can comprise other signal modules. For example, it may comprise a metabolic signal module, which can comprise a blood parameter signal unit capable of providing at least one blood parameter signal (e.g., blood glucose, blood pH, blood gas, etc). Alternatively or in addition, the metabolic signal module can comprise a hormone signal unit capable of providing at least one hormone signal.

A detection module 285, as shown in FIG. 3C, is generally described in U.S. patent application Ser. No. 12/896,525, filed Oct. 1, 2010.

The above methods may be performed by a computer readable program storage device encoded with instructions that, when executed by a computer, perform the method described herein.

All of the methods and apparatuses disclosed and claimed herein may be made and executed without undue experimentation in light of the present disclosure. While the methods and apparatus of this invention have been described in terms of particular embodiments, it will be apparent to those skilled in the art that variations may be applied to the methods and apparatus and in the steps, or in the sequence of steps, of the method described herein without departing from the concept, spirit, and scope of the invention, as defined by the appended claims. It should be especially apparent that the principles of the invention may be applied to selected cranial nerves other than, or in addition to, the vagus nerve to achieve particular results in treating patients having epilepsy, depression, or other medical conditions.

What is claimed is:

1. A method, comprising:

receiving a signal relating to a cardiac activity from a patient;

deriving at least one cardiac index from the cardiac signal, wherein said at least one cardiac index is selected from a heart rate index and an EKG morphology index;

receiving a signal relating to a body movement from the patient;

deriving at least one body movement index from the body movement signal, wherein said at least one body movement index is selected from a body posture, a body position, a fall, and a body movement derived from an accelerometer;

detecting a possible epileptic seizure based on at least one of the at least one cardiac index and the at least one body movement index;

triggering a test of the patient's responsiveness based on said detecting;

performing one of

(a) confirming the detecting of the possible epileptic seizure; or

(b) overruling the detecting of the possible epileptic seizure,

wherein said confirming or overruling is based upon the result of the responsiveness test; and

performing a further action in response to said confirming the detecting of the possible epileptic seizure.

2. The method of claim 1, wherein the further action comprises one or more of:

logging the occurrence of at least one of said detecting and said confirming the detecting of the possible epileptic seizure;

logging the time of occurrence of at least one of said detecting and said confirming the detecting of the possible epileptic seizure;

providing at least one of a warning, alarm or alert to the patient, a caregiver or a health care provider;

providing a therapy to prevent, abort, and/or reduce the severity of the epileptic seizure;

logging the patient's response to said test of the patient's responsiveness;

assessing the severity of the epileptic seizure;

identifying the end of the epileptic seizure;

assessing the patient's degree of post-ictal impairment; and determining a time required for the patient to return to an interictal reference responsiveness level.

3. The method of claim 1, wherein confirming the detecting of the possible epileptic seizure is based on a finding that the patient's responsiveness differs from an interictal reference responsiveness level.

4. The method of claim 1 wherein said test of the patient's responsiveness is selected from one of:

a test requiring a simple motor response;

a test requiring a simple verbal response

a test requiring a complex motor response;

a test requiring a complex verbal response;

a test involving a noxious sensory stimulus;

a test involving an acoustic sensory stimulus;

a test involving a non-noxious sensory stimulus;

a complex reaction time test; and

a test comprising questions assessing at least one of knowledge, judgment, abstraction and memory.

5. The method of claim 1, wherein detecting a possible epileptic seizure is based at least in part on a determination of a correlation between the at least one cardiac index and at least one body movement index.

6. The method of claim 1, further comprising classifying said epileptic seizure based upon at least one of said at least one cardiac index;

said at least one body movement index, and

said result of said responsiveness test.

7. The method of claim 6, wherein said epileptic seizure is classified as a generalized tonic-clonic seizure when the following occur in a patient in a first, non-recumbent position:

a) said body movement comprises a fall from said first, non-recumbent position, wherein (i) said fall is associated with a loss of responsiveness, a loss of awareness, or both; and (ii) said fall is followed by generalized epileptic body movements.

8. A method, comprising:

receiving a signal relating to a body movement from the patient;

determining from said body movement signal that the patient is in a first, non-recumbent position;

23

detecting an epileptic seizure by determining from said body movement signal that the patient has had a fall from said first, non-recumbent position to a second position;

triggering a test of the patient's responsiveness based at least on part said determining that the patient has had a fall;

performing one of

(a) confirming the detecting of the epileptic seizure; or

(b) overruling the detecting of the epileptic seizure, wherein said confirming or overruling is based upon the result of the responsiveness test.

9. The method of claim 8 further comprising classifying said seizure as a generalized tonic-clonic seizure when

(a) the result of said responsiveness test indicates that the patient has had a loss of responsiveness, and

(b) the fall to said second position is followed by generalized epileptic body movements.

10. The method of claim 8 further comprising classifying said seizure as a tonic seizure when

(a) the body movement signal indicates an increase in muscle tone above a reference value and an absence of generalized body movements; and

(b) the result of the responsiveness test indicates that the patient has had a loss of responsiveness.

11. A method of detecting an epileptic seizure, comprising: receiving at least two body signals selected from a body movement signal, a cardiac activity signal, and a responsiveness signal;

determining at least one feature from each of said at least two body signals, wherein

(a) the feature determined from the cardiac signal is an increase in the patient's heart rate above an interictal reference value;

(b) the feature determined from the first body movement signal is selected from

(i) an increase in axial or limb muscle tone substantially above an interictal or exercise value for the patient;

(ii) a decrease in axial muscle tone when the patient is in a non-recumbent position;

(iii) a fall followed by an increase in body muscle tone; or

(iv) a fall followed by generalized epileptic body movements; and

(c) the feature determined from the responsiveness signal is (i) a decrease in the patient's responsiveness below an interictal reference value;

(ii) a decrease in the patient's awareness below an interictal reference value; and

performing a further action in response to said confirming the detecting of the possible epileptic seizure.

24

12. The method of claim 11, further comprising classifying said epileptic seizure

(a) as a complex partial seizure based upon a finding the patient's change in cardiac activity is associated with impaired awareness and is not associated with (i) a fall, (ii) generalized increase in muscle tone, or (iii) generalized body movements; and

(b) as a simple partial seizure based upon a finding the patient's change in cardiac activity is not associated with impaired awareness.

13. The method of claim 11 wherein performing a further action comprises logging one or more of a time of onset of the epileptic seizure, a time of termination of the epileptic seizure, a severity of the epileptic seizure, an impact of the epileptic seizure on the patient, an interval between the epileptic seizure and at least one preceding epileptic seizure, an epileptic seizure frequency over a time window, an epileptic seizure burden over a time window, time spent in epileptic seizures over a time window, or a type of epileptic seizure.

14. A system for detecting an epileptic seizure, comprising: an autonomic signal module for receiving a cardiac signal and determining at least one cardiac feature selected from an increase in the patient's heart rate above an interictal value and a heart beat morphology feature;

a neurological signal module for receiving at least one of a kinetic signal and a cognitive signal and determining at least one of a kinetic feature from the kinetic signal and a cognitive feature from the cognitive signal, wherein

said kinetic feature is selected from (a) an increase in axial or limb muscle tone substantially above an interictal or exercise value for the patient, (b) a decrease in axial muscle tone when the patient is in a non-recumbent position, (c) a fall followed by an increase in body muscle tone, or (d) a fall followed by generalized epileptic body movements; and

said cognitive feature is selected from (a) a decrease in the patient's responsiveness below an interictal reference value, (b) a decrease in the patient's awareness below an interictal reference value, (c) a memory feature, (d) an attention feature, and (e) a language feature; and

a detection module for (a) detecting an epileptic seizure based on at least two of a cardiac feature, a kinetic feature, an awareness feature, and a responsiveness feature, and (b) performing a further action in response to said detecting.

15. The system of claim 14, wherein said cardiac signal is at least one of an electrocardiogram (EKG) signal, a phonocardiogram (PKG) signal, an apexcardiography signal, a blood pressure signal, and an echocardiogram signal.

16. The system of claim 14, wherein said kinetic signal is at least one of an accelerometer signal, an inclinometer signal, an actigraph signal, an imaging signal, a dynamometer signal, a gyroscope signal, and an electromyogram (EMG) signal.

\* \* \* \* \*

专利名称(译)	使用多模态数据检测，量化和/或分类癫痫发作		
公开(公告)号	<a href="#">US8852100</a>	公开(公告)日	2014-10-07
申请号	US13/776176	申请日	2013-02-25
[标]申请(专利权)人(译)	FLINT HILLS SCI L LC		
当前申请(专利权)人(译)	FLINT HILLS科技有限责任公司		
[标]发明人	OSORIO IVAN		
发明人	OSORIO, IVAN		
IPC分类号	A61B5/00 A61B5/0205 A61B5/0245 A61B5/11 A61N1/36 A61N1/365		
CPC分类号	A61B5/0205 A61B5/4094 A61B5/7264 A61B5/1117 A61N1/36064 A61N1/36135 A61B5/0245 A61B5/686 A61N1/36585 A61B5/0402 A61B5/113 A61N1/36139 A61B5/0816 G16H50/20 A61B5/02055 A61B5/021 A61B5/02405 A61B5/026 A61B5/0488 A61B5/0531 A61B5/4266 A61B5/746 A61B7/04 A61B8/0883 A61B2562/0219		
优先权	13/098262 2013-02-26 US 12/896525 2012-12-25 US		
其他公开文献	US20130225992A1		
外部链接	<a href="#">Espacenet</a> <a href="#">USPTO</a>		

摘要(译)

一种方法，包括从患者接收与第一心脏活动有关的信号和与第一身体运动有关的信号中的至少一个；基于至少一个触发患者的响应性，意识，第二心脏活动，第二身体运动，第二心脏活动的光谱分析测试和第二身体运动的光谱分析测试的测试中的至少一个与第一心脏活动有关的信号和与第一身体运动有关的信号；至少部分地基于所述一个或多个触发的测试来确定癫痫事件的发生；响应于所述癫痫事件发生的所述确定，执行进一步的动作。进一步的方法允许对癫痫事件进行分类。能够实现该方法的装置和系统。

