

US008628472B2

(12) **United States Patent**  
**Beck-Nielsen**

(10) **Patent No.:** **US 8,628,472 B2**  
(45) **Date of Patent:** **\*Jan. 14, 2014**

- (54) **METHOD AND APPARATUS FOR PREDICTION AND WARNING OF HYPOGLYCAEMIC ATTACK**
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- (\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **13/398,382**

(22) Filed: **Feb. 16, 2012**

(65) **Prior Publication Data**  
US 2012/0209133 A1 Aug. 16, 2012

**Related U.S. Application Data**

(63) Continuation of application No. 11/793,271, filed as application No. PCT/DK2005/000739 on Nov. 21, 2005, now Pat. No. 8,118,741.

(30) **Foreign Application Priority Data**  
Dec. 20, 2004 (DK) ..... 2004 01955

- (51) **Int. Cl.**  
**A61B 5/00** (2006.01)
- (52) **U.S. Cl.**  
USPC ..... **600/365; 600/544; 600/545; 600/347**
- (58) **Field of Classification Search**  
USPC ..... **600/365, 544, 545**  
See application file for complete search history.

(56) **References Cited**  
U.S. PATENT DOCUMENTS

2,046,188 A	6/1936	Spencer
2,220,584 A	11/1940	Seeley
2,346,195 A	4/1944	Spalding
2,413,490 A	12/1946	Evans
2,747,832 A	5/1956	Vischer, Jr.
3,057,747 A	10/1962	Hargreaves

(Continued)

FOREIGN PATENT DOCUMENTS

DE	10248894 A1	5/2004
EP	1419731 A1	5/2004
WO	2005037092 A1	4/2005

OTHER PUBLICATIONS

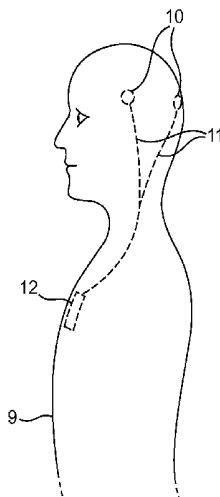
Bendtsen, I., et al., "Nocturnal Electrocephalogram Registration in Type 1 Insulin-Dependent Diabetic Patients with Hypoglycaemia," *Diabetologia* 1991, vol. 34, nr. 10, pp. 750-756, ISSN 0012-186X.

(Continued)

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(57) **ABSTRACT**  
A method and device for warning diabetics of imminent hypoglycaemic attacks. EEG signals are collected from a person using subcutaneously placed electrodes and the signals are led via wires drawn under the person's skin to a subcutaneously placed signal interface unit from where they are transmitted to an externally worn signal processing unit. The signal processing analyzes the EEG signals and when the pre-seizure characteristics signal changes are detected, a warning signal is given to the person from an alarm giver built into the signal processing unit, e.g., in form of a vibrator. When a person detects a warning signal, the person can prevent the hypoglycaemic attack by, e.g., consuming a sugary food.

**10 Claims, 3 Drawing Sheets**



(56)

References Cited

U.S. PATENT DOCUMENTS

3,686,382	A	8/1972	Fairbanks	
3,709,204	A	1/1973	Noponen	
3,719,320	A	3/1973	Morris et al.	
3,799,432	A	3/1974	Schneider	
4,295,474	A	10/1981	Fischell	
4,615,482	A	10/1986	Marusiak et al.	
4,734,559	A	3/1988	Fortune et al.	
4,830,277	A	5/1989	Hood	
6,354,299	B1	3/2002	Fischell et al.	
6,360,122	B1	3/2002	Fischell et al.	
6,572,542	B1	6/2003	Houben	
6,583,796	B2	6/2003	Jamar et al.	
7,029,443	B2	4/2006	Kroll	
7,136,703	B1	11/2006	Cappa et al.	
7,299,085	B2	11/2007	Bergelson et al.	
7,299,086	B2	11/2007	McCabe et al.	
8,118,741	B2*	2/2012	Beck-Nielsen	600/365
8,348,842	B1*	1/2013	Osorio et al.	600/365
2002/0099412	A1	7/2002	Fischell et al.	
2006/0020184	A1*	1/2006	Woods et al.	600/319
2006/0049957	A1	3/2006	Surgenor et al.	
2007/0016117	A1	1/2007	Sliwa, Jr. et al.	
2007/0225577	A1*	9/2007	Mathan	600/301
2008/0183097	A1	7/2008	Leyde et al.	
2008/0234598	A1	9/2008	Snyder et al.	

OTHER PUBLICATIONS

Bjorgaas, M. et al., "Quantitative EEG During Controlled Hypoglycaemia in Diabetic and Non-Diabetic Children," Diabetic

Medicine 1998, vol. 15, nr. 1, pp. 30-37, ISSN 0742-3071(Print).  
 Heger, G. et al., "Monitoring Set-Up for Selection of Parameters for Detection of Hypoglycaemia in Diabetic Patients," Medical & Biological Engineering & Computing 1996, vol. 34, pp. 69-75.  
 Howorka, K. et al., "Severe Hypoglycaemia Unawareness is Associated With an Early Increase in Vigilance During Hypoglycaemia,"  
 Tupola, S. et al., "Abnormal Electroencephalogram at Diagnosis of Insulin-Dependent Diabetes Mellitus May Predict Severe Symptoms of Hypoglycemia in Children," Journal of Pediatrics, Dec. 1998, vol. 133, nr. 6, pp. 792-794, ISSN 0022-3476.  
 Published PCT International Search Report; PCT/DK2005/000739, dated Apr. 11, 2006.  
 Stig Pramming et al, "Glycaemic threshold for changes in electroencephalograms during hypoglaecemia in patients with insulin dependent diabetes," British Medical Journal, vol. 206, Mar. 5, 1998, pp. 665-667.  
 G. Tribl et al, "EEG topography during insulin-induced hypoglycemia," European Neurology, 1996, 36(5) pp. 303-309.  
 Oxford University, Oxford Press, Oxford English Dictionary, definition of 'clamp' [online], [retrieved on Dec. 28, 2010]. Retrieved from the Internet:<URL:http://www.oed.com:80/Entry/33715.  
 Supplementary European Search Report for EP05803996 dated Oct. 4, 2011.  
 F. Iaione et al, "Methodology for hypoglycaemia detection based on the processing, analysis and classification of the electroencephalogram", Medical & Biological Engineering & Computing, vol. 43, No. 4, Jul. 1 2005, pp. 501-507 XP001508909.  
 J. Gade et al, Detection of EEG Patterns Related to Nocturnal Hypoglycemia, Methods of Information in Medicine, vol. 33, No. 1, Mar. 1994, pp. 153-156 XP000002659531.

\* cited by examiner

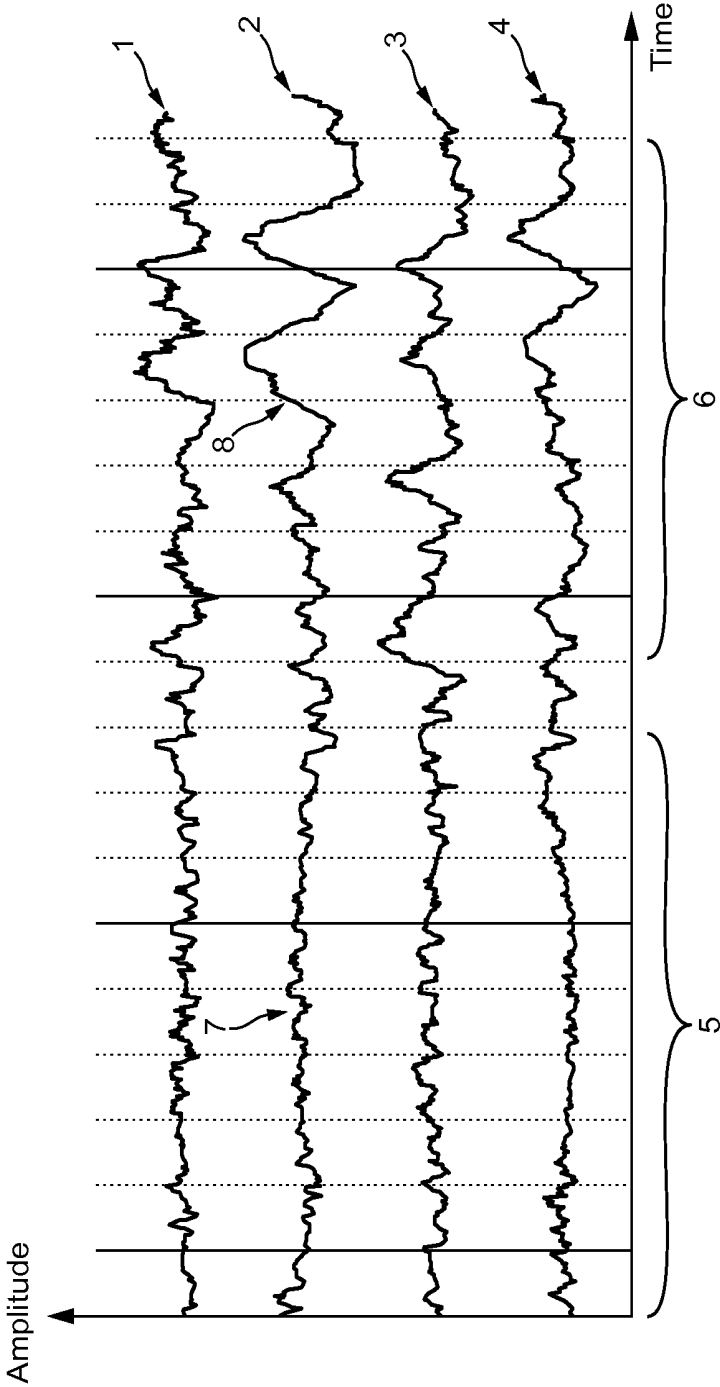


FIG. 1

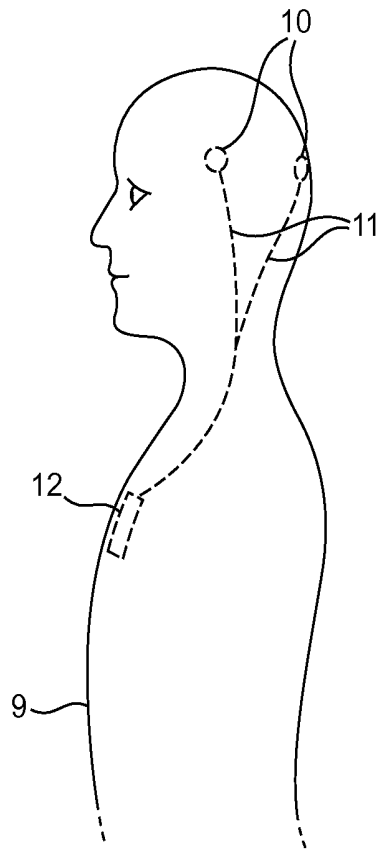


FIG. 2

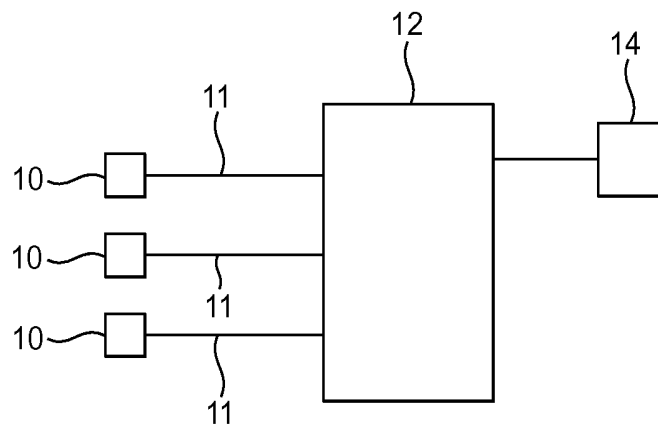


FIG. 3

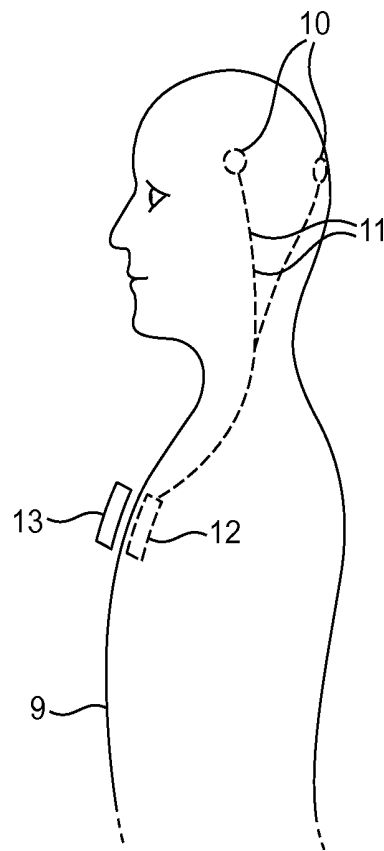


FIG. 4

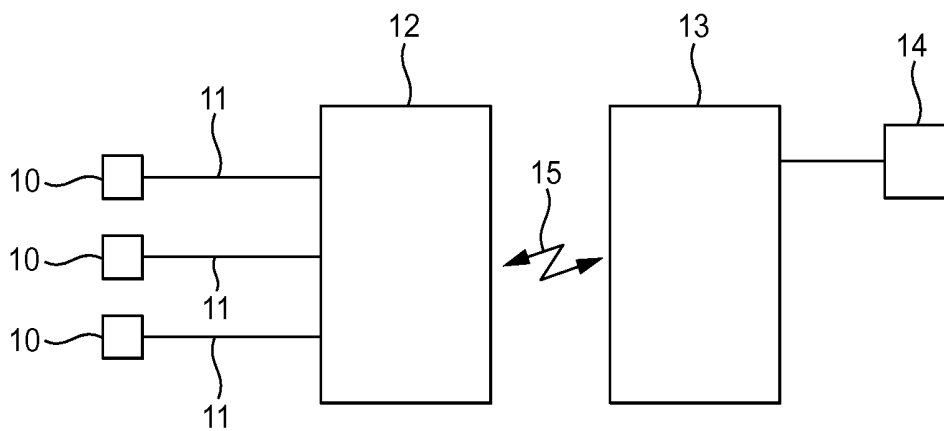


FIG. 5

## METHOD AND APPARATUS FOR PREDICTION AND WARNING OF HYPOGLYCAEMIC ATTACK

### CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation of U.S. application Ser. No. 11/793, 271 filed Feb. 19, 2008, which is the national stage of PCT/DK2005/000739 filed Nov. 21, 2005, which claims priority from Danish Application PA200401955 dated Dec. 20, 2004, the disclosures of which are incorporated in their entirety herein.

### BACKGROUND OF THE INVENTION

The invention relates to a method of predicting and warning of hypoglycaemic attacks for people such as diabetics.

Moreover the invention relates a device for prediction and warning of hypoglycaemic attacks for people such as diabetics.

Hypoglycaemic attacks occur as a result of too low a blood sugar concentration, which is mostly a problem for diabetics, who are treated with insulin or other blood sugar regulating medical drugs.

The attacks can be highly severe and often entail unconsciousness.

The risk of an attack therefore often limits the possible activities of the people, which furthermore decreases the quality of life for these people.

Attacks can be prevented in a simple way if the people e.g. consume appropriate food when the glucose values become critical.

The problem is however that many in the risk group cannot by themselves feel when the blood sugar concentration reaches a critically low level with risk of an attack.

The number of people in the risk group is approximately 1 million.

There are known methods and devices for prediction of hypoglycaemic attacks.

In U.S. Pat. No. 6,572,542 a method and a device are described, which among others have the purpose of warning of hypoglycaemic attacks. The known technique primarily uses registration of changes in a person's ECG (electrocardiographic) signals as a result of a critically low level of blood sugar, to emit a signal of warning. The changes in the ECG signals are in an example described in the patent specification linked with EEG (electroencephalographic) signals from the person in order to clarify the blood sugar dependent changes in the ECG signal.

It has been found, however, that this prior art involves some drawbacks.

Since the technique requires signal analysis of both the ECG and EEG signals from the person on whom the measurements are being taken, the algorithms for calculating become relatively complex, which specifies high demands for hardware processing power and at the same time demands a high power draw.

If this is linked together with the fact that a relatively high number of electrodes for both ECG and EEG signal collection are necessary, it results in a relatively big and complex product, which is difficult to apply in the daily life of a person.

It is furthermore generally known that the greater complexity a product contains, the greater is the risk that the product will become unstable.

The mentioned drawbacks have overall meant that the hitherto known technique has not resulted in the manufacturing of products, which can enhance the quality of life for wide parts of the risk group.

### SUMMARY OF THE INVENTION

It is therefore a purpose of the invention to improve the known method and the known device. The object of the invention is achieved by a method for warning of hypoglycaemic attacks, which is characterized in that the warning is based on analysis of one or more EEG signals from the person.

Hereby, it is thus possible to reduce the number of electrodes, since the ECG signal is not going to be used, simultaneously the complexity is reduced, and the demands for processing power and the need for power draw is also reduced.

In this way it is possible to manufacture a simple, robust and highly portable alarm system, which basically everyone in the seizure risk group can have advantage of. It is furthermore a preferred feature of the invention that the warning is given after signal analytic identification of pre-seizure characteristic EEG changes such as decrease in frequency and increase in amplitude.

Tests have shown that the EEG signal changes in a simple and characteristic way in the time leading to a hypoglycaemic attack. A signal analytic identification of the characteristic changes in the frequency and amplitude has shown to be a good, safe and robust basis for release of an alarm signal.

The alarm signal can be released in sufficient time before a seizure is triggered, so that the person can easily have time to prevent an attack.

It is furthermore a preferred characteristic of the invention that the EEG signals are registered from two or more electrodes placed intracranially or extracranially on the skin surface or subcutaneously. By placing the EEG electrodes outside the skin the electrode to skin contact impedance and thus the signal detection will vary with e.g. the moisture of the skin and the head movement of the patient. If the electrodes are placed subcutaneously the location will be permanent and the electro impedance more stable, which makes the whole warning system more robust.

It is furthermore a preferred characteristic of the invention that the EEG signals from the electrodes are transmitted via subcutaneously drawn wires to a subcutaneous placed signal interface unit or signal-processing and alarm unit.

With these characteristics it is among other things made possible to manufacture a warning system for hypoglycaemic attacks, which is not visible, since the whole unit can be placed subcutaneously.

Further preferred embodiments of the method of the invention are described below

As mentioned the invention also relates to a device.

This is characterized in that the device collects EEG signals from two or more electrodes and by signal analysis identifies pre-seizure characteristic changes in the EEG signal such as declining frequency content and increasing amplitude and after identification of the characteristic EEG changes delivers a warning signal.

The device thereby becomes simple, robust and highly portable.

Further preferred embodiments of the device are also described below.

### BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be explained more fully with reference to the drawings, in which:

FIG. 1 shows an example of EEG signal sequences with both normal signals and the pre-seizure characteristic changes.

FIG. 2 shows a person with a subcutaneously placed hypoglycaemic seizure warning system.

FIG. 3 shows a block diagram of the warning system from FIG. 2.

FIG. 4 shows a person with a warning system, which is partly subcutaneously placed and is partly external.

FIG. 5 shows a block diagram of the warning system shown in FIG. 4.

#### DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

In FIG. 1 is shown part of four EEG signals derived from a person in advance of a hypoglycaemic attack. The four signals, which originate from different electrodes placed on the person's head skin, have been given the numbers 1 through 4.

The EEG signals are drawn in a co-ordinate system with indication of time on the horizontal axis and the signal amplitude on the vertical axis.

The time sequence specified with 5 shows a normal process of the EEG signals, while the time sequence specified with 6 shows the EEG signal in advance of a hypoglycaemic attack.

In the normal time phase 5 the EEG signals as shown with 7 are characterized in that they oscillate with a given mean frequency and with a given mean amplitude, which is comparable for all the four shown EEG signal derivations. In the pre-seizure time phase 6 it is clearly seen, as indicated with 8, that the EEG signal in this phase is changed both significantly and characteristically. The wavelength of the signal becomes notably increased, similar to a comparable frequency reduction, concurrent with the signal amplitude being strongly increased.

The listed characteristic changes in the EEG signals in the pre-seizure phase often occur several minutes before a hypoglycaemic attack is triggered. Hereby there is sufficient time to give an early warning to the person on the basis of the detected EEG signal changes. The person can then prevent the seizure, e.g. by consuming a sugary food product.

As it appears from FIG. 1 there are relatively notable changes in the EEG signal in the phase in advance of a hypoglycaemic attack. For the same reason it is relatively simple to detect these changes by the use of appropriate signal analysis algorithms.

The signal analysis can be performed in both the time- and frequency domain and can be based on more in other applications well-proven algorithms such as e.g. Bayes' methods, logistic regression or neural networks. Tests have shown that algorithms based on Bayes' methods, including Bayesian classifier has been especially appropriate in order to, with high precision, detect the pre-seizure characteristic changes in the EEG signals.

It can be appropriate to build in dynamics in the signal processing algorithms in such a way that these are continuously adapted to the single person, who is going to be warned. Such a dynamic adaptation of the warning algorithms is a part of the present invention. In order to achieve the best possible result of the signal processing it is appropriate to pre-filter the EEG signals including e.g. by band-pass filtering these, in order to eliminate noise from other signal sources in the highest possible extent.

Regarding signal analysis, it is always aimed for to get the best possible signal/noise ratio. It will therefore be optimal to place the signal electrodes directly in the brain, from where the signal activity, which it is desired to measure, originates.

Tests have shown that recording of the blood sugar concentration occurs in the brain's hypothalamus area.

It is thus a part of the present invention to place electrodes directly in the hypothalamus area in order to achieve the best possible signal/noise ratio on signals for warning of hypoglycaemic attacks.

FIG. 2 shows a person 9 provided with a warning system in accordance to the invention. Subcutaneously placed electrodes 10 record the EEG signals, which via wires 11, drawn under the skin, are lead to a signal processing unit 12, which is also placed below the skin.

The signal processing unit 12 processes via the implemented signal processing algorithms the measured EEG signals, and when the previously mentioned pre-seizure characteristic changes in the signals are detected, the unit 12 delivers a warning signal to the person 9.

The unit 12 is in FIG. 2 shown placed in the person's upper chest region, but can obviously also be placed a random place, e.g. behind the neck or where it seems the most appropriate for the single individual. A block diagram for the system shown in FIG. 2 appears in FIG. 3.

Since the unit 12 is placed below the skin the alarm to the person can e.g. be delivered via a vibrator 14 integrated in the unit 12.

In FIG. 3 is shown 3 EEG electrodes from where the signals are lead to the signal processing unit 12. In practice any number of electrodes from two and more can be used, and the shown number is therefore not any limitation of the invention.

Even though the system in terms of signal is designed in order to achieve as high a signal/noise ratio as possible, there can probably arise situations where loud noise from the environment will reduce the possibility of sufficiently detecting the characteristic pre-seizure changes in the EEG signals.

In such a situation the system unit 12 can be programmed to deliver a warning signal to the person 9, which indicates that the seizure surveillance efficiency is lowered because of external noise. Such a warning signal, which must be separable from the normal pre-attack warning signal, can help the person, if possible, to remove or reduce the external noise source.

By differentiating the signal giver, e.g. by giving each signal a particular vibration frequency, several types of alarm- or information signals can be delivered, e.g. about the charging state of the energy supply.

The unit 12 must in order to function optimally be provided with electronics for adaptation of impedance for the electrodes and signal boosters and means for digitization of the analogue EEG signals. The digitized signals are subsequently processed in a calculation circuit such as a digital signal processor. The unit 12 can be provided with a battery for energy supply.

The service life of the battery obviously depends of the choice of the electronic components, which are a part of the unit 12.

With present-day technique a service life of several years will be achievable. The service life and the size of the product will, however, to a certain extent always be proportional.

In those cases where e.g. the product's size is of decisive importance, it can be an advantage to split the system into a part, which is placed under the patient's skin and which only demands a minimum of power and an external part, which demands more power.

A warning system, which consists of an internally placed part below the patient's skin and an external part, is shown in FIG. 4.

In a system as shown in FIG. 4, the internal unit 12 can solely consist of an interface unit with a low power draw,

which gathers the EEG signal from the electrodes and transmits them wirelessly through the skin to an external unit 13, which can e.g. be placed in the breast pocket of a shirt.

A block diagram of the system shown in FIG. 4 is seen in FIG. 5.

The unit 13 can in this example contain the more power demanding components, including the signal processing unit and the alarm signal giver 14, and electronics for wireless communication with the unit 12, which is placed under the skin.

When the signal giver is externally placed, the alarm, which is delivered from 14, can e.g. be an acoustic warning device as an alternative to a vibrator.

It is also possible to have a configuration like the one shown in FIG. 4, where the unit 12 is the complete unit with integrated signal processor and alarm giver, and where 13 in the principle is just a battery charging circuit, which wirelessly through the skin can charge the batteries in the unit 12. Such a battery charging can be produced on the basis of known techniques for wireless charging of batteries, e.g. through magnetic interaction of spools in respectively the charger/sender 13 and the receiver 12, which is going to be charged.

In case the unit 12 is provided with a signal processor, it will often be appropriate to provide the unit 12 with a communication circuit so that the signal processing program can wirelessly be updated from an external computer unit. With the application of a wireless communication circuit, it will at the same time be possible to transfer data from the unit 12 to the external unit 13 or one or more substituting external units in the form of data collection units or computers.

The present invention covers all combinations of system compositions, which directly or indirectly can be derived from the drawings 2 through 5 and the supplemental description to these.

What is claimed:

1. A method for warning of imminent hypoglycaemic attacks for people such as diabetics, the warning being based on analysis of one or more Electroencephalography (EEG) signals from a person without the use of Electrocardiography (ECG) signals, said method comprising:

providing the person with a portable hypoglycaemic attack warning system comprising EEG signal gathering electrodes and a signal processing unit,

receiving in said signal processing unit EEG signals derived from said signal gathering electrodes,

performing analysis of said signals for identifying characteristics therein indicative of an imminent hypoglycaemic attack by signal analytic identification of pre-seizure characteristic EEG changes which include at least one of decrease in frequency and increase in amplitude,

and giving a warning to said person that a said attack is determined to be imminent when said characteristics are identified in said EEG signals.

2. The method according to claim 1, wherein said EEG signals are received first in an interface unit connected to said electrodes and comprising a wireless transmitter, and are wirelessly transmitted by said wireless transmitter of said interface unit to said signal processing unit.

3. The method according to claim 2, wherein said interface unit is implanted beneath the skin of the person and said signal processing unit is externally worn.

4. The method according to claim 2, wherein the electrodes are connected to said interface unit by subcutaneously drawn wires and said interface unit is subcutaneously placed.

5. The method according to claim 1, wherein the EEG signals are registered from two or more said electrodes placed intracranially, or placed extracranially on or below the skin surface.

6. The method according to claim 1, wherein the EEG signals prior to the signal analysis are filtered through band-pass filtering.

7. The method according to claim 1, wherein the signal analysis of the EEG signal is carried out in the time domain or in the frequency domain.

8. The method according to claim 1, wherein pre-seizure characteristic EEG signal changes are detected by application of signal analysis based on a logistic regression algorithm, a Bayesian classifier algorithm, or a neural network algorithm.

9. A hypoglycaemic attack warning device for warning of an imminent hypoglycaemic attacks for people such as diabetics, said device comprising:

Electroencephalography (EEG) signal gathering electrodes and a signal processing unit connected to receive in said signal processing unit EEG signals derived from said signal gathering electrodes in use,

said signal processing unit being adapted to perform analysis of said signals for identifying characteristics therein indicative of an imminent hypoglycaemic attack by signal analytic identification of pre-seizure characteristic EEG changes which include at least one of decrease in frequency and increase in amplitude,

and an alarm unit connected to said signal processing unit and adapted to give a warning that a said attack is determined to be imminent when said characteristics are identified in said EEG signals.

10. The device according to claim 9, further comprising an interface unit physically connected to said electrodes and comprising a wireless transmitter for transmitting EEG signals received from said electrodes in use, wherein said signal processing unit comprises a wireless receiver for receiving said transmitted EEG signals for processing.

\* \* \* \* \*

专利名称(译)	用于预测和警告低血糖发作的方法和装置		
公开(公告)号	<a href="#">US8628472</a>	公开(公告)日	2014-01-14
申请号	US13/398382	申请日	2012-02-16
[标]申请(专利权)人(译)	HYPO SAFE		
申请(专利权)人(译)	HYPO-SAFE A / S		
当前申请(专利权)人(译)	HYPO-SAFE A / S		
[标]发明人	BECK NIELSEN HENNING		
发明人	BECK-NIELSEN, HENNING		
IPC分类号	A61B5/00		
CPC分类号	A61B5/7264 A61B5/14532 A61B5/048 A61B5/0031 A61B5/4094		
代理机构(译)	萨格鲁MION, PLLC		
优先权	PCT/DK2005/000739 2005-11-21 WO 200401955 2004-12-20 DK		
其他公开文献	US20120209133A1		
外部链接	<a href="#">Espacenet</a> <a href="#">USPTO</a>		

摘要(译)

一种用于警告即将发生的低血糖发作的糖尿病患者的方法和装置。使用皮下放置的电极从人收集EEG信号，并且通过在人的皮肤下绘制的线将信号引导到皮下放置的信号接口单元，从那里它们被传输到外部佩戴的信号处理单元。信号处理分析EEG信号，并且当检测到癫痫发作前特征信号变化时，从内置于信号处理单元中的警报器给予人警告信号，例如以振动器的形式。当人检测到警告信号时，该人可以通过例如食用含糖食物来防止低血糖症发作。

