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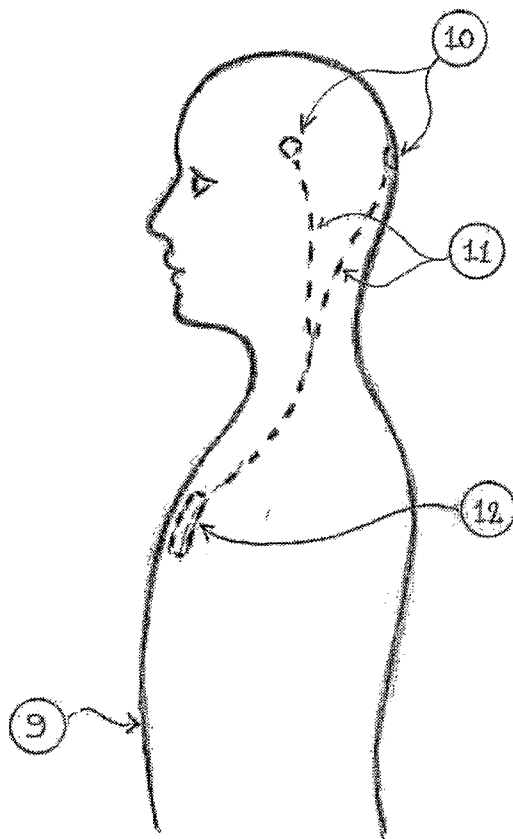
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(54) Title: METHOD AND APPARATUS FOR PREDICTION AND WARNING OF HYPOGLYCAEMIC ATTACK



(57) Abstract: The present invention includes a method and device for warning of hypoglycaemic attacks, which is a big problem for especially diabetics, who are in insulin treatment. It is estimated that about 1 million people have a decreased quality of life as a result of hypoglycaemic attacks. The invention collects EEG signals from people, who must be supervised and analyses these in order to detect characteristic changes in the EEG signals, which occurs in advance of a hypoglycaemic attack. In a preferred embodiment the EEG signals are collected with subcutaneously placed electrodes and the signals are lead via wires drawn under the person's skin to a similar subcutaneously placed signal processing unit. The signal processing analyses 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 build 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.

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

Method and apparatus for prediction and warning of hypoglycaemic attack.

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

5

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

10

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.

15

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

20

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.

25

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

In US patent nr. 6,572,542 a method and a device are described, which among others have the purpose of warning hypoglycaemic attacks.

30

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
5 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.

10 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, who is being measured on, the algorithms for calculating become relatively complex, which specifies high demands for hardware processing power and at the same time demands a high power
15 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
20 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.

25 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.

30 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 of the type stated in the introductory portion of claim 1, which is characterized in that the warning is based on analysis of one or more EEG signals from the person.

5 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.

10 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.

As stated in claim 2 it is furthermore a special feature of the invention that
15 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
20 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.

25 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.

In claim 3 is stated that it is furthermore a special characteristic of the invention that the EEG signals are registered from two or more electrodes
30 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 subcutaneous the location will be permanent and the electro impedance more stable, which makes the whole warning system more robust.

It is stated in claim 4 that it is furthermore a 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 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 defined in claims 5 through 8.

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 defined in claim 10.

30

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.

5

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.

10

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.

15

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.

20

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.

25

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.

30

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 occurs 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. Baye's methods, logistic regression or neural networks. Tests have shown that algorithms based on Baye's 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.

5

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.

10

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.

20

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.

25

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.

30

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.

5

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.

10

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.

15

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.

20

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.

25

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.

30

The unit 12 can be provided with a battery for energy supply.

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

10 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.

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

20 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.

25 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.

30 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.

5 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
10 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
15 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.

20 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.

25

30

PATENT CLAIMS

- 5 1. Method for warning of hypoglycaemic attacks for people such as diabetics c h a r a c t e r i z e d in that the warning is based on analysis of one or more EEG signals from the person.
- 10 2. Method for warning of hypoglycaemic attacks according to claim 1 c h a r a c t e r i z e d in that the warning is given after signal analytic identification of pre-seizure characteristic EEG changes such as decrease in frequency and increase in amplitude.
- 15 3. Method for warning of hypoglycaemic attacks according to claim 1 or 2 c h a r a c t e r i z e d in that the EEG signals are registered from two or more electrodes placed intracranially or extracranially on the skin surface or subcutaneously.
- 20 4. Method for warning of hypoglycaemic attacks according to claim 3 c h a r a c t e r i z e d in that 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.
- 25 5. Method for warning of hypoglycaemic attacks according to claim 4 c h a r a c t e r i z e d in that the EEG signals from the signal interface unit communicates with a highly portable signal processing device from which the warning signal can be given.
- 30 6. Method for warning of hypoglycaemic attacks according one or more of claims 1-5 c h a r a c t e r i z e d in that the EEG signals in advance of the signal analysis are filtered through e.g. band-pass filtering

- 5 7. Method for warning of hypoglycaemic attacks according to one or more of claims 1-6 c h a r a c t e r i z e d in that the signal analysis of the EEG signal is carried out in the time- or frequency domain.
- 10 8. Method for warning of hypoglycaemic attacks according to one or more of claims 1-7 c h a r a c t e r i z e d in that the pre-seizure characteristic EEG signal changes are detected by application of signal analysis based on algorithms such as Baye's methods including bayesian classifier, logistic regression or neural network.
- 15 9. Device for warning of hypoglycaemic attacks for people such as diabetics c h a r a c t e r i z e d in that the device collects the EEG signal from 2 or more electrodes and by signal analysis identifies pre-seizure characteristic changes in the EEG signal such as a decrease in frequency content and an increase in amplitude and gives a warning signal after identification of the characteristic EEG changes.
- 20 10. Device for warning of hypoglycaemic attacks for people such as diabetics in accordance to claim 9 c h a r a c t e r i z e d in that the device is portable and fully or partly is placed subcutaneously.
- 25

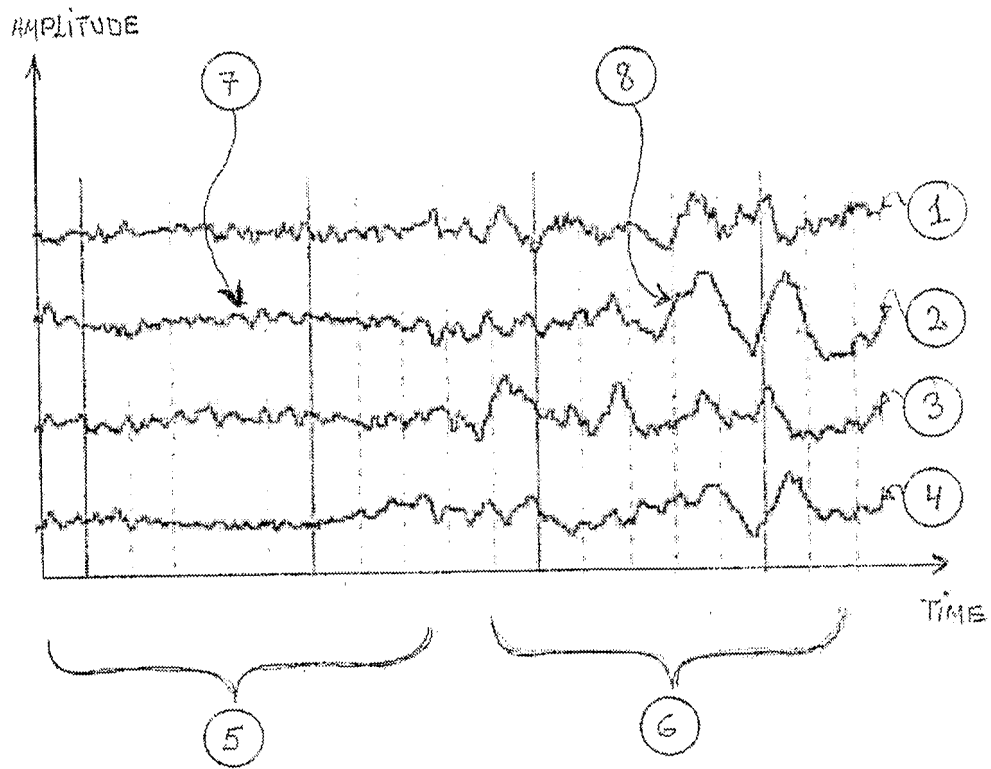


Fig. 1

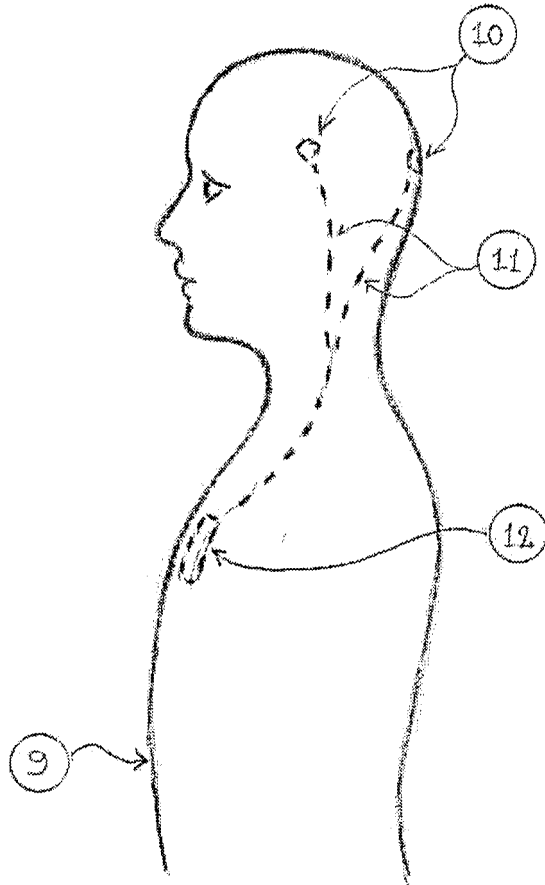


Fig. 2

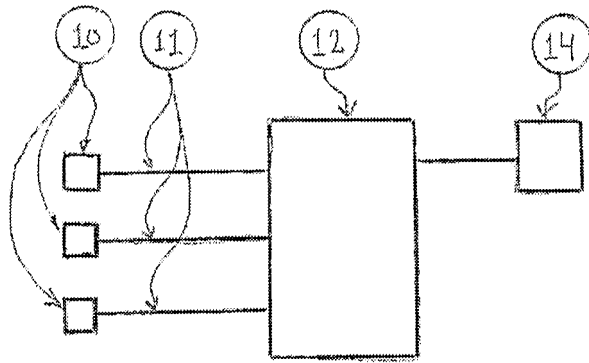


Fig. 3

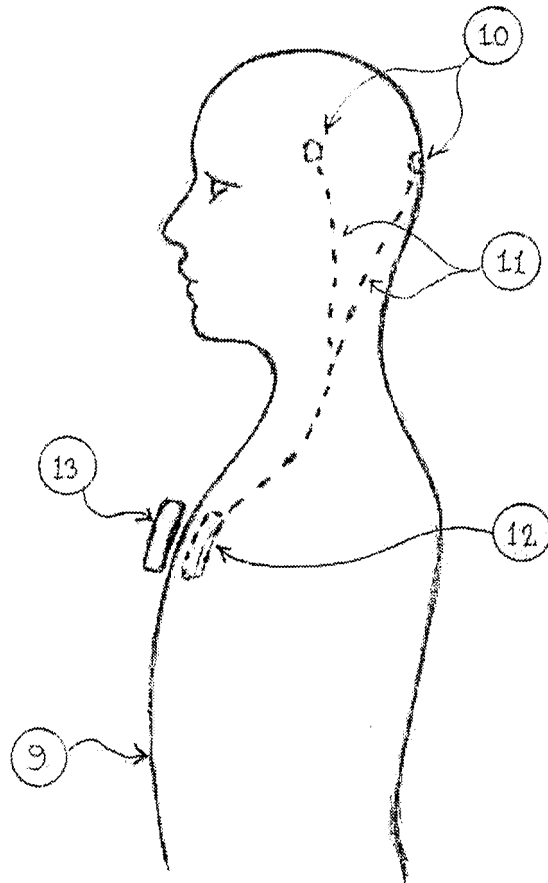


Fig. 4

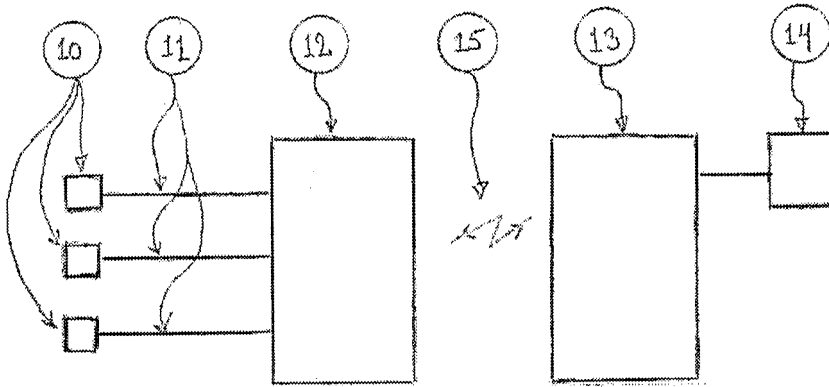


Fig. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2005/000739

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6572542 B1 (HOUBEN, R ET AL), 3 June 2003 (03.06.2003), column 5, line 8 - line 20; column 5, line 60 - line 61; column 11, line 14 - line 15, column 11, line 33 - line 57; column 17, line 44 - line 66; column 20, line 50 - line 52; column 22, line 12 - line 16, abstract	1
Y	--	2-10
X	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, pages 792-794, ISSN 0022-3476. See page 794 and abstract	1
Y	--	2-10

Further documents are listed in the continuation of Box C.

See patent family annex.

<p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK2005/000739

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BJORGAAS, M et al: "Quantitative EEG during controlled hypoglycaemia in diabetic and non-diabetic children". Diabetic medicine 1998, vol.15, nr.1, pages 30-37, ISSN 0742-3071 (Print). See page 32, figure 3 and abstract	1
Y	--	2-10
A	BENDTSON, I et al: " Nocturnal electroencephalogram registrations in type 1 insulin-dependent diabetic patients with hypoglycaemia". Diabetologia 1991, vol.34, nr.10, pages 750-756, ISSN 0012-186X. See abstract	1-10
A	HOWORKA, K et al: "Severe hypoglycaemia unawareness is associated with an early decrease in vigilance during hypohlycaemia". Psychoneuroendocrinology 1996, vol.21, nr.3, pages 295-312. See abstract	1-10
P,A	WO 2005037092 A1 (RANDLØV, J ET AL), 28 April 2005 (28.04.2005), claim 13, abstract	1-10
A	EP 1419731 A1 (PACESETTER, INC), 19 May 2004 (19.05.2004), abstract	1-10
A	DE 10248894 A1 (NIEHAUS, M, DR), 13 May 2004 (13.05.2004), abstract	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

04/03/2006

International application No.

PCT/DK2005/000739

US 6572542 B1 03/06/2003 NONE

WO 2005037092 A1 28/04/2005 NONE

EP 1419731 A1 19/05/2004 US 20040077962 A 22/04/2004
US 20040078065 A 22/04/2004

DE 10248894 A1 13/05/2004 NONE

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International patent classification (IPC)

A61B 5/00 (2006.01)

A61B 5/0476 (2006.01)

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Cited literature, if any, will be enclosed in paper form.

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	EP1827209A1	公开(公告)日	2007-09-05
申请号	EP2005803996	申请日	2005-11-21
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申请(专利权)人(译)	HYPOSAFE A / S		
当前申请(专利权)人(译)	HYPOSAFE A / S		
[标]发明人	BECK NIELSEN HENNING		
发明人	BECK-NIELSEN, HENNING		
IPC分类号	A61B5/00 A61B5/0476 A61B5/048 A61B5/145		
CPC分类号	A61B5/048 A61B5/0031 A61B5/14532 A61B5/4094 A61B5/7264		
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其他公开文献	EP1827209B1 EP1827209A4		
外部链接	Espacenet		

摘要(译)

本发明包括用于警告低血糖发作的方法和装置，这对于尤其是胰岛素治疗的糖尿病患者来说是一个大问题。据估计，由于低血糖发作，约有100万人的生活质量下降。本发明从人们收集EEG信号，他们必须受到监督并对其进行分析，以便检测在低血糖发作之前发生的EEG信号的特征变化。在优选实施例中，利用皮下放置的电极收集EEG信号，并且通过在人的皮肤下绘制的线将信号引导到类似的皮下放置的信号处理单元。信号处理分析EEG信号，并且当检测到癫痫发作前特征信号改变时，从警报器构建者向信号处理单元提供警告信号，例如，信号处理单元。以振动器的形式。当一个人检测到警告信号时，该人可以通过例如人防止低血糖发作。食用含糖食物。