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Granger et al.

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(54) **METHOD AND APPARATUS FOR ASSESSING SUSCEPTIBILITY TO STROKE**

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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.

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(22) Filed: **Jul. 19, 2001**

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Related U.S. Application Data

(63) Continuation-in-part of application No. 09/452,202, filed on Dec. 2, 1999, now Pat. No. 6,280,393.

(51) **Int. Cl.**⁷ **A61B 5/00**

(52) **U.S. Cl.** **600/544**

(58) **Field of Search** 600/544, 545, 600/547

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(57) **ABSTRACT**

A method is described for facilitating assessment of susceptibility to stroke. Electrical signals are collected from the brain of a patient under assessment. Data corresponding to the signals is then compared to a standard. The standard may represent a neural electrical signal taken from a person known to be susceptible to stroke. A positive comparison suggests susceptibility of the patient to stroke. The comparison can be used to characterize neural blood flow and the degree of susceptibility. This can be used in determining the need for additional testing and/or appropriate therapy. This information can also be used in categorizing the patient to determine enrollment in clinical trials. Alternatively, the standard represents a neural signal taken at an earlier time from the patient under assessment. A positive comparison suggests that the condition of the patient is unchanged. A negative comparison suggests that the neural activity of the patient has changed, implying changes in neural blood flow. This can suggest susceptibility.

16 Claims, 3 Drawing Sheets

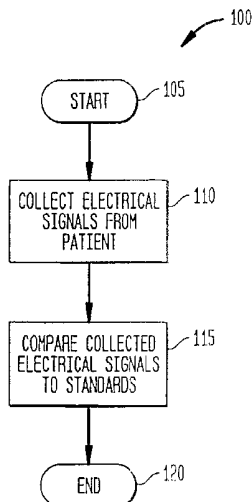


FIG. 1

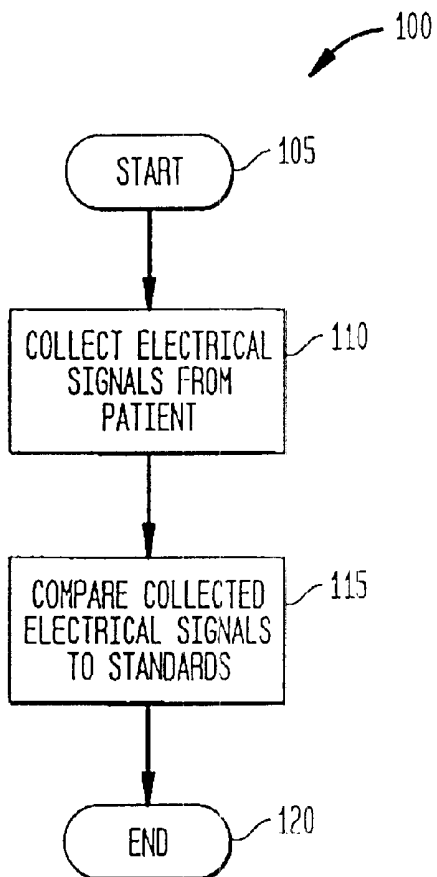


FIG. 2

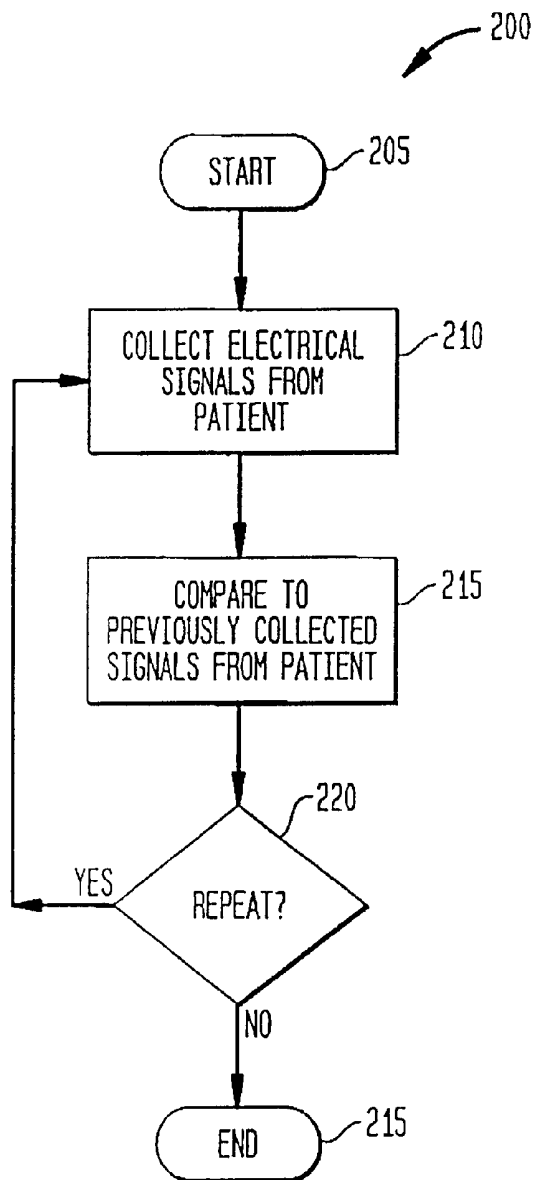


FIG. 3

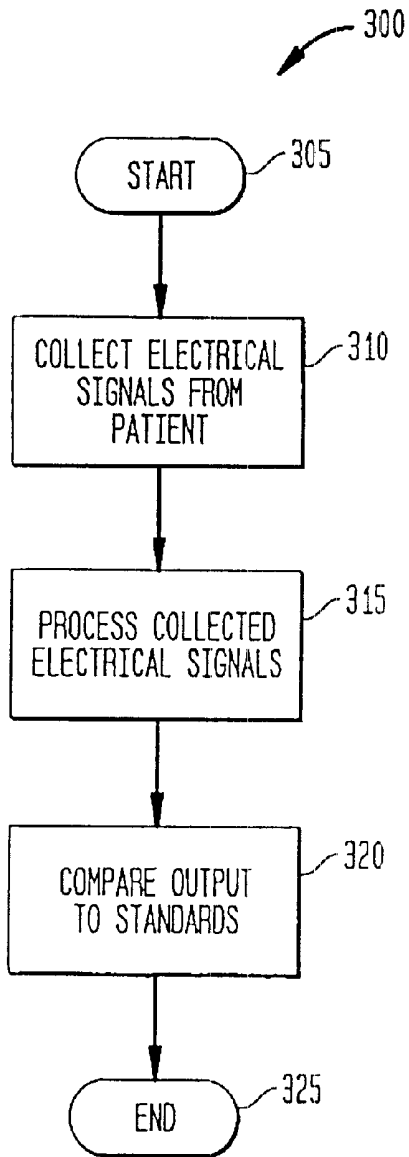


FIG. 4

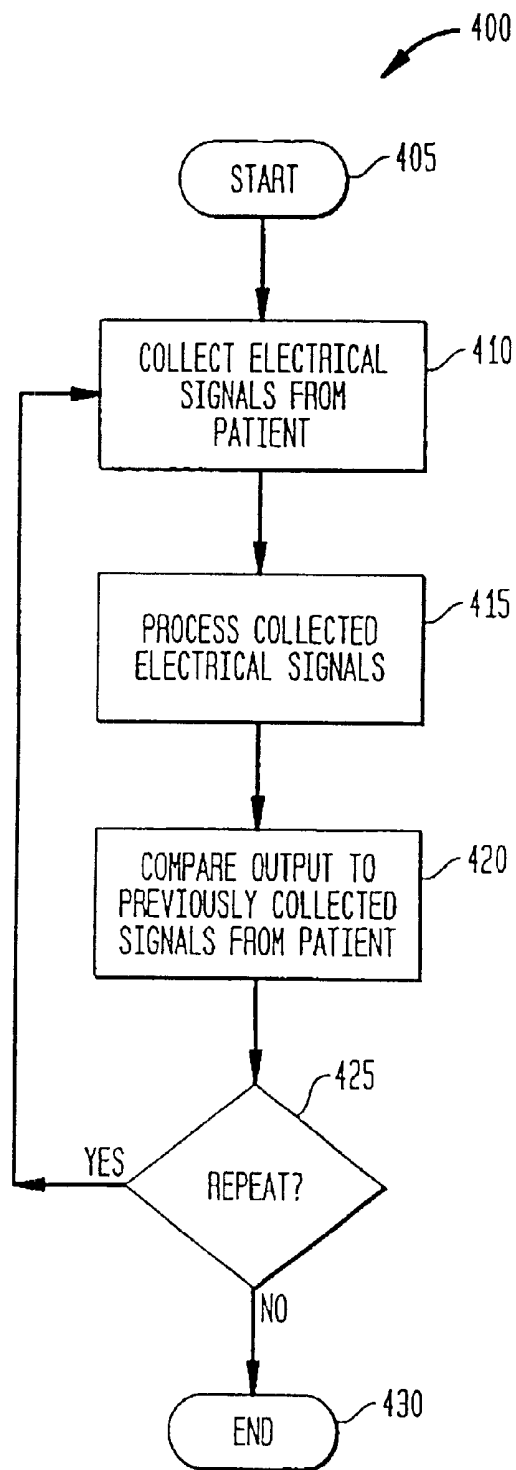


FIG. 5A

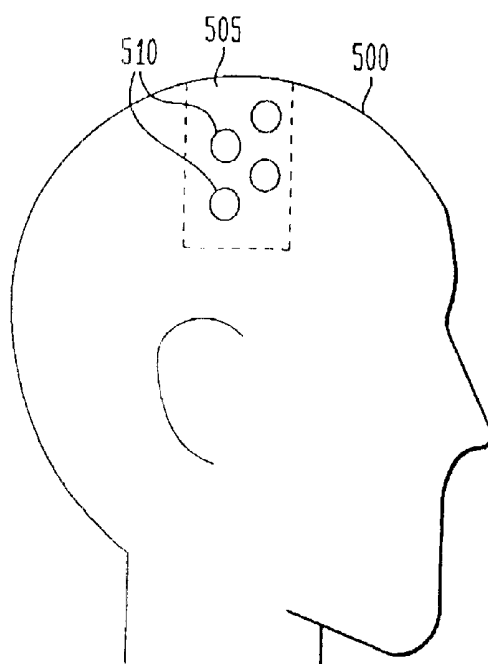
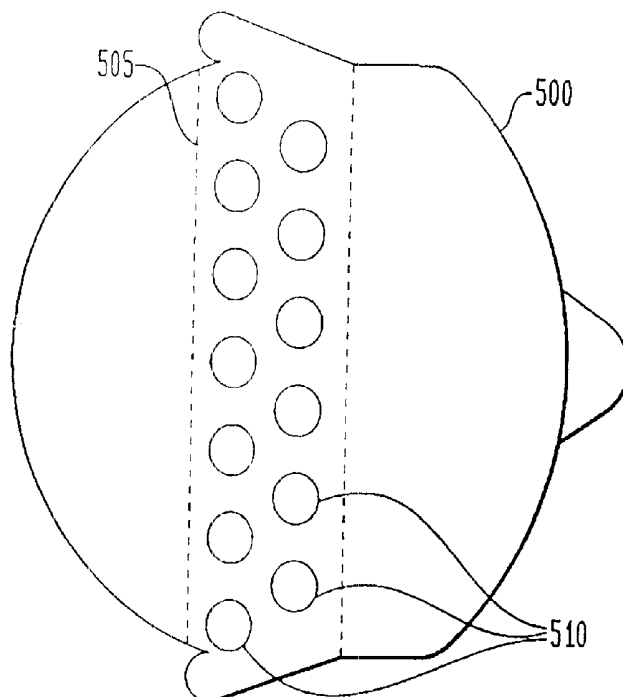


FIG. 5B



METHOD AND APPARATUS FOR ASSESSING SUSCEPTIBILITY TO STROKE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 09/452,202, filed Dec. 2, 1999, now U.S. Pat. No. 6,280,393 incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention described herein relates to medical assessment. In particular, the invention relates to early detection of potential dysfunction.

2. Background Art

Current methods for detecting a patient's susceptibility to stroke are well known, but tend to be costly and/or invasive. Examples include positron emission tomography (PET) and the use of sonogram technology to image capillaries in the brain. At the same time, a considerable amount is known about strokes, and about how and why they occur. It is well known that a stroke can be preceded by changes in blood flow in the brain. It is also well known that these changes can occur well in advance of the stroke, sometimes appearing months beforehand. Blood flow may be diminished in a blood vessel, for example, as a result of plaque build-up in the vessel. Moreover, this can lead to the generation of capillaries to compensate for the decreased blood flow in the original blood vessel. Plaque build-up may continue to the point of complete blockage, leading to a stroke. Alternatively, a sudden dislodging of the plaque can bring a sudden increase in blood flow to the newly developed capillaries, which can also lead to a stroke.

While such phenomenon are well understood, the only methods currently available for detection of changes in neural blood flow are costly. Such detection methods are therefore used judiciously; more widespread use would be prohibitively costly. As a result, strokes are not always anticipated. Hence, there is a need for a non-invasive and relatively inexpensive method for detecting a person's susceptibility to stroke.

BRIEF SUMMARY OF THE INVENTION

The invention described herein is a method and apparatus for facilitating assessment of a patient's susceptibility to stroke. The method begins with the step of collecting electrical signals from the brain of the patient under assessment. Signal data corresponding to the collected electrical signals is then compared to at least one standard. In an embodiment of the invention, the standard represents a neural electrical signal taken from a person known to be susceptible to stroke. A positive comparison result suggests susceptibility of the patient under assessment to stroke. Moreover, the comparison result can be used to characterize the pattern of neural blood flow and the degree of susceptibility to stroke. A strong similarity to a standard taken from another patient of known susceptibility suggests that the patient under assessment is experiencing similar neural blood flow and is susceptible to stroke to a similar degree. This information, in turn, can be used to determine the both the need for additional testing and/or the appropriate type and extent of therapy. In another application, this information can be used in categorizing the patient for purposes of determining enrollment in clinical trials.

In an alternative embodiment of the invention, the standard represents a neural electrical signal taken from the patient under assessment at an earlier point in time. A positive comparison in this case suggests that the condition of the patient under assessment has not changed. A negative comparison result suggests that the neural electrical activity of the patient under assessment has changed, implying possible changes in neural blood flow. This in turn can suggest susceptibility to stroke and the need for additional tests and/or for pharmaceutical or other therapeutic treatment. The apparatus for collection of electrical signals from the brain includes a headcap with electrodes concentrated in an area corresponding to a particular cranial region of interest.

BRIEF DESCRIPTION OF THE FIGURES

The foregoing and other features and advantages of the invention will be apparent from the following, more particular description of a preferred embodiment of the invention, as illustrated in the accompanying drawings.

FIG. 1 is a flowchart illustrating operation of an embodiment of the invention in a group testing environment, where unprocessed collected electrical signals are compared to one or more standards.

FIG. 2 is a flowchart illustrating operation of an embodiment of the invention where unprocessed electrical signals collected from a patient are compared to signals collected earlier from the patient.

FIG. 3 is a flowchart illustrating operation of an embodiment of the invention in a group testing environment, where processed collected electrical signals are compared to one or more standards.

FIG. 4 is a flowchart illustrating operation of an embodiment of the invention where electrical signals are collected from a patient and processed, then compared to signal data derived earlier from the patient.

FIGS. 5A and 5B illustrate a headcap that can be used in the collection of electrical signals from the brain of a patient under assessment.

DETAILED DESCRIPTION OF THE INVENTION

A preferred embodiment of the present invention is now described with reference to the figures where like reference numbers indicate identical or functionally similar elements. Also in the figures, the left most digit of each reference number corresponds to the figure in which the reference number is first used. While specific configurations and arrangements are discussed, it should be understood that this is done for illustrative purposes only. A person skilled in the relevant art will recognize that other configurations and arrangements can be used without departing from the spirit and scope of the invention. It will be apparent to a person skilled in the relevant art that this invention can also be employed in a variety of other devices and applications.

I. Overview

The invention provides a method that facilitates the identification of persons who may be susceptible to stroke and who may therefore require additional testing and/or pharmaceutical or other therapeutic treatment. The extent of a person's susceptibility and the pattern of the person's neural blood flow can also be characterized with the help of this invention. Stroke is typically preceded by irregularities in blood flow in the brain. These irregularities reveal themselves through changes in neural electrical activity. The

invention detects changes in neural electrical activity of a patient, thereby facilitating assessment of a patient's susceptibility to stroke.

The method of the invention begins with the step of collecting electrical signals from the brain of a patient under assessment. The collected electrical signals can then be compared to standards. For example, the collected electrical signals can be compared to signals taken from one or more persons known to be susceptible to stroke. Alternatively, the collected electrical signals of a patient under assessment can be compared to signals that were taken at one or more earlier points in time from the same patient. The latter approach allows a patient to be monitored over time to see whether the neural electrical activity has changed. Significant change could indicate a change in vascular condition of the patient, which could, in turn, suggest susceptibility to stroke.

II. Process

The process of the invention includes the collection of electrical signals from the brain of a patient under assessment. The signals can then be compared to signals of persons known to be susceptible to stroke. The signals can alternatively be compared to signals taken from the same patient at earlier points in time, in order to monitor changes in the neurological health of the patient over time. In alternative embodiments, the collected electrical signals can be processed prior to any comparison, yielding signal data, a form of the collected electrical signals that facilitates comparison.

A. Use of Raw Electrical Signals Collected from a Patient

An embodiment of the invention is illustrated in flowchart **100** of FIG. 1. The process begins with a step **105**. In a step **110**, electrical signals are collected from the brain of a patient under assessment. This can be done using a conventional electroencephalograph (EEG) apparatus and method, in which case the collected electrical signals represent one or more free running EEGs captured at various points on the surface of the brain. Alternatively, the electrical signals can be collected through an evoked response potential (ERP) apparatus and method. Here, electrical signals are captured at a plurality of points on the surface of the brain immediately after the patient under assessment has been exposed to a sensory stimulus, such as a flash of light, an auditory tone, or a tactile stimulus. An apparatus for capturing neural electrical signals is discussed in greater detail in section III below. In general, the use of EEGs and ERPs to capture neural electrical activity is well known to those skilled in the relevant art. In either case, the result of step **110** is a set of signals or graphs, where each graph represents electrical activity, over time, at a point on the brain surface.

In a step **115**, the collected electrical signals of the patient under assessment are compared to other signals that represent standards for comparison. In an embodiment of the invention, the signals of the patient under assessment are compared to signals taken from one or more persons known to be susceptible to stroke.

Persons known to be susceptible to stroke can be identified as such by using traditional longitudinal studies. The neural electrical activity of each person in a group of test patients is first benchmarked. The group is then tracked over time, and those who eventually suffer a stroke are identified. The benchmarked neural signals of those test patients who later suffered a stroke are then used as standards for comparison for the patient under assessment. Similarity between the collected electrical signals and the neural signals of persons who later suffered a stroke can indicate that the patient under assessment is likewise susceptible.

The comparison step **115** can be performed in any of several ways that are well known to those skilled in the

relevant art. Comparison may be done by statistical processing, for example, or by image analysis. A positive comparison result raises the possibility that the patient under assessment is susceptible to stroke and should be tested further and/or treated using pharmaceutical or other means. In particular, the comparison result can be used to determine the degree of susceptibility to stroke and to characterize the pattern of neural blood flow of the patient under assessment. In assessing the susceptibility of a patient to acute medial cerebral cortical infarction, for example, susceptibility can coincide with a state of hypoperfusion. Hypoperfusion refers to a condition wherein the volume of blood flowing through different neural blood vessels has changed. Step **115** can determine similarity between the state of hypoperfusion of the patient under assessment and the state of hypoperfusion indicated by the standard.

A strong similarity to a standard taken from another patient of known susceptibility suggests that the patient under assessment is susceptible to a similar degree, and is experiencing a similar pattern of neural blood flow, e.g., a similar state of hypoperfusion. This information, in turn, can be used to determine the both the need for additional testing and/or the appropriate type and extent of therapeutic treatment.

In another application, this information can be used in determining enrollment in clinical trials. In the course of researching the efficacy or safety of a medical treatment, for example, researchers typically require a set of subjects that are of a similar condition with respect to one or more attributes of interest. Researchers may require, for example, a set of patients having a similar pattern of neural blood flow. The invention described herein can facilitate assessment of the patient's condition and can therefore be of use in deciding whether the patient ought to be enrolled with a given set of subjects. Using information derived by the invention regarding the patient's pattern of neural blood flow, a decision can be made as to whether the patient's condition is sufficiently similar to that of others in a test group. If so, the patient can be enrolled; otherwise, the patient may not be used.

In an alternative embodiment, the signals of the patient under assessment are compared to signals collected from the same patient at one or more earlier points in time. This allows the detection of significant changes in the neural electrical activity of the patient under assessment. This is illustrated in flowchart **200** of FIG. 2. The process starts with a step **205**. In a step **210**, electrical signals are collected from the brain of the patient under assessment, as in the case of process **100**. In a step **215**, the collected electrical signals are compared to signals collected previously from the same patient. In this way, any significant changes in the neural electrical activity of the patient can be revealed. As in the case of process **100**, comparison can be performed using methods such as statistical processing or image analysis. A negative comparison result suggests that the condition of the patient under assessment has changed, and that the patient may be susceptible to stroke and should be tested further and/or treated using pharmaceutical or other therapeutic treatment.

In a step **220**, a determination is made as to whether additional signals are to be collected from the patient at some later point, e.g., one month hence. If so, the process continues at that time with step **210**. Process **200** therefore allows monitoring over time, so that a patient can be checked and rechecked for changes that can indicate irregularities in neural blood flow and possible susceptibility to stroke.

B. Use of Signal Data Derived from Collected Electrical Signals

In an alternative embodiment of the invention, the signals collected from the patient under analysis are processed prior to comparison with other signals. This processing, described below, results in signal data that is a function of the collected electrical signals. Signal data facilitates the subsequent comparison step. Such an embodiment is illustrated as flowchart **300** of FIG. **3**. The process begins with a step **305**. In a step **310**, electrical signals are collected from the brain of the patient under assessment. As described above, signal collection can be performed using an EEG procedure, an ERP procedure, or a similar method.

In a step **315**, the collected electrical signals are processed. The collected electrical signals can, for example, undergo a noise reduction process. The collected electrical signals can also be projected into an information subspace of lower dimensionality. In this process, each collected electrical signal is first sampled in the time domain to form an ordered set, or vector, of numerical values. The construction of a vector from an analog signal is known herein as vectorization. Some components of the vector are then deleted to form a vector of lower dimension, known as a projection. The deletion of components can be done either randomly or deterministically. The projections can then be compared to vectorized versions of one or more standard signals in a subsequent comparison step. The process of projecting collected electrical signals into an information subspace of lower dimensionality is described in greater detail in U.S. Pat. No. 6,223,074 B1 and U.S. patent application Ser. No. 09/773,732, incorporated herein by reference in their entirety.

Processing of collected electrical signals can also include the extraction of features of the signals. The overall power of a collected electrical signal is an example of a feature that can be extracted. Another example of an extractable feature is the degree of symmetry between the power in signals collected from the left and right hemispheres of the brain. Other features of a signal can be extracted, as is well known in the art. Extracted features can then be compared to analogous features of one or more standard signals in a subsequent comparison step. The procedures of noise reduction, projection, and feature extraction are presented merely as examples of the processes that can be used in step **315**, and are not meant to limit the scope of the invention. Moreover, the example processes described here can also be combined in step **315**. Noise reduction, for example, can be performed prior to projection or feature extraction.

In a step **320**, the signal data is compared to standard signals. In a manner analogous to step **115**, in an embodiment of the invention, the signal data of the patient under assessment is compared to signals taken from one or more persons known to be susceptible to stroke. If the signal data represents projections of the electrical signals originally collected from the patient under assessment, the projections are compared to vectorized versions of the standard signals. If the signal data represents features extracted from the collected signals, these features are compared to analogous features taken from the standard signals. If the signal data is a reduced noise version of the originally collected signals, then this noisereduced version is compared to the standard signals. In any event, as in the case of process **100**, a positive comparison result suggests the possibility that the patient under assessment is susceptible to stroke and should be tested further and/or treated using pharmaceutical or other means. In particular, the comparison result can be used in determining the degree of susceptibility to stroke, and to

characterize the pattern of neural blood flow, e.g., the state of hypoperfusion of the patient under assessment. A strong similarity to a standard signal taken from another patient of known susceptibility implies that the patient under assessment is susceptible to a similar degree, and is experiencing a similar pattern of neural blood flow. This information, in turn, can be used to determine the both the need for additional testing and/or the appropriate type and extent of therapeutic treatment.

In another application, this information can be used in determining enrollment in clinical trials, as discussed above. Using information derived by the invention regarding the patient's pattern of neural blood flow, a decision can be made as to whether the patient's condition is sufficiently similar to that of others in a test group. If so, the patient can be enrolled; otherwise, the patient may not be used.

An alternative embodiment is illustrated by flowchart **400** of FIG. **4**. Here, signal data of the patient under assessment is compared to signals previously collected from the same patient. The process begins with a step **405**. In a step **410**, electrical signals are collected from the brain of the patient under assessment. In a step **415**, the collected electrical signals are processed. As described above with respect to step **315**, processing can take the form of noise reduction, projection, or feature extraction, so as to yield signal data. Step **415** may alternatively include other forms of processing in other embodiments of the invention, wherein the processing facilitates a subsequent comparison step **420**. In step **420**, signal data is compared to neural electrical signals collected from the patient alone or more points in the past. If the signal data represents projections of the signals originally collected from the patient under assessment, the projections are compared to vectorized versions of the signals collected previously from the same patient. If the signal data represents features extracted from the collected electrical signals, these features are compared to analogous features taken from the previously collected signals. If the signal data is a reduced noise version of the originally collected electrical signals, then this noisereduced version is compared to the previously collected signals. In any event, as in the case of process **200**, a negative comparison result suggests that the patient under assessment may be susceptible to stroke and should be tested further.

III. Signal Collection Apparatus

As discussed above, apparatus for the collection of neural electrical signals is well known to persons skilled in the relevant art. The collection of such signals can be improved, for purposes of the above method, by modifying the conventional collection apparatus. Since the method described in section **11** collects signals related to blood flow in the brain, collection can be concentrated in those regions of the brain surface corresponding to blood vessels of interest.

Such a modified apparatus can consist of a conventional headcap as used in the collection of EEG or ERP signals, with additional electrodes placed in proximity to regions of the brain surface fed by a blood vessel of interest, such as the medial cerebral artery. This permits the collection of increased amounts of information from the regions of interest, improving the reliability of the process of section II.

An exemplary headcap apparatus, according to an embodiment of the invention, is illustrated in FIGS. **5A** and **5B**. These figures represent side and top views, respectively, of a headcap **505** as worn by a patient **500**. In the embodiment illustrated, the headcap **505** covers the region of the brain surface that is fed by the medial cerebral artery. Other embodiments of the headcap can concentrate electrodes on other regions of the brain surface, such as the region

associated with the somatosensory motor cortex. Headcap 505 includes electrodes 510. While FIG. 5B shows 13 electrodes 510, other embodiments can have a different number. In alternative embodiments, the headcap can cover the skull more completely. Moreover, such a headcap can include electrodes throughout, while concentrating electrodes in a region of interest.

Note that while an apparatus having an increased number of electrodes

II. The method described above can be performed with a conventional, unmodified headcap as used in the collection of EEG or ERP signals.

IV. Conclusion

While various embodiments of the present invention have been described above, it should be understood that they have been presented by way of example, and not limitation. It will be apparent to persons skilled in the relevant art that various changes in detail can be made therein without departing from the spirit and scope of the invention. Thus the present invention should not be limited by any of the above-described exemplary embodiments, but should be defined only in accordance with the following claims and their equivalents.

What is claimed is:

1. A method of collecting and processing information for determination of the susceptibility of a patient under assessment to suffering a stroke, the method comprising the steps of:

- (a) collecting electrical signals from the brain of the patient under assessment;
- (b) comparing signal data corresponding to the collected electrical signals to at least one standard to produce comparison results, wherein the signal data is derived from the collected electrical signals; and
- (c) interpreting the comparison results.

2. The method of claim 1, wherein said step (a) comprises the step of collecting at least one electroencephalograph (EEG).

3. The method of claim 1, wherein said step (a) comprises the steps of:

- (i) performing at least one evoked response potential (ERP) trial on the patient under assessment; and
- (ii) capturing the electrical signals that result from the at least one ERP trial.

4. The method of claim 1, further comprising the step of: (d) processing the collected electrical signals to derive signal data for subsequent comparison to the at least one standard; performed after step (a) and before step (b).

5. The method of claim 4, wherein said step (d) comprises the step of performing noise reduction on the collected electrical signals.

6. The method of claim 4, wherein said step (d) comprises the step of performing feature extraction on the collected electrical signals.

7. The method of claim 4, wherein said step (d) comprises the step of generating a plurality of projections of the collected electrical signals.

8. The method of claim 1, wherein said step (b) comprises the step of comparing the signal data corresponding to the collected electrical signals to at least one standard, wherein the at least one standard comprises signal data from a patient known to be susceptible to stroke.

9. The method of claim 1, wherein said step (b) comprises the step of comparing signal data corresponding to the collected electrical signals to at least one standard, wherein the at least one standard comprises signal data derived from electrical signals that were collected at an earlier time from the patient under assessment.

10. The method of claim 1, wherein said step (b) comprises the step of comparing signal data corresponding to the collected electrical signals to at least one standard using statistical processing.

11. The method of claim 1, wherein said step (b) comprises the step of comparing signal data corresponding to the collected electrical signals to at least one standard using image analysis.

12. The method of claim 1, wherein said step (c) comprises the step of determining whether the patient under assessment is susceptible to suffering a stroke.

13. The method of claim 1, wherein said step (c) comprises the step of determining a degree of susceptibility of the patient under assessment to suffering a stroke.

14. The method of claim 1, wherein said step (c) comprises the step of characterizing a pattern of neural blood flow in the patient under assessment.

15. The method of claim 1, wherein said step (c) comprises the step of categorizing the patient under assessment for purposes of enrollment in clinical trials, on the basis of the comparison results.

16. The method of claim 1, wherein said step (c) comprises the step of categorizing the patient under assessment for purposes of suggesting a type of therapeutic treatment on the basis of the comparison results.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,466,816 B2
DATED : October 15, 2002
INVENTOR(S) : Richard Granger et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:


Column 1,

Line 3, after the title of the invention and before the heading "BACKGROUND OF THE INVENTION" please insert the heading -- STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY-SPONSORED RESEARCH AND DEVELOPMENT --.

Line 5, under the heading "STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY-SPONSORED RESEARCH AND DEVELOPMENT" insert the paragraph -- This invention was made with Government support under N00014-97-C-0192 awarded by the Office of Naval Research. The U.S. Government has certain rights in this invention. --.

Signed and Sealed this

Eighteenth Day of February, 2003

A handwritten signature in black ink, appearing to read "James E. Rogan", written over a horizontal line.

JAMES E. ROGAN
Director of the United States Patent and Trademark Office

专利名称(译)	评估中风易感性的方法和装置		
公开(公告)号	US6466816	公开(公告)日	2002-10-15
申请号	US09/907914	申请日	2001-07-19
[标]申请(专利权)人(译)	THURIS CORP		
申请(专利权)人(译)	THURIS CORPORATION		
当前申请(专利权)人(译)	加利福尼亚州，第三的董事会		
[标]发明人	GRANGER RICHARD LYNCH GARY		
发明人	GRANGER, RICHARD LYNCH, GARY		
IPC分类号	A61B5/0476 A61B5/00		
CPC分类号	A61B5/0476		
其他公开文献	US20020016552A1		
外部链接	Espacenet USPTO		

摘要(译)

描述了一种用于促进评估中风易感性的方法。从评估的患者的大脑收集电信号。然后将对应于信号的数据与标准进行比较。该标准可以表示从已知易患中风的人获取的神经电信号。积极的比较表明患者对中风的易感性。该比较可用于表征神经血流和易感性程度。这可用于确定是否需要进行额外的测试和/或适当的治疗。该信息还可用于对患者进行分类以确定临床试验中的登记。或者，标准表示在较早时间从被评估的患者获取的神经信号。积极的比较表明患者的病情没有变化。负面比较表明患者的神经活动已发生变化，这意味着神经血流的变化。这可能表明易感性。

