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- (54) **FLICKER-INDUCED INTEROCULAR TRANSFER-OF-OXYGENATION FOR NON-INVASIVELY ASSESSING NEURAL INTEGRITY OF A PATIENT'S CENTRAL NERVOUS SYSTEM**
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- (51) **Int. Cl.⁷** **A61B 5/00**
- (52) **U.S. Cl.** **600/558**
- (58) **Field of Search** 600/544, 546,
600/558, 323, 355, 356

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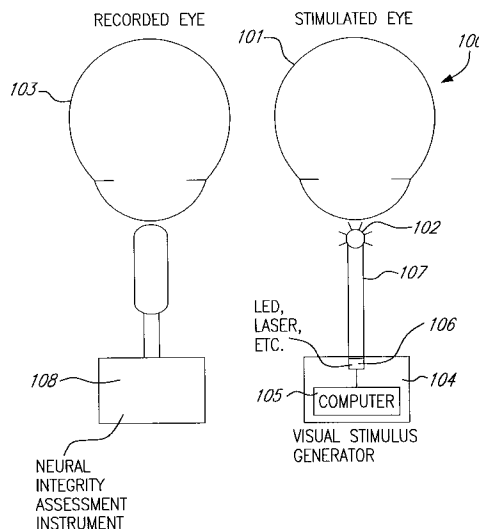
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(57) **ABSTRACT**

In the method and apparatus for assessing neural integrity of a patient's central nervous system, the patient is stimulated with a visual or auditory flickering stimulus, and oxygenation in the patient's second eye is sensed. Finally, the method and apparatus detects whether a change in the sensed oxygenation occurs in response to stimulation of the patient with the visual or auditory flickering stimulus. This change in the sensed oxygenation is indicative of neural integrity of the patient's central nervous system.

18 Claims, 4 Drawing Sheets



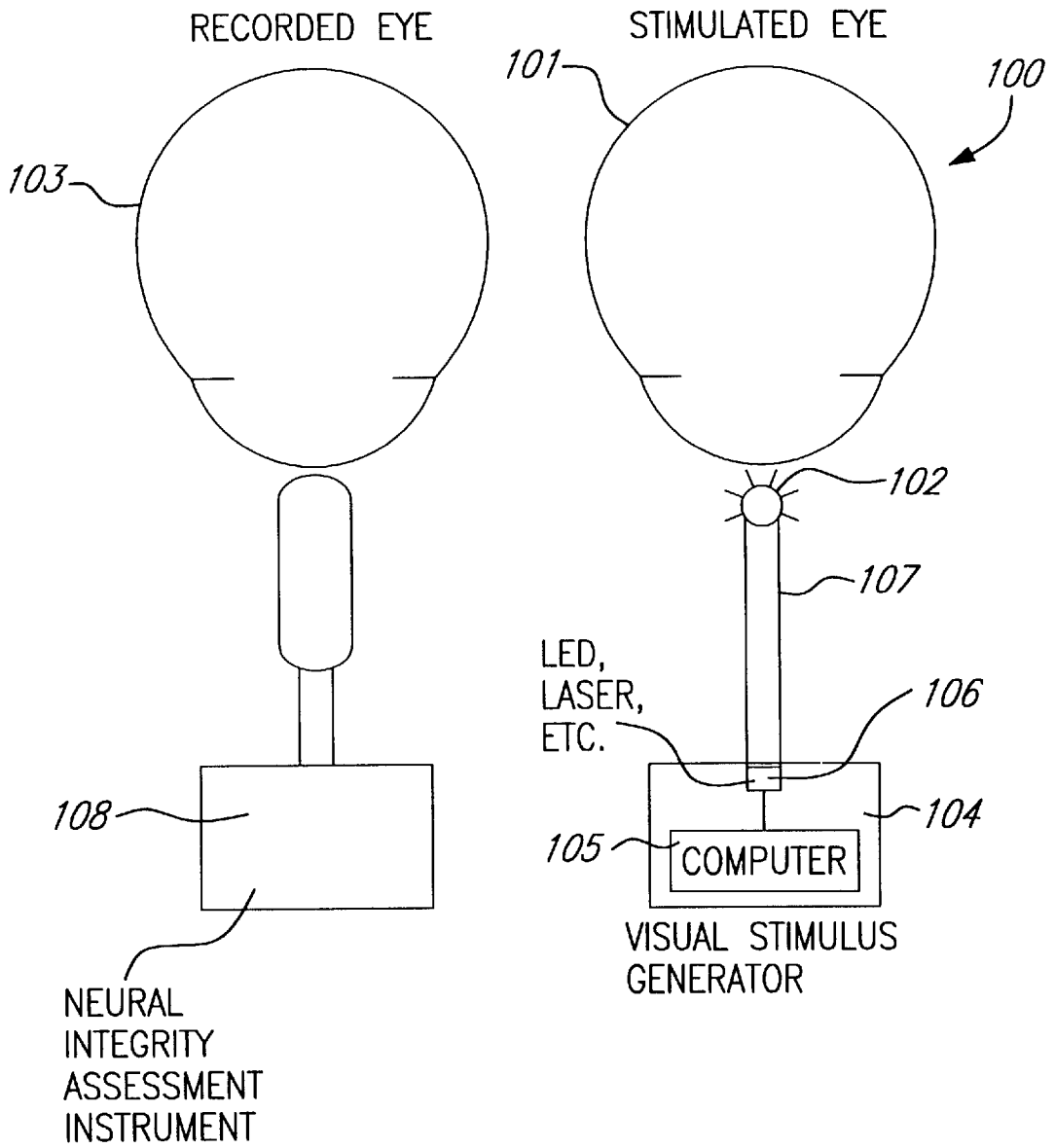


FIG. 1

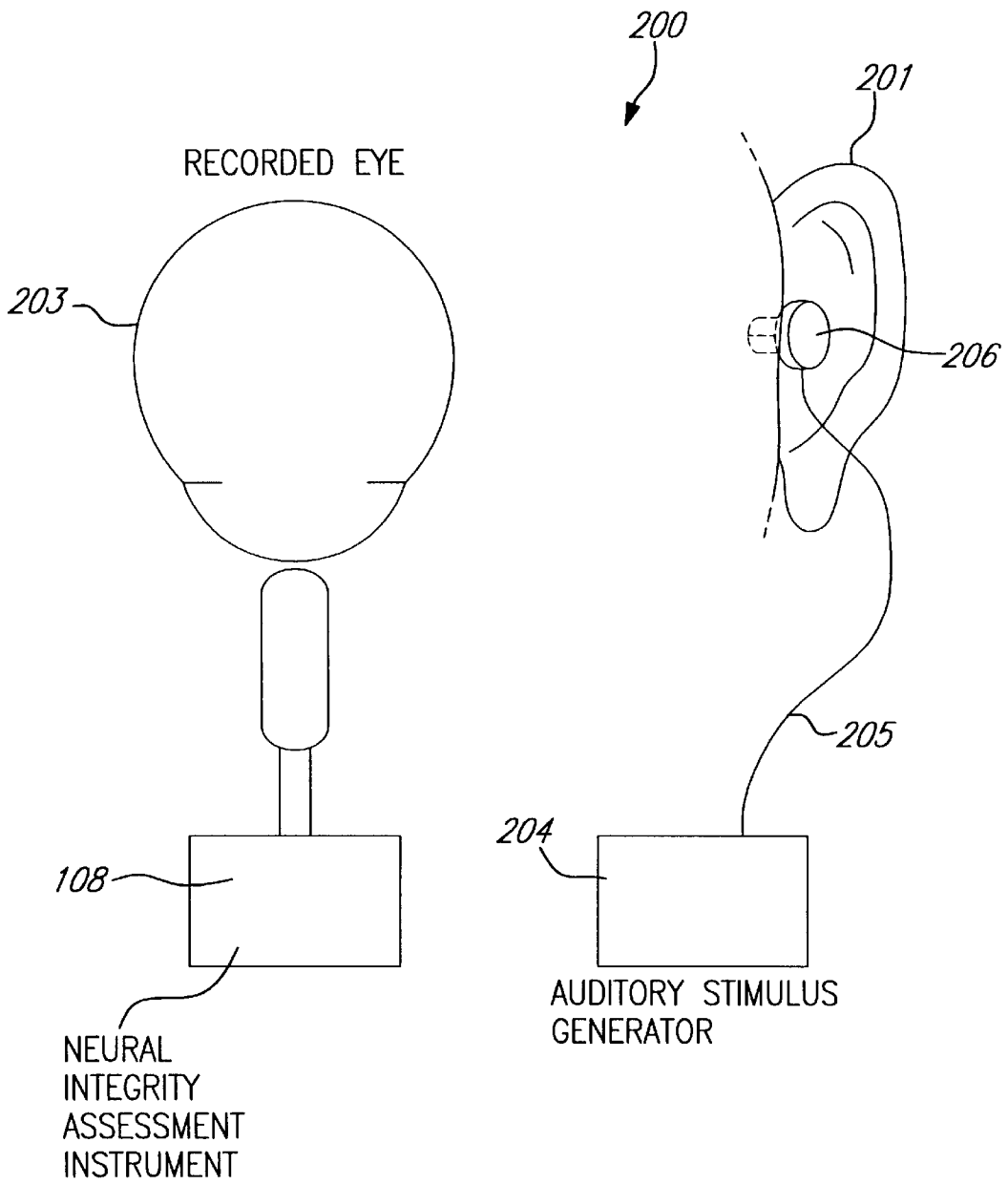
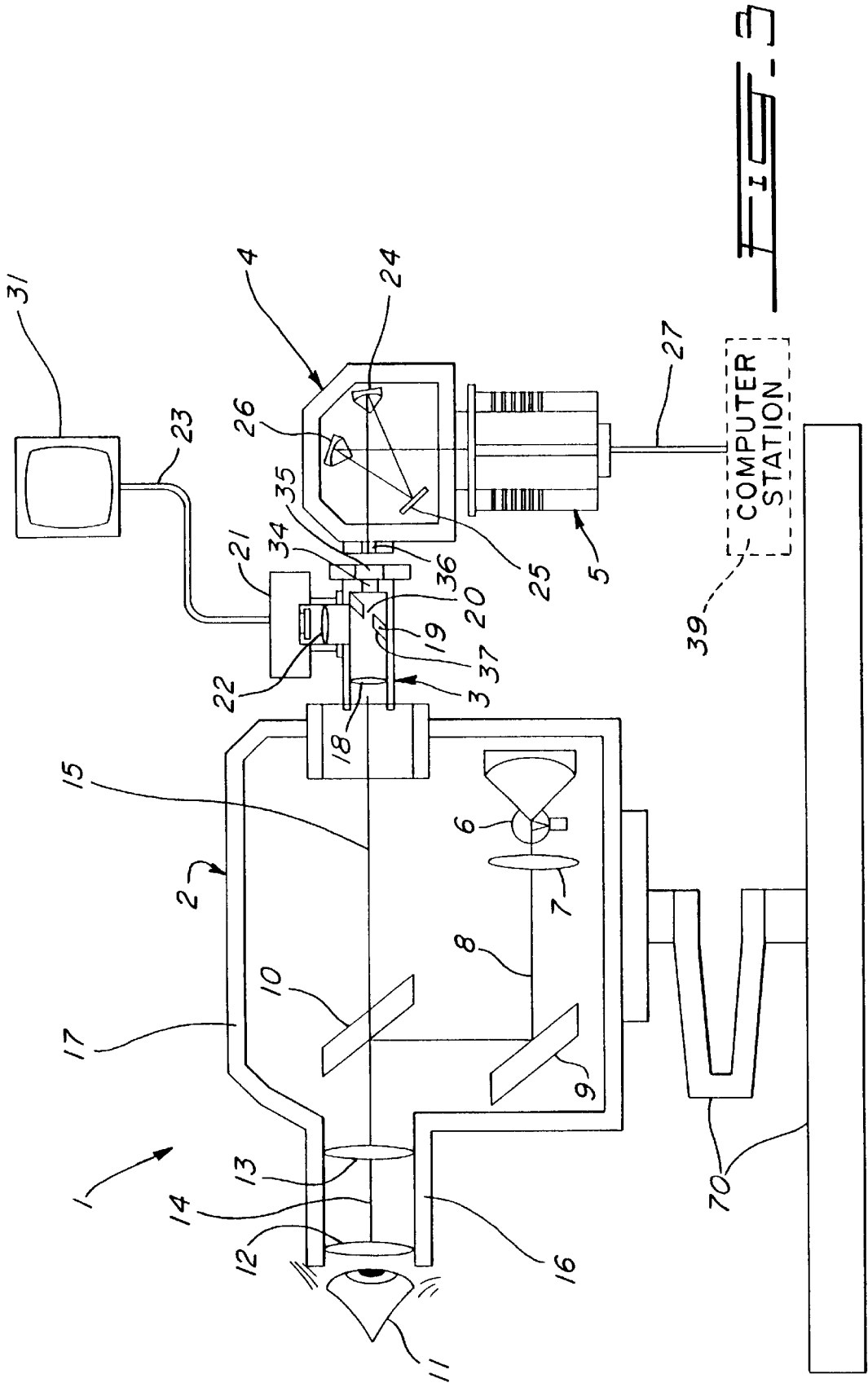
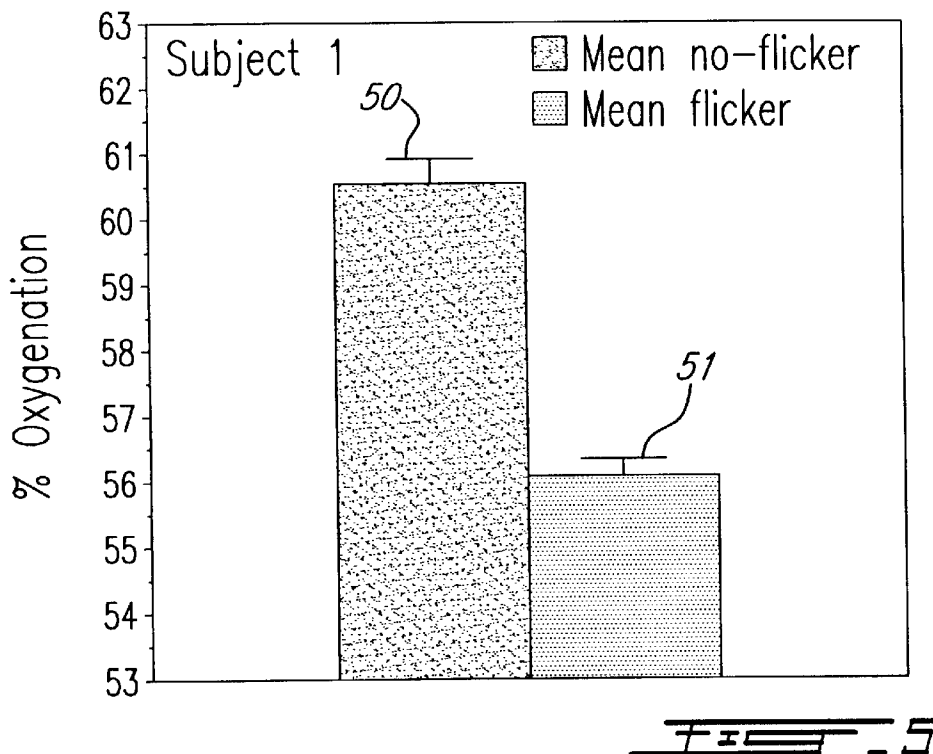
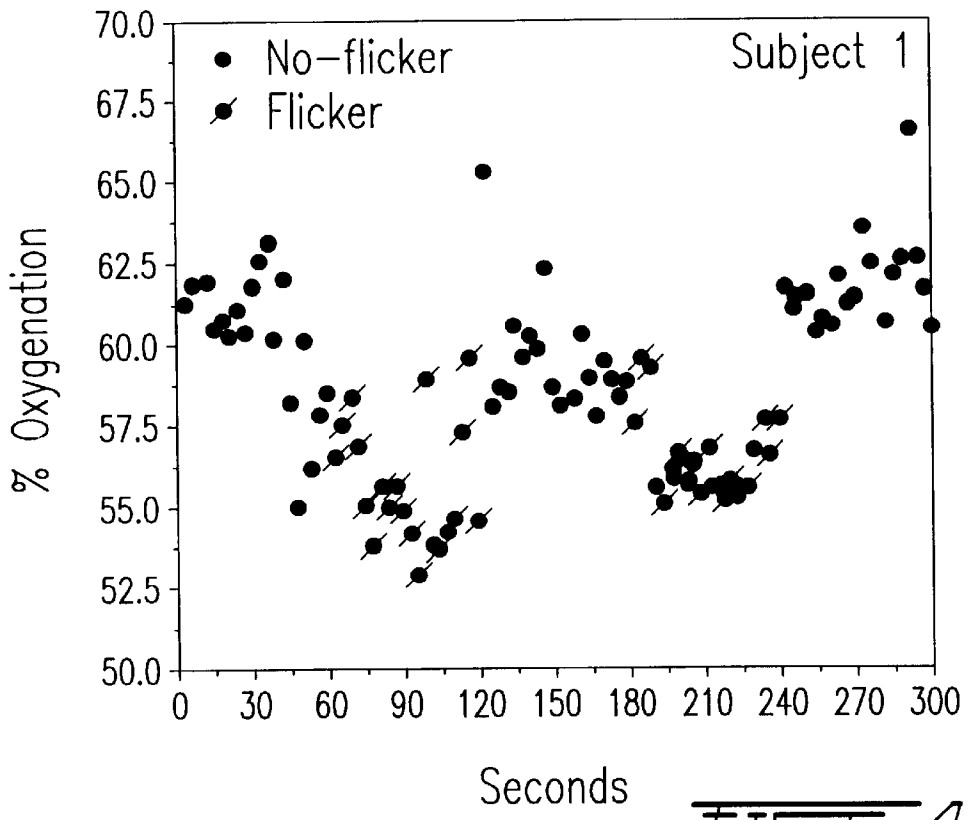


FIG. 2





**FLICKER-INDUCED INTEROCULAR
TRANSFER-OF-OXYGENATION FOR
NON-INVASIVELY ASSESSING NEURAL
INTEGRITY OF A PATIENT'S CENTRAL
NERVOUS SYSTEM**

This application claims benefit of 60/200,384 filed Apr. 28, 2000.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method and apparatus for assessing the neural integrity of a patient's central nervous system.

2. Brief Description of the Prior Art

It is well known to those of ordinary skill in the art that stimulating an eye with flickering light induces strong neural activity resulting in oxygen consumption of the human brain [Thomas, C. G.; Menon, R. S.; (1998); "Amplitude Response and Stimulus Presentation Frequency Response of Human Primary Visual Cortex Using BOLD EPI at 4 T"; *Magnetic Resonance Medicine*, 40, 203-209] and the optic nerve head of the cat [Ahmed J.; Linsenmeier, R. A.; Dunn, R. Jr.; (1994); "The Oxygen Distribution in the Prelaminar Optic Nerve Head of the Cat"; *Experimental Eye Research*, 59, 457-465]. It is also known from the literature that selective adaptation or stimulation of one eye will induce sensitivity changes in the other, contralateral eye; this phenomenon is called "interocular transfer" [Andrews T. J.; White, L. E.; Binder, D.; Purves, D.; (1996); "Temporal Events in Cyclopean Vision"; *Proceedings of the National Academy of Sciences USA*, 93, 3689-3692]. These studies imply the role of central mechanisms, e.g. the human brain, as being responsible for the control of the sensitivity changes observed in the contralateral eye. It is also reported that cerebral infarcts will induce oxygen changes measured at the level of the contralateral eye [Staedt, U.; Hutt M.; Herrmann B.; Seufzer, U.; Leweling H.; (1989); "Effect of Hemoglobin with 10% Hydroxyethyl Starch Solution (MW 200,000/9.5) on the Flow Properties of Blood, Arterial Blood Gases and Conjunctival Oxygen Partial Pressure in Patients with Cerebral Infarct"; *Infusionstherapie*, 16, 107-112].

Epilepsy, migraines with visual auras, and temporary amnesia have all been associated with cortical depression spreading (CD) in the brain, as reported in the following articles:

[Dahlem, M. A.; Engelmann, R.; Lowel, S.; Muller, S. C.; (2000); "Does the Migraine Aura Reflect Cortical Organization?"; *Eur J Neurosci*, 12, 767-770];

[Donnet A.; Bartolomei, F.; (1997); "Migraine with Visual Aura and Photosensitive Epileptic Seizures"; *Epilepsia*, 38, 1032-1034];

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[Pantoni, L.; Lamassa, M.; Inzitari, D.; (2000); "Transient Global Amnesia; A Review Emphasizing Pathogenic Aspects"; *Acta Neurol Scand.*, 102, 275-283]; and

[Sotak, C. H.; (1999); "New NMR Measurements in Epilepsy. Diffusion-Weighted Magnetic Resonance Imaging of Spreading Depression"; *Adv Neurol*, 79, 925-929].

Cortical depression spreading can be induced by stimulation and results in a widespread decrease in oxygenation of the brain followed by a change in neural potentials.

OBJECTS OF THE INVENTION

An object of the present invention is to assess the neural integrity of the central nervous system of a patient by stimulating the patient with a visual or auditory flickering stimulus and detecting oxygenation changes in at least one eye of the patient.

SUMMARY OF THE INVENTION

More specifically, in accordance with the present invention, there is provided a method for assessing neural integrity of a patient's central nervous system, comprising stimulating the patient with a visual or auditory flickering stimulus, sensing oxygenation in at least one eye of the patient, and detecting whether a change in the sensed oxygenation occurs in response to stimulation of the patient with the flickering stimulus. This change is indicative of neural integrity of the patient's central nervous system.

Also in accordance with the present invention, there is provided an apparatus for assessing neural integrity of a patient's central nervous system, comprising a generator of a visual or auditory flickering stimulus, and a neural integrity assessment instrument responsive to oxygenation in at least one eye of the patient. The flickering stimulus is applied to the patient to stimulate this patient, and the neural integrity assessment instrument comprises:

a sensor of oxygenation in at least one eye of the patient; and

a detector of a change in the level of the sensed oxygenation in response to stimulation of said patient with the flickering stimulus, this change being indicative of neural integrity of the patient's central nervous system.

The present invention further relates to method for assessing neural integrity of a patient's central nervous system, comprising stimulating a first eye of the patient with a flickering light, sensing oxygenation in the patient's second eye, and detecting whether a change in the sensed oxygenation occurs in response to stimulation of the patient's first eye with flickering light, this change being indicative of neural integrity of the patient's central nervous system.

In accordance with preferred embodiments of this method:

sensing oxygenation in the patient's second eye comprises sensing levels of oxygenation at the optic nerve head of the fundus of the patient's second eye; and

stimulating the patient's first eye comprises adjusting at least one of the following parameters to generate at least one desired neural response of the patient's central nervous system: an intensity of the flickering light, a contrast of the flickering light, a color of the flickering light, a flicker rate of the flickering light, and a duration of the stimulation of the patient's first eye with flickering light.

The present invention still further relates to an apparatus for assessing neural integrity of a patient's central nervous system, comprising a generator of flickering light applied to a first eye of the patient to stimulate this patient's first eye, and a neural integrity assessment instrument responsive to oxygenation in the patient's second eye. The neural integrity assessment instrument comprising:

a sensor of oxygenation in the patient's second eye; and a detector of a change in the level of the sensed oxygenation in response to stimulation of the patient's first eye

with flickering light, this change being indicative of neural integrity of the patient's central nervous system. According to preferred embodiments of this apparatus: the sensor is positioned to sense levels of oxygenation at the optic nerve head of the fundus of the patient's second eye;

the generator comprises a source of light operated through a flickering-light controller, the source of light is selected from the group consisting of a light-emitting diode and a laser, and a fiber optic cable is interposed between the source of light and the patient's first eye to guide light from the source of light to the patient's first eye; and

the neural integrity assessment instrument comprises an on-line oxygenation measurement device.

Still further in accordance with the present invention, there is provided a method for assessing neural integrity of a patient's central nervous system, comprising stimulating at least one ear of the patient with an auditory flickering stimulus, sensing oxygenation in at least one eye of the patient, and detecting whether a change in the sensed oxygenation occurs in response to stimulation of the patient's at least one ear with the auditory flickering stimulus, this change being indicative of neural integrity of the patient's central nervous system.

According to a preferred embodiment, stimulating the patient's at least one ear comprises adjusting at least one of the following parameters to generate at least one desired neural response of the patient's central nervous system: an amplitude of the auditory flickering stimulus, a frequency of the auditory flickering stimulus, a pitch domain of the auditory flickering stimulus, a flicker rate of the auditory flickering stimulus, and a duration of the stimulation of the patient's at least one ear with the auditory flickering stimulus.

Again in accordance with the present invention, there is provided an apparatus for assessing neural integrity of a patient's central nervous system, comprising:

- a generator of an auditory flickering stimulus, this auditory flickering stimulus being applied to at least one ear of the patient to stimulate this patient's at least one ear;
- a neural integrity assessment instrument responsive to oxygenation in at least one eye of the patient, this neural integrity assessment instrument comprising:
 - a sensor of oxygenation in the patient's at least one eye; and
 - a detector of a change in the level of the sensed oxygenation in response to stimulation of the patient's at least one ear with the auditory flickering stimulus, this change being indicative of neural integrity of the patient's central nervous system.

According to a preferred embodiment of this apparatus, the generator comprises a source of auditory flickering stimulus connected to an earphone.

The foregoing and other objects, advantages and features of the present invention will become more apparent upon reading of the following non restrictive description of preferred embodiments thereof, given for the purpose of illustration only with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the appended drawings:

FIG. 1 is a schematic block diagram of an apparatus according to the present invention, for assessing neural integrity of a patient's central nervous system by means of a visual stimulus;

FIG. 2 is a schematic block diagram of an apparatus according to the present invention, for assessing neural integrity of a patient's central nervous system by means of an auditory stimulus;

FIG. 3 is a schematic diagram of a spectrophotometry oxygenation measurement device used in the apparatuses of FIGS. 1 and 2, for assessing neural integrity of a patient's central nervous system;

FIG. 4 is a graph showing individual data points of the level of oxygenation in the patient's second eye with respect to time (seconds) obtained from a human observer for a 5 minute testing sequence where the flickering light was alternately off for 60 seconds and on for 60 seconds; and

FIG. 5 is a graph showing the mean level of oxygenation in the patient's second eye for the non-flicker and flicker conditions along with the standard error bars.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

At present, nobody has tested or proposed an apparatus for stimulating a first eye of a patient with flickering light and for measuring and detecting the effect of flicker-induced changes on the oxygen level of the second, contralateral eye of the same patient. Such an apparatus would have a great impact on assessing the integrity, in particular but not exclusively, of the human central nervous system (brain) as a consequence of cerebrovascular accidents, brain infarcts, brain traumas, epilepsy, migraines, or any other neuro-pathological condition produced by accidents (e.g. internal hemorrhaging), diseases, drugs, or toxins.

Such an apparatus would also have a great impact on measuring the widespread decrease in oxygenation of the brain (central nervous system) followed by a change in neural potentials, which results from cortical depression spreading; this would enable determination of whether patients are at risk and whether given medications are efficient in avoiding CD.

Such an apparatus would also have a great impact for evaluating treatment drugs for any neurological disorder such as anticonvulsive drugs for the treatment of epilepsy, migraine medication, neuro-protective agents, psychotropic medication, etc. Furthermore, testing the neural integrity with such a device could indicate the level of alertness for patients under anesthesia.

Visual Flickering Stimulus:

A first preferred embodiment of the present invention, as illustrated in FIG. 1, comprises an apparatus **100** for assessing neural integrity of a patient's central nervous system. This apparatus **100** stimulates a first eye **101** of the patient with flickering light **102** and senses oxygenation levels in the second, contralateral eye **103** of the same patient. Preferably, but not exclusively, these levels of oxygenation are sensed at the optic nerve head of the fundus of the eye. Of course, it is within the scope of the present invention to measure oxygenation levels at any other suitable locations in or on the second, contralateral eye **103**.

Referring to FIG. 1, the apparatus **100** comprises a visual stimulus generator **104**. This stimulus generator **104** essentially consists of a flickering-light controller, which can be a computer such as **105** coupled with a light-emitting diode (LED) (see **106**), a laser (see **106**), or any other suitable source of light (see **106**). The flickering light **102** can be guided from the light source **106** to the stimulated eye **101** via a fiber optic cable **107**. Alternatively, the LED, laser or any other source of light **106** can be placed directly in the proximity of the stimulated eye **101**.

The intensity, contrast, color, and flicker rate of the light **102**, as well as the duration of the test (duration of the stimulation of the eye **101** with flickering light) could all be adjusted to generate a desired neural response or different neural responses of the patient's central nervous system. Of course, it is important to adjust the above parameters to levels susceptible to cause no damage to the patient's eye **101**.

Still referring to FIG. 1, the apparatus **100** further comprises a neural integrity assessment instrument **108**. In the preferred embodiment, the neural integrity assessment instrument **108** comprises the device for on-line and real-time spectrorreflectometry measurement of oxygenation in a patient's eye as described in International patent application WO 99/48418 (Faubert et al.) published on Sep. 30, 1999. The subject matter of this International patent application WO 99/48418 is incorporated herein by reference. However, it should be kept in mind that it is within the scope of the present invention to use any other suitable type of neural integrity assessment device **108**.

Auditory Flickering Stimulus:

A second preferred embodiment of the present invention, as illustrated in FIG. 2, comprises an apparatus **200** for assessing neural integrity of a patient's central nervous system. This apparatus **200** stimulates at least one ear **201** of the patient with an auditory flickering stimulus and senses oxygenation levels in at least one eye **203** of the same patient. Preferably, but not exclusively, these levels of oxygenation are sensed at the optic nerve head of the fundus of the eye. Of course, it is within the scope of the present invention to measure oxygenation levels at any other suitable locations in or on the eye **203**.

Referring to FIG. 2, the apparatus **100** comprises an auditory stimulus generator **204**. This stimulus generator **104** essentially consists of a computer generating the auditory flickering stimulus applied to the patient's ear **201** through an electric wire **205** and an earphone **206**. Normally, the auditory flickering stimulus will consist of an audible sound.

The amplitude, frequency, pitch domain and flicker rate of the auditory flickering stimulus, as well as the duration of the test (duration of the stimulation of the ear **201** with the auditory flickering stimulus) could all be adjusted to generate a desired neural response or different neural responses of the patient's central nervous system. Of course, it is important to adjust the above parameters to levels susceptible to cause no damage to the patient's ear **201**.

Still referring to FIG. 2, the apparatus **100** further comprises a neural integrity assessment instrument **108**. In the second preferred embodiment, the neural integrity assessment instrument **108** again comprises the device for on-line and real-time spectrorreflectometry measurement of oxygenation in a patient's eye as described in International patent application WO 99/48418 (Faubert et al.) published on Sep. 30, 1999. The subject matter of this International patent application WO 99/48418 is incorporated herein by reference. However, it should be kept in mind that it is within the scope of the present invention to use any other suitable type of neural integrity assessment device **108**.

Neural Integrity Assessment Instrument:

A device as described in International patent application WO 99/48418, for on-line and real-time spectrorreflectometry measurement of oxygenation in a patient's eye is illustrated in FIG. 3 and generally identified by the reference **1**. This device **1** comprises a fundus camera **2**, a camera-to-spectrograph interface **3**, and a detector unit formed of a spectrograph **4** and a CCD (Charge Coupled Device) detector array **5**.

Sensor of the Neural Integrity Assessment Instrument:

The fundus camera **2** is supported by a mechanical frame **70** schematically illustrated in FIG. 3.

Still referring to FIG. 3, the fundus camera **2** comprises a light source **6** for producing light having a predetermined relatively wide spectral (frequency) bandwidth optimized for spectrorreflectometry oxygenation measurement. In this respect, the spectrorreflectometry oxygenation measurement of hemoglobin and its derivatives such as oxyhemoglobin and carboxyhemoglobin is preferably conducted within a spectral bandwidth including the range of wavelengths comprised between 450 nm and 850 nm.

Light is propagated from a light source **6** to a region of the fundus of the patient's eye **11** by a first optical system. As indicated in the foregoing description, oxygenation sensing is preferably made at the optic nerve head of the fundus of the eye. This first optical system comprises:

a lens **7** to concentrate light generated by the source **6** into a light beam **8**;

45° mirror **9** and 45° beam splitter **10** to reflect the light beam **8** twice and transmit that light beam **8** to the patient's eye **11** along a linear trajectory **14**; and

a pair of lenses **12** and **13** mounted along the trajectory **14** to propagate the light beam **8** toward the desired region of the fundus of the patient's eye **11**.

The intensity of the light beam **8** must be sufficiently low for being applied to the fundus of the patient's eye for the duration of the test without harming the patient's eye. Preferably, the light beam **8** will have an intensity lower than 5 mW/cm², which is safe for exposure time as long as 6 minutes.

As can be seen in FIG. 3, the fundus camera **2** is formed with a housing **17** defining a cylindrical portion **16** in which the pair of lenses **12** and **13** are mounted. The cylindrical portion **16** defines with the lens **12** the objective of the fundus camera **2**. Obviously, the patient places his (or her) eye **11** close to and in front of the lens **12** of the fundus camera **2**.

Light beam **8** is reflected at least in part by the fundus of the patient's eye **11** to produce a reflected light beam **15** having a geometrical longitudinal axis (not shown). A second optical system propagates the reflected light beam along a predetermined propagation path **14** from the fundus of the patient's eye **11** to the detector (**4, 5, 39**).

The second optical system comprises the pair of lenses **12** and **13**, and the 45° beam splitter **10** to propagate the reflected light beam **15** from the fundus of the patient's eye **11** along the propagation path **14** toward the camera-to-spectrograph interface **3**. 45° beam splitter **10** will cause no reflection of the reflected light beam **15** propagating along path **14** from the fundus of the patient's eye **11** to the interface **3**.

The second optical system also comprises a lens **18** and a 45° mirror **19** of the camera-to-spectrograph interface **3**. More specifically, the lens **18** propagates the reflected light beam **15** along the propagation path **14** toward the 45° mirror **19**. Mirror **19** defines an angle of 45° and comprises a central, axial opening **20** having a predetermined diameter centered on the geometrical longitudinal axis of the reflected light beam **15**. Of course, the central axial opening **20** will transmit to the detector (**4, 5, 39**) only the axial central portion of the reflected light beam **15**. The second optical system further comprises axial apertures such as **34, 35** and **36** provided in the housings of the camera-to-interface **3** and spectrograph **4** to enable the axial central portion of the reflected light beam **15** to reach the spectrograph **4**.

Just a word to mention that the use of the axial central portion of the reflected **37** lightbeam **15** enables selection of

a small precise area which is optimal for oxygenation sensing of specific structures such as the blindspot, arteries, veins, etc.

The mirror **19** comprises a light-reflecting annular surface **37** surrounding the axial central opening **20**. The reflected light beam **15** comprises an axial peripheral portion surrounding the axial central portion and reflected by the light-reflecting annular surface **37** of the mirror. The axial peripheral portion of the reflected light beam **15** is deviated by 90° by reflection on the light-reflecting annular surface **37** of the 45° mirror **19** to propagate toward a TV camera **21** through a lens **22** of the camera-to-spectrograph interface **3**.

The image sensed by the TV camera **21** is displayed on a TV monitor **31** through a cable **23**. This enables the operator to visualize the fundus of the patient's eye and the location of the axial central opening **20** on the fundus of the patient's eye, and therefore to select the small central area of interest where spectrophotometry oxygenation sensing is desired. Detector of the Neural Integrity Assessment Instrument:

The spectrograph **4** comprises a first concave mirror **24** having a generally elliptical cross section to receive the axial central portion of the reflected light beam **15** and to deflect this axial central light beam portion toward a generally planar diffraction grating **25**. Diffraction grating **25** consists of an array of narrow slits or grooves which produce a large number of beams interfering with each other to produce a light spectrum. As it is well known to those of ordinary skill in the art, this light spectrum includes light components of the axial central portion of the reflected light beam **15** arranged in order of wavelength. The produced light spectrum is reflected by a second concave mirror **26** also having a generally elliptical cross section and deviated toward the CCD detector array **5**.

In other words, the diffraction grating **25** separates the light components of different wavelengths within the range comprised between 450 nm and 850 nm. The intensities of the light components of different wavelengths of the light spectrum are detected and measured by the CCD detector array **5**. For example, the CCD detector array **5** consists of a two-dimensional array comprising 1024 columns and 256 rows of light detectors, in which the rows are summed for each column to give a readout (output signal) indicative of the spectral content of the reflected light beam **15**.

The readout (output signal) from the CCD detector array **5** is transmitted to a computer station **39** through an electric cable **27**. This computer station **39** is responsive to the measured intensities of the components of different wavelengths of the light spectrum for computing and eventually displaying a graph of absorbance of the precise small area of the fundus of the patient's eye as a function of wavelength. As this graph of absorbance depends on and is directly related to the level of oxygenation of the precise small area of the fundus of the patient's eye, it can be easily converted by the computer station **39** to this oxygenation level. The computer station **39** will detect whether a change has occurred in the oxygenation level in response to stimulation of the patient with the flickering stimulus. Such a change is indicative of neural integrity of the patient's central nervous system.

Experiments have been conducted to demonstrate that detection of the interocular transfer effect of oxygenation is possible. An example of these data is illustrated in FIGS. **4** and **5**. This example shows that the level of oxygenation measured at the optic nerve head of the second, recorded eye **103** (FIG. **1**) can change by 4 to 5% while simply stimulating the first eye **101** with a 5 Hz flickering light **102**. This is equivalent to the oxygenation changes produced in a given

eye by reducing its ocular perfusion pressure between 15 to 30% which corresponds to a relatively large change (Faubert, J.; Gagnon, M.; Diaconu V.; (1999); "The O.S.O.M.E. System: A New Real-Time Non-Invasive Technique for Measuring Oxygenation and Hemoglobin in the Human Eye"; *Investigative Ophthalmology and Visual Science*, 40, S977).

FIG. **4** is a graph of the level of oxygenation of the patient's recorded eye **103** with respect to time. The graph of FIG. **4** shows individual data points obtained from a human observer for a 5 minute testing sequence where the flickering light was alternately off for 60 seconds and on for 60 seconds. The results show clear changes in oxygenation level as a consequence of the flicker-induced neural activity. This demonstrates the sensitivity of the technique.

FIG. **5** is a graph showing the mean oxygenation level of the patient's recorded eye **103** for the non-flicker and flicker conditions along with the standard error bars **50** and **51** indicating that the technique is not only sensitive but is quite reliable for measuring the interocular transfer.

Just a word to mention that similar results are obtained with an auditory flickering stimulus according to the embodiment of FIG. **2**.

Although the present invention has been described hereinabove by way of a preferred embodiment thereof, this embodiment can be modified at will, within the scope of the appended claims, without departing from the spirit and nature of the subject invention.

What is claimed is:

1. A method for assessing neural integrity of a patient's central nervous system, comprising:
 - stimulating the patient with a visual or auditory flickering stimulus;
 - sensing oxygenation in at least one eye of the patient; and
 - detecting whether a change in the sensed oxygenation occurs in response to stimulation of the patient with the flickering stimulus, said change being indicative of neural integrity of the patient's central nervous system.
2. An apparatus for assessing neural integrity of a patient's central nervous system, comprising:
 - a generator of a visual or auditory flickering stimulus, said flickering stimulus being applied to the patient to stimulate said patient; and
 - a neural integrity assessment instrument responsive to oxygenation in at least one eye of the patient, said neural integrity assessment instrument comprising:
 - a sensor of oxygenation in at least one eye of the patient; and
 - a detector of a change in the level of the sensed oxygenation in response to stimulation of said patient with the flickering stimulus, said change being indicative of neural integrity of the patient's central nervous system.
3. A method for assessing neural integrity of a patient's central nervous system, comprising:
 - stimulating a first eye of the patient with a flickering light;
 - sensing oxygenation in the patient's second eye; and
 - detecting whether a change in the sensed oxygenation occurs in response to stimulation of the patient's first eye with flickering light, said change being indicative of neural integrity of the patient's central nervous system.
4. A method for assessing neural integrity of a patient's central nervous system as defined in claim **3**, wherein sensing oxygenation in the patient's second eye comprises sensing levels of oxygenation at the optic nerve head of the fundus of the patient's second eye.

5. A method for assessing neural integrity of a patient's central nervous system as defined in claim 3, wherein stimulating the patient's first eye comprises adjusting at least one of the following parameters to generate at least one desired neural response of the patient's central nervous system: an intensity of the flickering light, a contrast of the flickering light, a color of the flickering light, a flicker rate of the flickering light, and a duration of the stimulation of the patient's first eye with flickering light.

6. An apparatus for assessing neural integrity of a patient's central nervous system, comprising:

- a generator of flickering light, said flickering light being applied to a first eye of the patient to stimulate said patient's first eye;
- a neural integrity assessment instrument responsive to oxygenation in the patient's second eye, said neural integrity assessment instrument comprising:
 - a sensor of oxygenation in the patient's second eye; and
 - a detector of a change in the level of the sensed oxygenation in response to stimulation of the patient's first eye with flickering light, said change being indicative of neural integrity of the patient's central nervous system.

7. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 6, wherein said sensor is positioned to sense levels of oxygenation at the optic nerve head of the fundus of the patient's second eye.

8. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 6, wherein said generator comprises a source of light operated through a flickering-light controller.

9. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 8, wherein said source of light is selected from the group consisting of a light-emitting diode and a laser.

10. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 8, further comprising a fiber optic cable interposed between the source of light and the patient's first eye, said fiber optic cable guiding light from the source of light to the patient's first eye.

11. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 6, wherein the neural integrity assessment instrument comprises an on-line oxygenation measurement device.

12. A method for assessing neural integrity of a patient's central nervous system, comprising:

- stimulating at least one ear of the patient with an auditory flickering stimulus;
- sensing oxygenation in at least one eye of the patient; and

detecting whether a change in the sensed oxygenation occurs in response to stimulation of said patient's at least one ear with the auditory flickering stimulus, said change being indicative of neural integrity of the patient's central nervous system.

13. A method for assessing neural integrity of a patient's central nervous system as defined in claim 12, wherein sensing oxygenation in said patient's at least one eye comprises sensing levels of oxygenation at the optic nerve head of the fundus of said patient's at least one eye.

14. A method for assessing neural integrity of a patient's central nervous system as defined in claim 12, wherein stimulating said patient's at least one ear comprises adjusting at least one of the following parameters to generate at least one desired neural response of the patient's central nervous system: an amplitude of the auditory flickering stimulus, a frequency of the auditory flickering stimulus, a pitch domain of the auditory flickering stimulus, a flicker rate of the auditory flickering stimulus, and a duration of the stimulation of the patient's at least one ear with the auditory flickering stimulus.

15. An apparatus for assessing neural integrity of a patient's central nervous system, comprising:

- a generator of an auditory flickering stimulus, said auditory flickering stimulus being applied to at least one ear of the patient to stimulate said patient's at least one ear;
- a neural integrity assessment instrument responsive to oxygenation in at least one eye of the patient, said neural integrity assessment instrument comprising:
 - a sensor of oxygenation in said patient's at least one eye; and
 - a detector of a change in the level of the sensed oxygenation in response to stimulation of said patient's at least one ear with the auditory flickering stimulus, said change being indicative of neural integrity of the patient's central nervous system.

16. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 15, wherein said sensor is positioned to sense levels of oxygenation at the optic nerve head of the fundus of said patient's at least one eye.

17. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 15, wherein said generator comprises a source of auditory flickering stimulus connected to an earphone.

18. An apparatus for assessing neural integrity of a patient's central nervous system as defined in claim 15, wherein the neural integrity assessment instrument comprises an on-line oxygenation measurement device.

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