OBJECTIVE DETERMINATION OF CHRONIC PAIN IN PATIENTS

BACKGROUND OF THE INVENTION

[0001] This application relates to a method for objectively determining chronic pain in individuals.

[0002] Humans (as well as animals) suffer from two types of pain. Transitory pain, caused by external factors such as impacts, heat, etc. and injuries to tissue caused thereby, or by certain illnesses, can last for short moments to longer periods of time. It typically lasts until the effect on the person's tissue from injury or illness subsides, e.g. until a wound or burn, for example, has partially or fully healed. Humans also suffer long-term or chronic pain, which may or may not be the result of external factors and which typically persists for indeterminate lengths of time. Chronic pain can be debilitating and can prevent the person suffering such pain from leading a normal life, pursuing an occupation, performing many routine activities, and the like. Persons suffering chronic pain are often entitled to compensation from an insurance company, an employer, the government, individuals who negligently or intentionally inflicted the pain, etc. In the past, it was most difficult if not impossible to objectively determine the chronic pain allegedly suffered by a person. Making this determination, however, is important in order to fairly and adequately compensate the pain sufferer.

[0003] The root for the problem of objectively determining the presence of chronic pain and/or to quantify it is that pain is perceived by the brain, and there are presently no feasible tests or procedures which can objectively determine if chronic pain is present and, if so, the magnitude thereof. As a result, persons, such as physicians, psychologists, technicians and the like, had to principally rely on a subjective evaluation of the chronic pain by the patient. This is a difficult and highly inaccurate task, leading to unreliable results.

[0004] An individual's perception of chronic pain may be incorrect due to a variety of factors, such as his/her mental and/or emotional state, an objectively incorrect perception of the pain by the individual's brain, variations in pain tolerances by individuals, etc.

[0005] In addition, the pain sufferer may be motivated to embellish or diminish the chronic pain for purposes unrelated to the pain itself. Thus, an individual might exaggerate, embellish or completely fabricate the presence, description and/or magnitude of chronic pain.

Most often this occurs when an individual seeks to be compensated by a third party for the chronic pain he asserts to suffer. The individual may exaggerate or fabricate the chronic pain because he believes this may yield a higher payment from an insurance company, may lead to a higher settlement of a dispute, may assist the individual in prosecuting a lawsuit, may gain sympathy from others, and the like. Individuals also might minimize the chronic pain suffered by them, for example, in order to qualify for a position he/she seeks where chronic pain might be an obstacle.

[0006] The processing of insurance claims for compensation as a result of debilitating chronic pain is probably the most frequent occurrence requiring a determination of the presence and/or magnitude of chronic pain. Such claims may be for a one-time lump sum compensation, or for lifelong support as a result of actual, embellished or entirely fabricated assertions of high levels of chronic pain and the disabilities that can flow from them. Since a significant segment of the population suffers from chronic pain, the liabilities incurred by insurance companies and others obligated to compensate the sufferers are very large and typically lie in the billions of dollars per year nationwide.

[0007] Persons seeking compensation who do not suffer chronic pain, or suffer it at a non-debilitating level, would, if the claim is accepted, receive unfair compensation to which they are not entitled. This in turn burdens insurance companies and those insured by the insurance companies, because excessive or fraudulent claims lead to higher insurance premiums.

[0008] Up to now it has not been feasible to objectively determine the presence and/or amount of chronic pain, in an objective and reliable manner that is comparable, for example, to the way in which the cholesterol level in a patient can be determined with a simple blood test. Instead, claims for compensation due to chronic pain were in the past processed by persons who had experience in such matters. They looked at a variety of factors which can suggest the presence or absence and/or the level of chronic pain based on the patient's current behavior, background, personal and medical history, possible motivations for embellishing or fabricating their description of the chronic pain suffered by them, etc. Although such evaluations of claims are helpful, in that at least gross misstatements, exaggerations and outright untruths by the patient can sometimes be observed or detected, they are, at best, nonscientific, subjective and quite unreliable. As a result, a patient who suffers chronic pain might be wrongly judged as not having it, while another person who cleverly postures might be found to suffer such pain and be unjustifiably compensated.

[0009] It is well known that the presence of chronic pain is perceived and established in the brain. It has been suggested to more objectively determine the presence and/or level of chronic pain by observing brain activities that might evidence the presence of chronic pain and/or the level of such chronic pain.

[0010] U.S. patent 6,018,675 (Apkarian), for example, discloses to measure pain in a patient by applying a variable intensity pain stimulus in a time-dependent manner during which the patient's brain responses are recorded using imaging (for example, a functional MR) while the patient indicates the level of discomfort using a perceptometer or other similar pain rating device operated by the patient as the pain stimulus is applied and varied. The pain rating is correlated with the imaging results using a quantitative analysis to characterize the brain's representation of this pain. Color overlays are generated on high resolution anatomical images (MR or other modality) of the brain summarizing the calculated pain-related analysis information.

[0011] The Apkarian patent states that, during an examination, the patient is subjected to variable pain over a period of time during which brain responses of the patient are objectively imaged and during which time subjective indications of the level of discomfort of the patient are recorded. Thereafter, the subjective indications of the level of discomfort are correlated with the objectively imaged brain responses in order to characterize the brain's representation of the pain in relation to the patient's perception and irrespective of the details of the stimulus, which may be only weakly related to the perception. In this method, the patient may be externally manipulated in order to inflict a variable pain. Such manipulation may include the movement of a leg in the case of a patient experiencing chronic back pain. In other cases, the variable pain may be provided by the application of an external stimulus such as a thermal stimulus. In all cases, the stimulus perturbs the patient's pain perception and the patient himself/herself provides the perception signal used for analyzing the brain images.

[0012] The patient's subjective indications of pain are compared to the brain activities of a group of persons to whom the same pain stimuli were applied. Thus, the Apkarian patent further states that a large number of persons having the same pain-causing condition are tested using the above techniques in order to obtain an "aggregate" value for the condition. This sampling may also include persons who do not have the pain condition to test the reliability of the results obtained. For example, in order to establish an "aggregate" value of the brain images to be expected for a person having a lower back pain condition, several

persons are tested to obtain brain images for different levels of pain inflicted on them, for example by raising a person's leg to different angles to the horizontal. That is to say, with a person placed in a supine position, each leg of the person can be raised to different angles to the horizontal, for example in 5° increments. The brain images which are taken for each angular increment are then correlated with the pain rating indicated by that person. The resultant brain images relative to an indicated pain level may then be aggregated for these persons in order to establish an "aggregate" value to be expected for different levels of pain indicated by the rating device.

[0013] Once the "aggregate" value has been established, a patient may be subjected to a similar protocol to obtain his/her rating of pain for each angular increment of the leg relative to the horizontal. The brain image of the patient corresponding to the pain rating can then be compared to the aggregate brain image to be expected for the given pain rating. Deviations of the actual brain image from the expected aggregate brain image can then be used as objective evidence of feigned pain.

[0014] Thus, the Apkarian patent discloses a method of measuring brain activity in response to a number of pain stimuli successively applied to the patient. Although this approach may be helpful in discerning the pain generated by a number of pain stimuli, the method taught in the Apkarian patent does not and cannot distinguish between chronic pain and transitory pain and cannot establish the presence and/or magnitude of chronic pain on an objective basis.

[0015] As a result, these past attempts have not been adopted because of their questionable reliability, accuracy and/or practicability. Thus, there exists a need for a method to objectively determine chronic pain and chronic pain levels with a high degree of accuracy and reliability.

SUMMARY OF THE INVENTION

[0016] Sophisticated image scanning techniques are able to detect and quantify neuron activity in the brain. The present invention takes advantage of the discoveries that certain neuron activities which occur in the brain are related to pain sensations received by the brain, and that the pain-related neuron activity in the brain differs between patients suffering chronic pain and persons without chronic pain. In accordance with the present invention, this difference is advantageously used to detect whether a person suffers chronic pain on a purely

objective basis without requiring any input from the patient being examined. As a result, the patient cannot consciously influence the process and the ultimate determination whether he/she suffers chronic pain.

[0017] Pain occurring in a patient's body sends pain impulses to the brain, where they are initially processed at the prefrontal area of the brain, including the cortical and subcortical portions thereof. Such pain impulses cause neuron activity in the prefrontal area of the brain, which can be observed on functional magnetic resonance images ("f-MRI"). Thus, the application of a pain stimulus, such as vibration, pressure or heat, to any part of the patient's body can be observed by increased neuron activity in the brain, at least initially principally in the prefrontal area thereof. However, the observable neuron activity in response to an applied pain stimulus differs between patients who suffer chronic pain and persons who are free of such pain. Specifically, the chronic pain sufferer is much more sensitive to the applied pain stimulus than a person free of chronic pain, which shows up on the f-MRI as increased neuron activity in the brain as compared to the f-MRI of a person free of chronic pain to whom the same pain stimulus was applied.

[0018] Moreover, in a chronic pain sufferer, the observed brain activity in response to a given pain stimulus is a function of the amount of chronic pain that is present. Thus, the level of neuron activity in the brain bears a direct relationship to the amount of chronic pain suffered by the patient. This then provides a quantitative determination of the level of chronic pain the patient suffers.

[0019] To make the comparison between the neuron activity caused by a pain stimulus in a patient suffering chronic pain and in persons free of such pain, the patient's brain activity, as shown in his brain f-MRI, is compared to a standardized f-MRI that is assembled from brain activities in a representative sample of pain-free persons (control group) to whom the same pain stimulus was applied.

[0020] In its broadest form, the present invention involves applying a pain stimulus to the patient claiming to suffer chronic pain, observing changes in the brain caused by the stimulus, and comparing the observed brain changes to brain changes caused by the same stimulus applied to a group of persons who are free of chronic pain. An evaluator, such as a physician, for example, then judges if the differences between the observed brain changes in the patient and in the control group are statistically significant. If they are, the comparison results in an objective determination that the patient suffers from chronic pain. In addition, the

comparison of the quantitative changes to the brains of the patient and of the control group allows one to determine the level of chronic pain suffered by the patient with a high degree of objective accuracy.

[0021] In practical terms, the present invention involves initially preparing a library of standard f-MRIs for different control groups consisting of persons who are free of chronic pain. Standard f-MRIs are typically prepared by subjecting each member of the control group to the same pain stimulus while taking f-MRIs of the brain activity caused by the pain stimulus. All f-MRIs of the members of the control group are then statistically combined into the standard f-MRI for a given pain stimulus and for a control group the members of which have predetermined characteristics, as is further discussed below.

[0022] The patient claiming to suffer chronic pain is tested by applying the same pain stimulus to him/her as was applied to the members of the control group and taking an f-MRI of his/her brain activity. An evaluator then compares the patient's f-MRI to the standard f-MRI. If the patient's f-MRI shows a statistically significantly higher brain activity than is the case for the standard f-MRI, the patient is judged to suffer chronic pain. What is statistically significant can to some extent be left to the judgment but can at all times be objectively controlled, for example by defining that a standard deviation of 1 to 1½ from the mean of the standard, bell-shaped distribution of observed emissions is presently proposed, particularly for processing insurance claims as further discussed below.

[0023] Preferably, the process is computerized and automated so that the computer will provide an output which numerically (or otherwise, e.g. in graphic form) reflects the quantitative and qualitative differences between the patient's f-MRI and the standard f-MRI. In this manner, the process can be freed of most subjective inputs in determining the presence of chronic pain, including subjective inputs from an evaluator, by predefining computer output levels which indicate the presence of chronic pain.

[0024] The present invention is useful whenever the presence of chronic pain in a patient needs to be verified. The invention has particular applicability to the evaluation of insurance or other compensation claims based on chronic pain that may render the patient partially or wholly unable to perform certain tasks, hold jobs, and the like. A fairly substantial segment of the population suffers from chronic pain and makes claims for compensation. Unlike the past, when chronic pain could only be verified empirically and based on the evaluator's observations, including subjective input provided by the patient, which is quite inaccurate,

most difficult if not impossible to verify, and is subject to errors that might deny compensation to a person entitled to it, while unfairly awarding it to another person who does not suffer chronic pain, the present invention provides a completely objective determination of whether chronic pain is present in a manner that cannot be influenced by the patient.

[0025] Thus, another aspect of the invention provides a method for processing insurance claims by alleged sufferers of chronic pain which involves measuring the brain activity in the patient caused by a pain stimulus applied to his/her body and comparing the patient's brain activities to the brain activities of persons to whom the same stimulus was applied but who are free of chronic pain. If the comparison shows there is a statistically significant difference, the patient is judged to suffer chronic pain, and this information is then forwarded to the insurance company (or other entity against whom the patient made a claim for compensation) for further processing, such as determining whether the patient is entitled to compensation.

[0026] The present invention is particularly useful for processing insurance and other claims for compensation by chronic pain sufferers. The invention takes away the possibility for a patient to embellish, enhance or even entirely fabricate the presence of chronic pain, a tendency that has been observed to apply to as many as 40% of insurance claimants. Thus, insurance claims processed in accordance with the present invention will have a very high degree of accuracy, thereby ensuring that chronic pain sufferers are adequately compensated while preventing unscrupulous persons from effectively defrauding the insurance system by making inaccurate or outright false assertions, which, in the past, could not be readily verified.

Responses of the Brain to Pain

[0027] The human brain is not static, and with ongoing or chronic pain there is an adaptive reorganization of the brain. This has been observed on f-MRIs, MRSs (magnetic resonance spectrometer), PET-scans, MEGs (magnetoencephalography), etc. Scientific studies have shown that, with pain, there is brain plasticity and because of the brain plasticity there are changes in areas of the brain. For example, in the somatosensory map (how the body looks at itself), there is sensory reorganization, there is prefrontal cortical hyperactivity, there are changes in the brain neurotransmitter levels, and there are changes in pain-related neuron activity involving secondary pain and especially chronic pain.

[0028] Careful physical examinations have shown a relationship between, for example, patients with a low tender point count, and as the pain becomes more severe, the clinical

examination will change with an increase in the positive tender point count, allodynia (non-nociceptive stimulation which is painful) changes in the somatosensory map, etc. Even absent the scientific studies, careful clinical examinations demonstrate that there is plasticity in the central nervous system. Studies have also shown that with the healing or disappearance of the pain generator and a resulting decrease or absence of chronic pain, the nervous system will return to normal.

[0029] Clinical observation and/or examination of the patient may present confusing and variable findings to the unknowledgeable evaluator/physician. For example, in hysterical conversion reactions, individuals with chronic pain will exhibit non-anatomic and non-physiologic patterns of pain. With an f-MRI, these changes become explainable because they involve changes in the somatosensory map, or how the body looks at itself. These brain and neuro pattern changes are observable on f-MRIs.

[0030] Conventional MRIs allow imaging of both soft and hard tissue anatomy. Water is slightly magnetic in a high magnetic field. Some of the protons in the water line up and become a molecular compass. A radiofrequency ("RF") signal sent through the human body in a strong magnetic field will, depending on the amount of water/protons in the tissue, allow obtaining a cross-sectional image. The resultant image is based on the amount of water in the tissue. Bone, ligaments, muscle, etc. can be imaged. MRIs using this technique give a detailed cross-sectional image of the soft tissue which is impossible with x-rays.

[0031] F-MRIs go further and allow an indirect observation of neuron activation. The neural activation image production comes from the oxygen in the blood. The hemoglobin of blood contains iron, which can combine with oxygen carried by the blood. In brain tissue, the hemoglobin gives up its oxygen, which changes the magnetic properties of the hemoglobin. The change in the magnetic property of the hemoglobin results in a disturbance in the local magnetic field. Magnetized water molecules close to the hemoglobin oxygen exchange lose their magnetic orientation for a few nanoseconds, after which they will recover. RF signals beamed through the brain tissue pick up these magnetic alterations, which can be seen on the f-MRI, thereby identifying the changes that take place in the brain. Computers with appropriate software such as the AFNI (*Analysis of Functional Neuro Imaging by Robert Cox Ph.D.; Bio-research Institute, Medical College of Wisconsin and now at the National Institute of Health*) are used to create maps of the location of the neural

activation, and its strength, for example as a percentage of the neurons becoming active, and/or as a change of the pattern of the neuron activation.

[0032] More specifically, the intense magnetic field of the f-MRI allows a sufficient number of the water molecules (which are only slightly magnetic) to line up magnetically to permit depended level technique ("BOLD") to become effective. The BOLD technique takes advantage of the fact there are changes in the blood during nutrition of the neuron cells for activation. The hemoglobin will go from a diamagnetic oxyhemoglobin to paramagnetic deoxyhemoglobin. Change in the hemoglobin, in the red blood cell, from diamagnetic to paramagnetic results in a change in the magnetic signature of the molecule. The magnetic signature changes lead to a disturbance of the local magnetic field surrounding the hemoglobin. The magnetized water molecules, because of the disturbance in the local magnetic field, will lose their magnetic orientation. However, after the local magnetic signal change stabilizes, the molecules will again align themselves with the strong external magnetic field, and when the realignment occurs, there is a generation of RF signals. The realignment RF signal can be detected and the changes in the magnetic field recorded on the f-MRI.

[0033] In other words, with activation of the neurons by stimulation, there is a requirement for oxygen to complete the chemical reactions necessary for brain/neuron metabolism. This metabolic requirement occurs when the neuron is stimulated and then becomes metabolically active. The metabolism requires oxygen, and there is passage of the oxygen from the hemoglobin, or blood, to the neuron. This involves a momentary loss of magnetic orientation, which generates RF signals and becomes visible on the f-MRI scan. Magnetic changes can be mapped showing location of the activation, the magnitude thereof, the percentage of neurons becoming active, and the pattern of neuron activation that becomes visible on the f-MRI.

[0034] Thus, input to the brain from the body caused by sensory dysfunction or pain results in changes in the brain responses. These changes include neurochemical changes/molecular changes and the functional alterations of normal excitement and inhabitation of neurotransmissions. There are also new neural connections made and a reorganization, or makeover, of the somatosensory section of the brain. These changes are modulated by nociceptive or pain input. The changes are essentially hyper-responsiveness associated with reorganization.

[0035] Research has been carried out to identify pain generators in the back. This has shown that back pain can be due to injuries to back muscles, intraspinous ligaments, the dura matter, the sacroiliac joint, etc. All these can be pain generators. Studies have shown 41% of back pain is secondary to discogenic disease, 34.4% is secondary to sacroiliac joint pain, and 18% originates from the zygapophyseal joint.

[0036] One of the major pain generators in the spine is "tumor necrosis factor alpha" from a pain-generating disc of the spinal cord. After approximately the age of 20 there is a decreased blood supply to the human intervertebral disc. This results in "apoptosis", which is a non-necrotic or programmed death of the cell. A by-product of the cell breakdown is "tumor necrosis factor alpha".

[0037] Leaking of "tumor necrosis factor alpha" through rents or tears in the annulus fibrosis, which holds the disc nucleus pulposus in place, causes a chemical irritation of the spinal nerve root and its investments. X-rays, MRIs, electrodiagnostic studies, physical examination, etc. will frequently demonstrate no pathology. Discograms will be positive and MRI gadolinium studies will also show positive results. Vibratory testing will also cause significant increase in pain.

[0038] With chronic pain there are associated chemical changes in the brain. There is a decrease in N-acetyl aspartate and changes in other brain metabolites. The chemical changes will result in depression, anxiety and/or a loss of cognitive memory functions. The pain and discomfort, coupled with depression, can become so severe that, on occasion, chronic pain/ongoing pain individuals will commit suicide.

[0039] Chronic pain also involves changes in somatosensory cortical inhibition of the pain perceived and changes in reflexes, as well as changes in the excitability, for example in the motor cortex. The somatosensory maps of individuals with chronic pain show changes in perception of the body by the brain, which do not occur in persons without chronic pain.

[0040] A central feature made use of by the present invention is the difference in which transitory pain or a "pain stimulus" temporarily applied to a patient leads to different brain activities, or changes in brain activity, depending on whether the person has chronic pain. Changes in the brain due to brain plasticity, new neurons growing, as well as inhibition or augmentation of other pain pathways which are secondary to changes in the neurotransmitters and the nerve activity, are different in chronic pain patients as compared to persons free of chronic pain. As a result, there is a difference in the pattern of activity in the brain between

chronic pain and non-chronic pain patients. Further, studies show that individuals who carry a significant chronic pain load take about a nanosecond more time to process a pain stimulus applied to them as compared to a normal individual free of chronic pain, because there is an increased number of excited or activated neurons.

[0041] An important feature of the present invention is therefore to determine the difference in the pattern and/or number of neurons being activated in a chronic pain patient as compared to the activation and patterns of neurons in a normal, chronic pain-free person and, preferably, in a number of persons free of chronic pain (control group).

[0042] Additionally, brain (neuron) activity in a chronic pain patient is significantly and statistically meaningfully different from that in a pain-free patient. The brain activity in response to a pain stimulus can therefore be employed to objectively determine and quantify the presence of chronic pain by comparing the patient's brain activities (on an f-MRI) to the brain activities in a pain-free control group (on the standard f-MRI).

BRIEF DESCRIPTION OF THE DRAWINGS

[0043] Fig. 1 is a flow diagram of the method for objectively determining if a patient has chronic pain; and

[0044] Fig. 2 is a flow diagram which illustrates the processing of a claim for compensation for chronic pain disability.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0045] Pain that stops activity amounts to a disability. Pain is a subjective, unpleasant sensation that varies, depending on a variety of factors, such as genetics, brain chemistry, past pain experience, culture, emotion, suggestions, etc. Pain can be secondary to actual, potential tissue damage and also secondary to brain abnormal/pathological nociception information processing.

[0046] Clinicians, insurance companies and the courts have relied on physical examination and a variety of examination techniques to identify and quantify pain. For example, in the evaluation of chronic pain patients, routine MRI scans, CT scans, electromyelograms, etc. have been employed as providing at least a measure of non-subjective findings, but they are not objective. A routine MRI may show pathology that is or is not a pain generator. The

levels of the pain and/or disability stated by a patient are subjective complaints that are highly variable and not objectively reliable. However, on an f-MRI, pain perception by the brain, as distinguished by statements from the patient, can be objectively observed.

[0047] The patient may have one or multiple painful body parts, for example. Chronic low back pain is a number one cause of disability in individuals under age 45. After age 45 it is the third leading cause of disability. Body areas that are affected with chronic pain vary, but involve the cervical spine, shoulders, arms, wrists and hands, dorsal and lumbar spine, hips, knees, ankles, entire arms, entire legs, etc. These same anatomical areas are amenable to pain stimulation evaluation by comparing the patient's f-MRI to the standard f-MRI (or "chart") at the same level of pain stimulation applied to the same anatomical areas.

[0048] One of the objectives of the present invention is to provide the requesting person or agency (e.g. the insurance company) with an objective statistical comparison of a patient with ongoing pain to normal pain-free persons. The results are based on the pattern and/or the percentage of neuron activation compared to standard normal pain-free persons when a pain-producing stimulus is applied at or near the suspected pain generator. Alterations and pattern changes will occur in pain processing between normal and chronic pain subjects when the same stimulation is applied such as heat, pressure, vibration or cold to the same anatomic area.

[0049] This invention benefits insurance companies, courts, etc. as well as the chronic pain patients themselves. Insurance company studies have shown an estimated 20% to 46% of litigation involving chronic pain and suffering is based on either fraudulent behavior or misrepresentations by the plaintiff. Other insurance company-funded studies have shown that up to approximately 40% of the population feels that it is acceptable to misrepresent their chronic pain and suffering symptomatology in order to obtain a favorable insurance or other settlement.

[0050] The invention will also benefit the individual with a considerable chronic pain who was not diagnosed as having chronic pain when evaluated/examined in accordance with past practice. Without objective findings, a chronic pain sufferer will occasionally go without appropriate compensation and/or further medical treatment, even though he/she will have continued pain and significant functional activity restrictions limiting his/her income, decreasing the quality of life, and/or impacting his/her family's future. The present invention

can identify patients with significant chronic pain, sort out the embellishers and fraudulent claims, and facilitate proper decision making for the appropriate institution or person.

[0051] As discussed above, the pain pattern and neuron activation in the brain of a patient with chronic pain is different from that of normal persons with no such pain. Chronic pain patients have an increased pain sensitivity, hyperalgesia and frequently also a central augmentation of pain. For example, a patient with chronic lower back pain or with fibromyalgia who receives a painful stimulus applied to his/her thumbnail will have an f-MRI that differs from that for the control group when the same pain stimulus is applied. Differences in the brain regions and pattern of neuron activation between the two sets of f-MRIs can be objectively observed. Both the fibromyalgia patient and the chronic lower back pain patient will exhibit extensive common patterns of neuron activation of pain in related cortical areas.

[0052] Chronic back pain patients and patients with fibromyalgia require a lower magnitude or intensity of pain stimulation than a pain-free person who received the same pain stimulus. Thus, chronic pain patients require a lesser pain stimulus to activate the same painful response than is required for pain-free persons.

[0053] Further, depending on his/her current chronic brain pain burden, patients with ongoing chronic pain will reach a maximum of pain and neuron activation even if the magnitude or intensity of the pain stimulus is increased; that is, an even greater pain stimulus will not lead to greater pain after a maximum pain level has been reached. Thus, as compared to a control group, a given pain stimulus applied to a chronic pain patient leads to increased neuron activation and a greater level of pain as compared to pain-free persons. Conversely, the intensity needed to observe a common pain level on the f-MRI will be less for the chronic pain patient than for the pain-free persons. In addition, the chronic pain patient will normally have a different regional cerebral blood flow as compared to the pain-free control group.

[0054] Referring to Fig. 1, the actual evaluation whether a given person claiming to suffer chronic pain in fact has chronic pain is conducted in an f-MRI machine by initially placing the patient in a comfortable position within the bore of the magnet of the machine. The patient's head is immobilized, for example with a vacuum bean bag, a foam headrest and a removable plastic bar across the bridge of the nose, although if there is concern about a tremor or movement, a bite bar can be used instead to hold the head steady, and a pain

stimulus 2 is applied while the patient's brain is scanned at 4 and an f-MRI image of the brain activity is taken. To avoid the effect of sensitization, the pain stimulus is applied in a random order. The modality of the stimulus will also be random.

[0055] Members of the control group were previously subjected to the same pain stimulus 1 at intervals, initially up to a sensation threshold level which lies just below the pain threshold level, and thereafter to the pain threshold level and, finally, to the maximum tolerable pain level, while their brains are scanned at 3 and f-MRI images thereof are taken. The f-MRI images of the members of the control group are statistically combined at 5 into a standard f-MRI image or chart of the average brain activities of the members of the group. The standard chart is then stored at 7, for example in a computer memory or other suitable memory or storage device.

[0056] The same protocol used for the control group is used on the chronic pain patient by preferably applying the pain stimulus to the painful body part and the contralateral body part. It should be noted, however, that for purposes of the present invention the pain stimulus can be applied to parts of the body not affected with chronic pain in order to generate f-MRI images that reflect the presence or absence of chronic pain. During scanning, the patient in the f-MRI machine has access to an alarm so that in the event pain becomes intolerable during testing, he/she can stop the test.

[0057] The f-MRIs generated during testing of the chronic pain patient are fed into a computer which preferably includes in its database 7 at least the standard f-MRIs which are relevant to the test in progress. In a preferred embodiment, the computer is appropriately programmed to compare the patient's f-MRI or f-MRIs with the standard f-MRIs at 6 and to appropriately quantify the difference, for example in terms of a percentage difference, which can be further processed and can be used by an evaluator, a physician, an insurance company and the like to judge at 8 whether the patient suffers chronic pain and, if so, to preferably also quantify the chronic pain so that, if appropriate, required compensation can be paid. Alternatively, the comparison of the patient's f-MRI to the standard f-MRI can be done manually, for example by a physician.

[0058] Although not necessary for the objective determination of the patient's chronic pain level, in a preferred embodiment of the invention the patient can be asked to rate the perceived pain level while the test is in progress, for example to differentiate between mild pain (25%), slight pain (50%), moderate pain (75%) and severe pain (100%). This subjective

pain rating provides helpful verification of the objectively conducted pain level tests. As such, it will preferably also be provided to the requestor, e.g. the insurance company, for review and evaluation. However, the objective determination of the chronic pain level in accordance with the invention is based solely on the above-described comparison of the patient's f-MRI with the standard f-MRI to remove all subjective inputs from the evaluation.

[0059] The pain stimulus that is applied to both the members of the control group and the individual patients can be selected from a variety of different technologies, which, moreover, are subject to change as new methods become available. Principally, the pain stimulus is applied to the patient and the members of the control group in similar and preferably in an identical manner. As previously mentioned, the pain stimulus is preferably applied to the area from which the pain originates and to the contralateral side thereof.

[0060] The pain stimulus is initially applied at a magnitude so that the sensation perceived by the patient is just below his/her pain threshold level. The pain threshold level is reached when the pain stimulus applied to the patient changes from a mere sensation to perceived pain. Thereafter the pain stimulus is increased past the threshold level and up to a maximum stimulation pain level. At each interval or pain level, at least one complete f-MRI showing the patient's brain activity in response to the applied stimulus is taken. Generally speaking, the pain threshold levels will vary from patient to patient (at least in part depending on the patient's level of chronic pain), and they will dictate the amount of pain stimulus that can be applied to any given patient (or member of the control group). Further, tests stopped at the request of the patient are significant and useful as studies that had to be terminated. Both completed and terminated studies will show a difference in the pain level in the patient's brain for comparison to the corresponding pain level in the standard f-MRI for the control group.

[0061] Vibratory devices are useful for applying pain stimuli for eliciting pain responses from inflamed/irritated tissue. Vibratory devices are clinically useful in identifying individuals with discogenic back pain. Vibratory devices also cause pain and discomfort when applied to individuals with SI joint dysfunction, painful joints and painful muscles. MVDs (magneto-mechanical vibrotactile device) placed in the static magnetic field of an f-MRI scanner can be used to generate vibration. The MVDs work on the principle of wire coils with small oscillatory currents in a large static magnetic field. The resulting Lorentz forces can be oriented to generate large vibrations that are easily converted to transitional

motion of as much as several centimeters. This vibration can also be converted into oscillating motion. Vibratory frequencies of 1hz to 130hz and displacement amplitudes of .5mm to 4mm will produce a positive vibratory response in inflammation. This device is well-described by Golaszewski, SM, et al., in Neuroimaging 2002, September 17 (1): 421-30, *Functional Magnetic Resonance Imaging of the Human Sensorimotor Cortex Using Noval Vibrotactile Stimulator*, and also described by Graham, SJ, published in Magnetic Resonance Medicine, 2001, September 46 (3): 436-42, *New Devices Deliver Somatosensory Stimuli During Functional MRI.*

[0062] The MVD will be applied with a very mild amount of pressure to make certain there is good tissue contact. This can be accomplished by using a 1mm to 2mm raised 1-2 cm diameter soft round pressure point. In patients with hyperalgesia, application with pressure may not be possible, because of pain, however the f-MRI will show positive findings and a change in the pain threshold compared to the normal pain-free members of the control group.

[0063] Heat can be applied as a pain stimulus by using a modified thermal stimulator. This can be a Peltier device, also known as thermal electric (TE) modules. It is a small solid state device that acts as a heat pump. When a direct current is applied, heat is moved from one side of the device to the other. Such devices can be used to apply either heat or cold.

[0064] Lasers can be used as a pain stimulus to apply heat to peripheral body parts. A CO_2 laser that produces infrared radiation will activate nocioceptors in the hand or foot, for example. A thulium-YAG (Yttrium-aluminum-granage) laser will also produce nociception. These lasers act as a pain stimuli without concomitant tactile contact or stimulation. Using lasers will also allow rapid alternation in pain manipulation between each side of the body. The use of lasers for stimulating pain is described by Bingel, U, et al., in Neuroimaging 2003, March 18 (3): 740-8, *Single Trial f-MRI Reveals Significant Contralateral Bias in Response to Laser Pain Within Thalamus and Somatosensory Cortexes.*

[0065] Pressure pain may be applied as a stimulus with a tensiometer that has a rounded surface with a 3 cm diameter. Pressure may be applied at 4 to 6 mm of mercury, or the lowest level at which the patient reports a beginning of pain. The pain threshold is typically at about 15 to 18 mm in mercury. Pressure may also be applied using a water actuator.

[0066] One or more of vibration, pressure, heat, lasers, light touch and cold are used as a pain stimulus, depending on the clinical situation, the patient, the location of the chronic pain, etc. For example, in long-term unilateral muscle pain there is a significant increase in

sensitivity to pressure compared to the homologous contralateral area, but there will be no difference in the outcome of thermal testing. Also, in muscle pain, in the painful area there will frequently be a decreased sensitivity to light touch. For such a case, heat or another non-contact device will normally be the preferred pain stimulus.

[0067] Transitory or acute pain also causes pain changes in the central nervous system. Such pain is temporary and the nervous system will return to normal when the pain stops. However, with chronic/ongoing pain, there are continued central nervous system changes in the patient's brain which lead to enhanced brain responses (neuron activity and/or patterns of neuron activity) as compared to what occurs in patients without chronic pain.

[0068] Depending on intensity of the stimulus, there is an increase in referred pain. (For example, an intense deep pain stimulus will travel to the spinal cord in the unmyelinated C nerve fibers. With the intense stimulation, neighboring neurons will also become active and a lower pain threshold hyperalgesia will result. With significant stimulation of the spinal cord neurons, an associated burning referred pain will develop. This burning referred pain results in an increased area of pain generation. The increased area of referred pain results in increased stimulus size. The increased size of the pain stimulus results in further neuro changes, which results in even further central nervous system changes.

[0069] Referring briefly to Fig. 2, the above-discussed method of the present invention for processing claims by an asserted chronic pain sufferer for reimbursement from an insurance company or any other third party involves initially receiving the request for compensation at 20, for example at an insurance company. The request is referred to an evaluator 22 who then examines the patient by applying pain stimuli to the patient at 24 in the manner described above. With the pain stimulus applied, an f-MRI image of the patient's brain activity is prepared at 26.

[0070] The patient's f-MRI is then compared to the standard f-MRI image or chart from the members of the control group at 28, either by a computer (which compares the patient's f-MRI with the standard f-MRI and provides an output that reflects the difference between the two) or, in the alternative, by the evaluator, preferably but not necessarily a physician. At 30, the evaluator judges if the difference between the patient's f-MRI and the standard f-MRI is statistically significant, which means that the differences between the two f-MRIs are sufficiently large so that they are not the result of random variations, but are caused by the presence of chronic pain in the patient. If the difference is judged to be statistically

significant, the evaluator informs the requestor at 32 that the patient suffers chronic pain. Conversely, if the difference between the two images is judged to be statistically not significant, the evaluator informs the requestor (e.g. the insurance company) that the patient does not have chronic pain.

[0071] Although it is entirely feasible to leave the judgment whether the difference between the two sets of f-MRIs is statistically significant to a computer analysis and use the output (e.g. a numerical output that is reflective of the difference) as the criterion whether the patient suffers chronic pain, for example whenever the difference rises above a predetermined threshold level, review of the respective images by a trained person, such as a physician, will typically be desirable, and he/she may supplement the computer output with additional comments concerning the computer output and/or the testing of the patient and the observed results.

WHAT IS CLAIMED IS:

1. A method for determining the presence of chronic pain in a patient comprising applying a pain stimulus to a part of the body of the patient, observing changes in the brain caused by the pain stimulus, comparing observed brain changes to brain changes caused by the stimulus when applied to a plurality of persons who are free of chronic pain, and deciding that the patient suffers chronic pain if the brain changes observed in the patient while the stimulus is applied are judged to be statistically significantly different from the brain changes in the plurality of patients who are free of chronic pain.

2. A method according to claim 1 wherein the patient is judged to have chronic pain if brain changes observed in the patient are statistically significantly greater than brain changes observed in the person free of chronic pain.

3. A method according to claim 1 wherein observing changes in the patient's brain comprises observing physical emissions generated by the brain of the patient.

4. A method according to claim 3 wherein observing physical emissions comprises observing radiofrequency (RF) emissions generated by the brain.

5. A method according to claim 3 wherein observing changes in the RF emissions comprises observing an intensity of the RF emissions and comparing them to an intensity of RF emissions from the plurality of persons who are free of chronic pain.

6. A method according to claim 4 wherein observing RF emissions comprises observing a pattern of RF emissions generated by the patient's brain, and wherein comparing comprises comparing the observed RF emission pattern in the patient's brain with an RF emission pattern for the persons who are free of chronic pain.

7. A method according to claim 6 wherein observing patterns of RF emissions includes observing patterns of RF emissions in the patient and in the plurality of patients who are free of chronic pain in prefrontal areas of the brains.

8. A method according to claim 4 wherein comparing comprises comparing f-MRIs of the patient with a standard f-MRI based on RF emissions by the brains of the persons who are free of chronic pain.

9. A method according to claim 8 wherein observing changes in the brain of the patient includes generating an f-MRI of RF emissions by the patient's brain.

10. A method according to claim 9 including preparing a standard f-MRI for RF emissions by the brains of persons who are free of chronic pain which is a statistical summary of the f-MRIs of the persons who are free of chronic pain, and wherein comparing comprises comparing the f-MRI of the patient with the standard f-MRI.

11. A method according to claim 10 wherein comparing comprises processing the patient's f-MRI and the standard f-MRI in a computer and generating a computer output which quantifies a difference between the patient's f-MRI and the standard f-MRI.

12. A method according to claim 11 including judging if the difference between the patient's f-MRI and the standard f-MRI is statistically significant.

13. A method according to claim 12 including deciding that the patient has chronic pain if the difference between the patient's f-MRI and the standard f-MRI is statistically significant.

14. A method according to claim 1 wherein comparing comprises preparing a standard chart of brain changes caused by the stimulus in the plurality of persons who are free of chronic pain, and comparing comprises comparing the changes in the patient's brain with the standard chart.

15. A method according to claim 14 wherein preparing the standard chart comprises comparing a standard f-MRI reflective of the brain changes in the plurality of persons who are free of chronic pain.

16. A method according to claim 15 wherein the standard f-MRI is an f-MRI of a statistically significant number of persons who are free of chronic pain.

17. A method according to claim 14 wherein observing the changes in the patient's brain comprises preparing an f-MRI which reflects the changes in the patient's brain, wherein preparing the standard chart includes preparing a standard f-MRI which is reflective of the changes in the brains of the plurality of persons who are free of chronic pain,

and wherein deciding if the patient suffers chronic pain includes judging if a difference between the patient's f-MRI and the standard f-MRI is statistically significant.

18. A method according to claim 17 wherein deciding if the patient suffers chronic pain includes analyzing the difference between the patient's f-MRI and the standard f-MRI with a computer.

19. A method according to claim 18 including generating a computer output which reflects the difference between the patient's f-MRI and the standard f-MRI.

20. A method according to claim 19 wherein the output of the computer is a numerical output.

21. A method according to claim 19 including evaluating the computer output and therewith judging if the patient is likely to have chronic pain.

22. A method according to claim 1 wherein applying the pain stimulus comprises applying at least one of vibrations, pressure, heat, cold and brushing to an external surface of the part of the patient's body.

23. A method for determining if a patient has chronic pain by applying a pain stimulus to the patient, observing changes occurring in the patient's brain in response to the applied pain stimulus, comparing observed changes in the patient's brain to changes caused by the same stimulus in brains of persons without chronic pain, analyzing results from comparing the observed changes in the respective brains to determine if the difference is statistically significant and, if so, judging that the patient is likely to suffer chronic pain.

24. A method according to claim 23 wherein applying comprises applying an external pain stimulus to the patient.

25. A method according to claim 23 including judging that the person is likely to suffer chronic pain if the results of analyzing show that changes in the patient's brain caused by the applied stimulus are statistically significantly higher than changes in the brains of persons without chronic pain generated by the same stimulus to such persons.

26. A method according to claim 23 wherein comparing comprises preparing an f-MRI of radiofrequency (RF) emissions in the patient's brain while the pain

stimulus is applied, preparing a standard f-MRI for the persons without chronic pain by combining individual f-MRIs of changes in the brains of the persons without chronic pain so that the standard f-MRI is reflective of approximately an average change in the brains of the persons without chronic pain, and wherein analyzing comprises evaluating the difference between the patient's f-MRI and the standard f-MRI.

27. A method for verifying a claim for compensation made to a receiver of the claim resulting from an assertion of chronic pain by a patient comprising subjecting the patient to a pain stimulus, observing changes occurring in a brain of the patient in response to the pain stimulus, comparing the observed changes in the patient's brain to changes in the brains of a multiplicity of persons who are free of chronic pain and who have been subjected to the same pain stimulus, determining if a difference between the changes occurring in the patient's brain and the changes observed in the brains of the persons without chronic pain is statistically significant, and if the difference is statistically significant informing the receiver that the patient is judged to likely suffer chronic pain.

28. A method according to claim 27 including preparing f-MRIs reflective of changes occurring in the patient's brain and of changes occurring in the brains of persons who are free of chronic pain, and wherein determining if the difference is statistically significant comprises comparing the f-MRIs.

29. A method according to claim 28 wherein comparing f-MRIs comprises feeding the f-MRIs into a computer, and analyzing the difference between the patient's f-MRI and the f-MRIs of the persons without chronic pain.

30. A method according to claim 28 including informing the receiver that the patient is likely to suffer chronic pain when the difference between the respective f-MRIs is statistically significant.

31. A method according to claim 27 including judging that the patient is likely to suffer chronic pain if the difference between the changes observed in the patient's brain and the changes observed in the brains of the persons who are free of chronic pain shows that the changes observed in the patient's brain are statistically significantly higher than the changes observed in the brains of the persons without chronic pain.

32. A method according to claim 27 wherein the receiver is an entity requested to compensate the patient.

33. A method according to claim 32 wherein the entity is an insurance company.

34. A method for processing an insurance claim submitted by a patient asserting to suffer chronic pain comprising observing a multiplicity of persons who are free of chronic pain while subjecting the persons to a given pain stimulus, measuring radiofrequency (RF) emissions generated by the brains of the persons who are free of chronic pain while the persons are subjected to the pain stimulus, preparing a chart which statistically reflects an average of RF emissions generated by the brains of the persons who are free of chronic pain while subjected to the pain stimulus, applying the given pain stimulus to the patient, sensing RF emissions generated by a brain of the patient while the given pain stimulus is applied, comparing the RF emissions from the patient's brain with the chart and determining if the RF emissions from the patient's brain are statistically different from the approximately average RF emissions from the persons who are free of chronic pain, and advising the insurer that the patient is likely to suffer chronic pain if the difference between the RF emissions from the patient's brain and from the brains of persons who are free of chronic pain is statistically significant.