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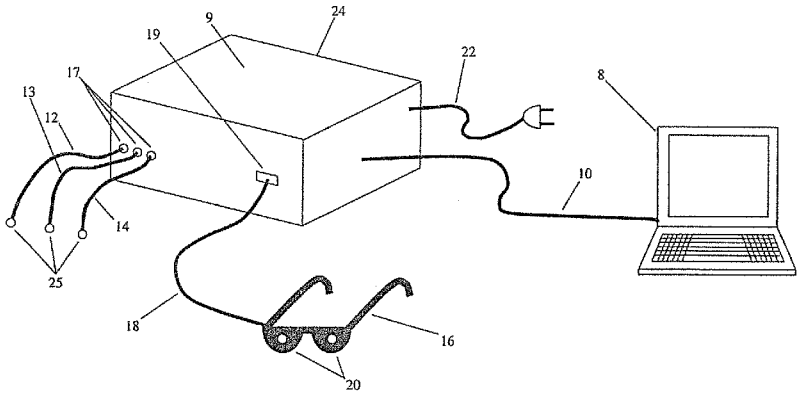

Figure 4

(57) Abstract: Methods are disclosed for stimulating targeted regions of a brain to alleviate symptoms, treat conditions and/or modify brain activities associated with central sensitivity in a subject. The methods may include selecting a subject suffering from central sensitivity, identifying regions of the brain involved in central sensitivity, and stimulating one or more of these regions of the brain.

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AMENDED CLAIMS
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What is claimed is:

1. A method for alleviating symptoms associated with central sensitivity in a subject, the method including the steps of:

selecting a subject suffering from pathological brain activity associated with central sensitivity in a target region of the brain of a subject; and

alleviating one or more symptoms associated with the central sensitivity by stimulating the target region of the brain of the subject.

2. The method of claim 1, in which:

the one or more symptoms associated with central sensitivity include one or more symptoms from the group of such symptoms consisting of pain, musculoskeletal pain, pain at multiple sites, generalized hyperalgesia, stiffness, swollen feeling in soft tissues, fatigue, poor sleep, paresthesia, anxiety, chronic headaches, tension headaches, dysmenorrhea, irritable bowel syndrome, periodic limb movements, symptoms of restless leg syndrome, depression, symptoms of Sjogren's syndrome, symptoms of Raynaud's Phenomenon, symptoms of female urethral syndrome, impaired memory, impaired concentration, cognitive impairment, tender cervical lymph nodes, tender axillary lymph nodes, post-exertion malaise, tender points, sensory hypersensitivity, sleep disturbances, immune dysfunction, history of viral illness, neurohormonal dysfunction, neuroendocrine dysfunction, or a lack of macroscopic or microscopic pathological findings in peripheral tissues; and

the alleviating step includes alleviating one or more of the symptoms of the group of symptoms by stimulating the target region of the brain.

3. The method of claim 1, wherein the stimulating step includes at least one administration of electrical stimulation to a target region of the brain of the subject.

4. The method of claim 1, wherein the stimulating step includes at least one administration of magnetic stimulation to the target region of the brain of the subject.

5. The method of claim 1, wherein the stimulating step is performed in a noninvasive manner.

6. The method of claim 5, wherein the noninvasive manner includes stimulation applied to the target region of the brain from outside the subject and transmitted through intervening tissues.

7. The method of claim 1, wherein the stimulating step is performed in an invasive manner.

8. The method of claim 3, wherein the step of administering electrical stimulation includes administration of an AMPWM signal.

9. A method for treating a condition associated with central sensitivity in a subject, the method including the steps of:

selecting a subject suffering from pathological brain activity associated with central sensitivity in a target region of the brain; and

treating one or more conditions associated with the central sensitivity by stimulating the target region of the brain of the subject.

10. The method of claim 9, in which:

the one or more conditions associated with central sensitivity include one or more conditions from the group of such conditions consisting of chronic pain of unknown origin, fibromyalgia, osteoarthritis, depression, complex regional pain syndrome, phantom pain, chronic fatigue syndrome, irritable bowel syndrome, functional dyspepsia, migraine headaches, tension-type headaches, temporomandibular disorder, myofascial pain syndrome, regional soft-tissue pain syndrome, restless leg syndrome, periodic limb movements, multiple chemical sensitivity, primary dysmenorrhea, female urethral syndrome, interstitial cystitis, premenstrual tension syndrome, vulvodynia, Sjogren's syndrome, Raynaud's Phenomenon, post-traumatic stress disorder, Gulf War Syndrome, chronic low back pain, or mild traumatic brain injury; and

the treating step includes treating the one or more conditions of the group of conditions by stimulating the target region of the brain.

11. The method of claim 9, wherein the stimulating step includes at least one administration of electrical stimulation to the target region of the brain of the subject.

12. The method of claim 9, wherein the stimulating step includes at least one administration of magnetic stimulation to the target region of the brain of the subject.

13. The method of claim 9, wherein the stimulating step is performed in a noninvasive manner.

14. The method of claim 13, wherein the noninvasive manner includes stimulation applied to the target region of the brain from outside the subject and transmitted through intervening tissues.

15. The method of claim 9, wherein the stimulating step is performed in an invasive manner.

16. The method of claim 11, wherein the step of administering electrical stimulation includes administration of an AMPWM signal.

17. A method for altering brain activity associated with central sensitivity in a subject, the method including the steps of:

selecting a subject suffering from pathological brain activity associated with central sensitivity in a target region of the brain of the subject; and

stimulating the target region of the brain of the subject.

18. The method of claim 17, in which:

the selecting step includes selecting a subject exhibiting, in one or more regions of the subject's brain in response to one or more peripheral stimuli, one or more brain activities from the group of brain activities consisting of abnormal function, abnormal response, abnormal regions of activation, abnormal network

connectivity, abnormal release of neurochemicals, abnormal uptake of neurochemicals, abnormal electrical activity or abnormal metabolism; and

the stimulating step includes altering the one or more brain activities exhibited by the subject's brain by stimulating the target region of the brain.

19. The method of claim 17, wherein the stimulating step includes at least one administration of electrical stimulation to the target region of the brain of the subject.

20. The method of claim 17, wherein the stimulating step includes at least one administration of magnetic stimulation to the target region of the brain of the subject.

21. The method of claim 17, wherein the stimulating step is performed in a noninvasive manner.

22. The method of claim 21, wherein the noninvasive manner includes stimulation applied to the target region of the brain from outside the subject and transmitted through intervening tissues.

23. The method of claim 17, wherein the stimulating step is performed in an invasive manner.

24. The method of claim 19, wherein the step of administering electrical stimulation includes administration of an AMPWM signal.

25. A tissue stimulation apparatus for use in alleviating symptoms associated with central sensitivity in a subject, the apparatus comprising:

a neuroimaging device configured to obtain neuroimaging data from tissues in a target region of a brain of a subject suffering from pathological brain activity associated with central sensitivity in the target region and exhibiting one or more symptoms associated with central sensitivity;

a stimulation device including a stimulation signal generation circuit configured to generate and deliver a tissue stimulation signal to the target region of the subject's brain; and

a computing device configured to set one or more parametric values of the electrical tissue stimulation signal in response to neuroimaging data obtained by the neuroimaging device.

26. The apparatus of claim 25 for use in alleviating one or more of the following symptoms associated with central sensitivity: pain, musculoskeletal pain, pain at multiple sites, generalized hyperalgesia, stiffness, swollen feeling in soft tissues, fatigue, poor sleep, paresthesia, anxiety, chronic headaches, tension headaches, dysmenorrhea, irritable bowel syndrome, periodic limb movements, symptoms of restless leg syndrome, depression, symptoms of Sjogren's syndrome, symptoms of Raynaud's Phenomenon, symptoms of female urethral syndrome, impaired memory, impaired concentration, cognitive impairment, tender cervical lymph nodes, tender axillary lymph nodes, post-exertion malaise, tender points, sensory hypersensitivity, sleep disturbances, immune dysfunction, history of viral illness, neurohormonal dysfunction, neuroendocrine dysfunction, or a lack of macroscopic or microscopic pathological findings in peripheral tissues.

27. The apparatus of claim 25, wherein the stimulation device is configured to administer magnetic stimulation to a target region of the brain of the subject.

28. The apparatus of claim 25, wherein the stimulation device is configured to deliver an electrical stimulation signal to a target region of the subject's brain.

29. The apparatus of claim 28, wherein the electrical stimulation signal is an AMPWM signal.

30. The apparatus of claim 25, wherein the stimulation device is configured to deliver the stimulation signal to a target region of the brain from outside the subject and to transmit the signal through intervening tissues.

31. The apparatus of claim 25 for use in alleviating one or more symptoms associated with central sensitivity in a subject exhibiting, in one or more regions of the subject's

brain in response to one or more peripheral stimuli, one or more of the following brain activities: abnormal function, abnormal response, abnormal regions of activation, abnormal network connectivity, abnormal release of neurochemicals, abnormal uptake of neurochemicals, abnormal electrical activity or abnormal metabolism; the apparatus being configurable to alter the one or more brain activities exhibited by the subject's brain by stimulating the target region of the brain.

32. A tissue stimulation signal comprising one or more parametric values tailored in response to neuroimaging data obtained from tissues in a target region of the brain of a subject suffering from pathological brain activity associated with central sensitivity in the target region and exhibiting one or more symptoms of central sensitivity, and deliverable to the target region for use in alleviating the one or more symptoms.

33. A tissue stimulation signal as set forth in claim 32, wherein the stimulation signal is adapted for use in alleviating symptoms associated with central sensitivity by tailoring the signal to mitigate a central sensitivity condition causing the symptoms.

34. A tissue stimulation signal as set forth in claim 32, wherein the stimulation signal is an amplitude modulated pulse width modulated (AMPWM) signal for use in penetrating tissues between the signal source and the target region of the subject's brain.

35. A tissue stimulation signal as set forth in any one of claims 32-34, wherein the stimulation signal is tailored in response to neuroimaging data obtained from tissues in a target region of the brain of a subject suffering from one or more of the following central sensitivity symptoms: pain, musculoskeletal pain, pain at multiple sites, generalized hyperalgesia, stiffness, swollen feeling in soft tissues, fatigue, poor sleep, paresthesia, anxiety, chronic headaches, tension headaches, dysmenorrhea, irritable bowel syndrome, periodic limb movements, symptoms of restless leg syndrome, depression, symptoms of Sjogren's syndrome, symptoms of Raynaud's Phenomenon, symptoms of female urethral syndrome, impaired memory, impaired concentration,

cognitive impairment, tender cervical lymph nodes, tender axillary lymph nodes, post-exertion malaise, tender points, sensory hypersensitivity, sleep disturbances, immune dysfunction, history of viral illness, neurohormonal dysfunction, neuroendocrine dysfunction, or a lack of macroscopic or microscopic pathological findings in peripheral tissues.

36. A tissue stimulation signal as set forth in any one of claims 32-34, wherein:

the stimulation signal is tailored in response to neuroimaging data obtained from the brain of a subject exhibiting, in one or more regions of the subject's brain in response to one or more applied peripheral stimuli, any one or more of the following abnormal brain activities: abnormal function, abnormal response, abnormal regions of activation, abnormal network connectivity, abnormal release of neurochemicals, abnormal uptake of neurochemicals, abnormal electrical activity or abnormal metabolism; and

the signal is tailored for use in altering any one or more of the brain activities exhibited by the subject's brain.

37. A tissue stimulation signal as set forth in any one of claims 32-34, wherein the signal is a composite signal comprising two or more components configured for use in providing two or more frequency-dependent beneficial effects on tissues in a target region of a subject's brain.