

Claims:

1. A method of diagnosing an impending agitation episode in a subject predisposed to agitation comprising:

(a) monitoring one or more physiological signals of sympathetic nervous system activity in the subject using an automated sensing device placed or mounted on the subject's skin surface; and

(b) identifying, via the processing of incoming data in the device, when the subject is about to have an agitation episode.

2. A method of alerting a caregiver to an impending agitation episode in a subject predisposed to agitation comprising:

(a) monitoring one or more physiological signals of sympathetic nervous system activity in the subject using an automated sensing device placed or mounted on the subject's skin surface;

(b) identifying, via the processing of incoming data in the device, when the subject is about to have an agitation episode; and

(c) sending a signal from the device to a compatible device monitored by a caregiver alerting the caregiver to an impending agitation episode in the subject.

3. A method of preventing the emergence of agitation in a subject predisposed to agitation comprising:

(a) monitoring one or more physiological signals of sympathetic nervous system activity in the subject using an automated sensing device placed or mounted on the subject's skin surface;

(b) identifying, via the processing of incoming data in the device, when the subject is about to have an agitation episode;

(c) sending a signal from the device to a remote compatible device monitored by a caregiver alerting the caregiver to an impending agitation episode in the subject; and

(d) administering by the caregiver an anti-agitation agent which decreases sympathetic nervous activity in said subject.

4. A method of treating the early stage emergence of agitation or the signs of agitation in a subject predisposed to agitation comprising:

(a) monitoring one or more physiological signals of sympathetic nervous system activity in the subject using an automated sensing device placed or mounted on the subject's skin surface;

(b) identifying, via the processing of incoming data in the device, when the subject is having an agitation episode;

(c) sending a signal from the device to a remote compatible device monitored by a caregiver alerting the caregiver to the start of agitation episode in the subject; and

(d) administering by the caregiver an anti-agitation agent which decreases sympathetic nervous activity in said subject.

5. The method according to claim 3 or claim 4, wherein agitation is prevented or treated without causing significant sedation.

6. The method according to any one of claims 1 to 5, wherein the automated sensing device is a wearable device.

7. The method according to any one of claims 1 to 6, wherein the physiological signals of sympathetic nervous system activity are selected from one or more of the following: change in electrodermal activity; heart rate variability (e.g. resting EEG, ECG); cognitive assessments such as pupil size; secretion of salivary amylase; blood pressure; pulse; respiratory rate; temperature variability and level of oxygen in the blood.

8. The method according to claim 7, wherein sympathetic nervous system activity is assessed by measuring any change in electrodermal activity or any change in electrodermal activity together with any change in resting EEG.

9. The method according to any one of claims 1 to 8, wherein the automated sensing device sends data of physiological signals related to sympathetic nervous system activity in the patient to a remotely situated apparatus (e.g. a computer database) that includes one or more early warning algorithm.
10. The method according to claim 9, wherein the device sends a signal to the remotely situated apparatus through Bluetooth.
11. The method according to any one of claims 3 to 10, wherein the anti-agitation agent is an alpha-2 adrenergic receptor agonist.
12. The method according to claim 11, wherein the alpha-2 adrenergic receptor agonist is selected from the group consisting of clonidine, guanfacine, guanabenz, guanoxabenz, guanethidine, xylazine, tizanidine, medetomidine, dexmedetomidine, methyl dopa, methylnorepinephrine, fadolmidine, iodoclonidine, apraclonidine, detomidine, lofexidine, amitraz, mivazerol, azeperol, talipexol, rilmenidine, naphazoline, oxymetazoline, xylometazoline, tetrahydrozoline, tramazoline, talipexole, romifidine, propylhexedrine, norfenefrine, octopamine, moxonidine, lidamidine, tolomidine, UK14304, DJ-7141, ST-91, RWJ-52353, TCG-1000, 4-(3-aminomethyl-cyclohex-3-enylmethyl)-1,3-dihydro-imidazole-2-thione, and 4-(3-hydroxymethyl-cyclohex-3-enylmethyl)-1,3-dihydro-imidazole-2-thione or a pharmaceutically acceptable salt thereof.
13. The method according to claim 12, wherein the alpha-2 adrenergic receptor agonist is dexmedetomidine or a pharmaceutically acceptable salt thereof.
14. The method according to claim 13, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered parenterally by intravenous injection.
15. The method according to claim 13, wherein dexmedetomidine or a pharmaceutically acceptable salt thereof is administered sublingually using a self-supporting, dissolvable film.
16. The method according to any one of claims 13 to 15, wherein dexmedetomidine is administered as the hydrochloride salt.
17. The method according to claim 16, wherein dexmedetomidine hydrochloride is administered at unit dose in the range of about 5 micrograms to about 250 micrograms, preferably about 5 micrograms to about 200 micrograms.

18. The method according to claim 16, wherein dexmedetomidine hydrochloride is administered at unit dose of 180 micrograms.

19. The method according to any one of claims 1 to 18, wherein the patient is suffering from a neuropsychiatric disease selected from the group consisting of schizophrenia, bipolar disorder, bipolar mania, delirium, major depressive disorders and depression.

20. The method according to any one of claims 1 to 18, wherein the patient is suffering from a neurodegenerative disease selected from the group consisting of Alzheimer's disease, frontotemporal dementia (FTD), dementia, dementia with Lewy bodies (DLB), post-traumatic stress disorder, Parkinson's disease, vascular dementia, vascular cognitive impairment, Huntington's disease, multiple sclerosis, Creutzfeldt-Jakob disease, multiple system atrophy, traumatic brain injury and progressive supranuclear palsy.

21. The method according to any one of claims 1 to 18, wherein the patient is predisposed to agitation associated with opioid withdrawal, substance abuse withdrawal (including cocaine amphetamine), or alcohol withdrawal.

22. A method, comprising:

receiving first physiological data of sympathetic nervous system activity;

establishing a baseline value of at least one physiological parameter by training at least one machine learning model using the first physiological data;

receiving, from a first monitoring device attached to a subject, second physiological data of sympathetic nervous system activity in the subject;

analyzing, using the at least one machine learning model and based on the baseline value of at least one physiological parameter, the second physiological data to predict an agitation episode of the subject; and

sending, based on predicting the agitation episode of the subject, a signal to a second monitoring device to notify the second monitoring device of the prediction of the agitation episode of the subject such that treatment can be provided to the subject to decrease sympathetic nervous system activity in the subject.

23. The method of claim 22, wherein: the first monitoring device is a wearable device in contact with the subject.

24. The method of claim 22, wherein the second monitoring device is monitored by a caregiver of the subject.

25. The method of claim 22, wherein: the analyzing to predict the agitation episode includes determining a time period within which the agitation episode of the subject will occur.

26. The method of claim 22, wherein:

the analyzing to predict the agitation episode includes determining a degree of the agitation episode of the subject.

27. The method of claim 22, wherein:

the analyzing to predict the agitation episode includes:

comparing the second physiological data with the baseline value of at least one physiological parameter;

when the second physiological data exceeds a first threshold of the baseline value, the signal is a first signal, the treatments are first treatments;

when the second physiological data exceeds a second threshold of the baseline value, the signal is a second signal different from the first signal, the treatments are second treatments different from the first treatments.

28. The method of claim 22, wherein the receiving the second physiological data is during a first time period; the method further comprises:

receiving, during a second time period after the first time period, third physiological data of sympathetic nervous system activity in the subject; and

generating, based on the second physiological data and the third physiological data, a report of sympathetic nervous system activity in the subject to identify a pattern of a change of sympathetic nervous system activity in the subject.

29. The method of claim 22, wherein:

the treatment includes administering an anti-agitation agent to the subject.

30. The method of claim 22, wherein:

the second physiological data of sympathetic nervous system activity include at least one of a change in electrodermal activity, heart rate variability, cognitive assessments such as pupil size, secretion of salivary amylase, blood pressure, pulse rate, respiratory rate, or level of oxygen in blood.

31. The method of claim 22, wherein:

the sympathetic nervous system activity is assessed by measuring any change in electrodermal activity or any change in electrodermal activity together with any change in resting electroencephalography.

32. The method of claim 22, further comprising:

receiving an indication associated with the agitation episode after sending the signal to the second monitoring device; and

further training the at least one machine learning model based on the indication.

33. The method of claim 22, further comprising:

receiving an indication associated with the agitation episode after sending the signal to the second monitoring device, the indication indicating at least one of (1) whether or not the agitation episode occurs, (2) when the agitation episode occurs, (3) a degree of the agitation episode, (4) a time period for which the agitation episode lasts, or (5) a symptom of the agitation episode; and

further training the at least one machine learning model based on the indication.

34. The method of claim 22, wherein:

the at least one machine learning model includes at least one of a linear regression, logistic regression, a decision tree, a random forest, a neural network, a deep neural network, or a gradient boosting model.

35. The method of claim 22, wherein:

the at least one machine learning model is trained based on at least one of supervised learning, unsupervised learning, semi-supervised learning, or reinforcement learning.

36. The method of claim 22, wherein:

the analyzing to predict the agitation episode includes determining, based on a comparison between the second physiological data and the baseline value, a degree of the agitation episode of the subject.

37. The method of claim 22, further comprising:

receiving, from the first monitoring device, additional data of sympathetic nervous system activity in the subject, the additional data including at least one of audio data, motion data, or location data,

the analyzing includes analyzing, using the at least one machine learning model, the additional data to predict the agitation episode of the subject.

38. An apparatus, comprising:

a memory; and

a processor operatively coupled to the memory, the processor configured to:

receive, from a first monitoring device attached to a subject, physiological data of sympathetic nervous system activity in the subject;

analyze, using at least one machine learning model, the physiological data to detect an anomaly from a reference pattern of sympathetic nervous system activity to determine a probability of an occurrence of an agitation episode of the subject; and

send a signal to a second monitoring device to notify the second monitoring device of the probability of the occurrence of the agitation episode of the subject such that treatment can be provided to the subject to decrease sympathetic nervous system activity in the subject.

39. The apparatus of claim 38, wherein:

the processor is configured to:

receive an indication associated with the agitation episode after sending the signal to the second monitoring device; and

further train the at least one machine learning model based on the indication.

40. The apparatus of claim 38, wherein:

the processor is configured to:

receive an indication associated with the agitation episode after sending the signal to the second monitoring device, the indication indicating one of (1) whether or not the agitation episode occurs, (2) when the agitation episode occurs, (3) a degree of the agitation episode, (4) a time period for which the agitation episode lasts, or (5) a symptom of the agitation episode; and

further train the at least one machine learning model based on the indication.

41. A processor-readable non-transitory medium storing code representing instructions to be executed by a processor, the code comprising code to cause the processor to:

receive, from a first monitoring device attached to a subject, physiological data of sympathetic nervous system activity in the subject;

analyze, using at least one machine learning model, the physiological data to detect an anomaly from a reference pattern of sympathetic nervous system activity to determine a probability of an occurrence of an agitation episode of the subject; and

send a signal to a second monitoring device to notify the second monitoring device of the probability of the occurrence of the agitation episode of the subject such that treatment can be provided to the subject to decrease sympathetic nervous system activity in the subject.

42. The processor-readable non-transitory medium of claim 41, wherein the code comprises code to cause the processor to:

train, prior to analyzing using the at least one machine learning model, the at least one machine learning model based on training physiological data of sympathetic nervous system

activity associated with a plurality of subjects, the at least one machine learning model including a plurality of physiological parameters as input, each physiological parameter from the plurality of physiological parameters associated with a weight from a plurality of weights of the machine learning model;

determine, based on the at least one machine learning model, the reference pattern of at least one physiological parameter from the plurality of physiological parameters.

43. The processor-readable non-transitory medium of claim 41, wherein the code comprises code to cause the processor to:

train, prior to analyzing using the at least one machine learning model, the at least one machine learning algorithm based on training physiological data of sympathetic nervous system activity associated with a plurality of subjects, the at least one machine learning model including a plurality of physiological parameters as input, each physiological parameter from the plurality of physiological parameters associated with a weight from a plurality of weights of the machine learning models;

determine, based on the at least one machine learning model, the reference pattern of at least one physiological parameter from the plurality of physiological parameters.

receive an indication associated with the agitation episode after sending the signal to the second monitoring device; and

further train, based on the indication, the at least one machine learning model to adjust the reference pattern of the at least one physiological parameter and a weight associated with the at least one physiological parameter.

44. The method, apparatus and processor-readable non-transitory medium of any of the claims 1 to 43, wherein additional signals of sympathetic nervous system activity include audio and motion.