to treatment can result in diminished adherence, which affects success of treatment, risk of relapse, and cost of the illness. For example, it has been observed that the first 6 weeks of treatment is a particularly critical period to promote adherence, with increased risks of treatment dropout, relapse, medication discontinuation, vulnerability to suicide, and greater economic burden among those who show early nonadherence to antidepressants. The fear of and experience of side effects also contribute to patients failing to adhere to medications. Less commonly prescribed controlled substances, such as ketamine, and electroconvulsive therapy (ECT) are fast acting, but are extremely expensive to administer, and often cause significant side effects.

[0004] Accordingly, there is a need for rapid-acting depression treatments that pose low risk to patients, promote adherence, are self-administered and inexpensive, and may also significantly reduce anxiety.

SUMMARY

[0005] Transcranial Alternating Current Stimulation (tACS) has been investigated as another approach to treat depression. tACS is a form of non-invasive neurostimulation that delivers low dose alternating current to the brain to induce neuroplasticity. Accordingly, tACS has shown promise as an effective for treatment for depression, as well as anxiety, insomnia, and other neuropsychiatric and cognitive disorders.

[0006] tACS devices can be self-administered by a patient, and used safely as a standalone treatment or in combination with medications. While regulated as medical devices, tACS devices are not complex or expensive to manufacture. Importantly, there is growing scientific evidence that tACS is safer than medications, and in certain forms, rapid acting.

[0007] A challenge facing the development of tACS devices has been discovering a method of delivering electrical current that is simultaneously therapeutic, comfortable for the patient, and able to successfully maintain blinding in a sham controlled clinical trial. If patients find the stimulation to be uncomfortable, they may avoid using the device; if participants in a clinical trial can easily differentiate an active device from a sham device (a device that appears to function normally but does not produce any stimulation), the results of the trial may not be easily defended.

[0007a] In an aspect, the present disclosure refers to a device for transcranial alternating current (tACS) stimulation, comprising:

a controller including a processor configured to generate and transmit an electrical current,

two electrodes configured to contact opposing lateral sides of a patient's scalp and to receive the electrical current to deliver a therapeutic dose of tACS for a predetermined treatment time;

wherein the generated electrical current has a constant, an average amplitude of about 2.2 mA and a bidirectional square waveform utilizing a carrier waveform having a frequency of about 15 kHz, a first modulating waveform having a frequency of about 15 Hz, and a second modulating waveform having a frequency of about 500 Hz;

wherein the generated current includes a plurality of sub-bursts within a burst duration, the burst duration including a burst on duration of about 50 ms including the plurality of sub-bursts followed by a burst off duration of about 16.7 ms without the plurality of sub-bursts;

wherein the current switches polarity after each burst duration;

wherein each sub-burst includes a plurality of pulses within a sub-burst duration, the sub-burst duration including a sub-burst on duration of 1 ms including the plurality of pulses followed by a sub-burst off duration of about 1 ms without the plurality of pulses;

wherein each pulse of the plurality of pulses extends for about 33.33 μs followed by a pause of about 33.33 μs.

[0008] Examples of the present disclosure provide systems and methods for improved tACS that are suitable for treatment of depression (e.g., Major Depressive Disorder; MDD), as well as anxiety (e.g., Generalized Anxiety Disorder; GAD), insomnia, and other neuropsychiatric and cognitive disorders. As discussed in greater detail below, a tACS device is provided that has been demonstrated to provide therapeutically effective treatment using a rapidly pulsed, alternating current (AC) output in the form of a bipolar (bi-directional) square waveform that employs a high carrier frequency and modulates to two lower frequencies, with a current amplitude of 2.2 mA (+/- 5% manufacturing tolerance). By conducting large-scale, randomized, controlled clinical trials, it has been discovered that this combination of amplitude, pulse rate, waveform and frequency, delivered to the human brain on a daily basis for a predetermined treatment time (e.g., about 20 minutes), twice per day (once soon after the patient wakes, and again before bed), through two electrodes placed in specific locations on either side of the head, provides effective treatment for depression and anxiety. The ability to provide effective therapy at lower current amplitude reduces or substantially eliminates discomfort experienced by patients.

[0009] In an example, a method of transcranial alternating current (tACS) stimulation is provided. The method includes generating and transmitting, by a controller including a processor, an electrical current for receipt by two electrodes in contact with opposing lateral sides of a patient's scalp to deliver a therapeutic dose of tACS for a predetermined treatment time. The generated electrical current has a constant, an average amplitude of about 2.2 mA and a bidirectional square waveform utilizing a carrier waveform having a frequency of about 15 kHz, a first modulating waveform having a frequency of about 15 Hz, and a second modulating waveform having a frequency of about 500 Hz. The generated current includes a plurality of sub-bursts within a burst duration, the burst duration including a burst on duration of about 50 ms including the plurality of sub-bursts followed by a burst off duration of about 16.7 ms without the plurality of sub-bursts. The current switches polarity after each burst duration. Each sub-burst includes a plurality of pulses within a sub-burst duration, the sub-burst duration including a sub-burst on duration of 1 ms including the plurality of pulses followed by a sub-burst off duration of about 1 ms without the plurality of pulses. Each pulse of the plurality of pulses extends for about 33.33 μs followed by a pause of about 33.33 μs.

[0010] In another example, each of the two electrodes is positioned on the squamous temporal bone, above the posterior aspect of the zygomatic arch and maintained in place

during delivery of the therapeutic dose of tACS for the treatment of Major Depressive Disorder (MDD) or Generalized Anxiety Disorder (GAD). The diameter of each of the electrodes is about 36 mm. The method further includes retrieving, by the processor, the predetermined treatment time from a memory in communication with the processor, wherethe predetermined treatment time is about 20 minutes. The method also includes measuring a treatment time during which the therapeutic dose of tACS is delivered to the patient, comparing the treatment time to the predetermined treatment time; and ceasing transmission of the generated electrical current when the elapsed time is equal to the predetermined treatment time.

[0011] In a further example, the method further includes administering the therapeutic dose of tACS to the patient twice daily for the predetermined treatment time, one administration occurring within two hours after waking from sleep and another administration occurs within two hours prior to sleeping.

[0012] In an example a method for transcranial alternating current (tACS) stimulation is provided. The method includes positioning two electrodes in contact with opposing lateral sides of a patient's scalp. The method further includes generating, by a controller including a processor, an electrical current. The method additionally includes transmitting the generated electrical current to the electrodes to deliver a therapeutic dose of tACS for a predetermined treatment time (e.g., about 20 minutes). The generated electrical current has an amplitude of about 2.2 mA. The generated electrical current further has a waveform including a carrier waveform having a frequency of about 15 kHz, a first modulating waveform having a frequency of about 15 Hz, and a second modulating waveform having a frequency of about 500 Hz.

[0013] In another example, each of the two electrodes is positioned on the squamous temporal bone, above the posterior aspect of the zygomatic arch and maintained in place during stimulation.

[0014] In another example, each of the two electrodes has a diameter of about 36 mm.

[0015] In another example, the therapeutic dose of tACS is sufficient for treatment of at least one of Major Depressive Disorder (MDD) or Generalized Anxiety Disorder (GAD).

[0016] In another example, the method further includes retrieving, by the processor, the predetermined treatment time from a memory in communication with the processor. The method also includes measuring a treatment time during which the therapeutic dose of tACS is delivered to the patient. The method additionally includes comparing the treatment time to the predetermined treatment time. The method also includes ceasing transmission of the therapeutic dose of tACS to the patient when the elapsed time is equal to or greater than the predetermined treatment time.

[0017] In another example, the waveform is a pulsed, alternating current in the form of a bidirectional square wave.

[0018] In another example, the waveform includes a plurality of first square wave sub-bursts having a first polarity that repeats for a burst duration followed by a plurality of second square wave sub-bursts having a second, opposite polarity that repeats for the burst duration.

[0019] In another example, the burst duration is about 66.7 ms and includes an on duration and an off duration, wherein the on duration is about 50 ms and extends from the start of the first sub-burst of the burst duration to the end of the last sub-burst of the burst duration, and wherein the off duration is about 16.7 s and extends from the end of the last sub-burst of the burst duration to the end of the burst duration.

[0020] In another example, each of the plurality of first sub-bursts and second sub-bursts extends a sub-burst duration of about 2 ms that includes a sub-burst on duration of about 1 ms followed by a sub-burst off duration of about 1 ms.

[0021] In another example, each of the first and second plurality of square wave sub-bursts includes a plurality of pulses that extend a pulse duration of about 66.7 ms that includes a pulse on duration of about 33.3 ms followed by a pulse off duration of about 33.3 ms.

[0022] In an example, a transcranial alternating current stimulation (tACS) device is provided. The device includes a stimulator including a strap and two electrodes coupled to the strap. The strap is configured to be secured to a human head and position the two electrodes in contact with opposing lateral sides of a patient’s scalp. The method also includes a controller including a processor. The controller is in electrical communication with the plurality of electrodes and configured to perform a variety of operations. The

controller is configured to generate an electrical current. The controller is further configured to transmit the electrical current to the electrodes to deliver a therapeutic dose of tACS for a predetermined treatment time. The generated electrical current has an amplitude of about 2.2 mA. The generated electrical current has a waveform including a carrier waveform having a frequency of about 15 kHz, a first modulating waveform having a frequency of about 15 Hz, and a second modulating waveform having a frequency of about 500 Hz.

[0023] In an example, the strap is configured to maintain each of the two electrodes on the squamous temporal bone, above the posterior aspect of the zygomatic arch.

[0024] In an example, each of the two electrodes has a diameter of about 36 mm.

[0025] In an example, the controller is further configured to retrieve the predetermined treatment time from a memory in communication with the processor, to measure a treatment time during which the therapeutic dose of tACS is delivered to the patient, to compare the treatment time to the predetermined treatment time; and to cease transmission of the therapeutic dose of tACS to the patient when the elapsed time is equal to or greater than the predetermined treatment time.

[0026] In an example, the waveform is a pulsed, alternating current in the form of a bidirectional square wave.

[0027] In an example, the waveform includes a plurality of first square wave sub-bursts having a first polarity that repeats for a burst duration followed by a plurality of second square wave sub-bursts having a second, opposite polarity that repeats for the burst duration.

[0028] In an example, the burst duration is about 66.7 ms and includes an on duration and an off duration, wherein the on duration is about 50 ms and extends from the start of the first sub-burst of the burst duration to the end of the last sub-burst of the burst duration, and wherein the off duration is about 16.7 s and extends from the end of the last sub-burst of the burst duration to the end of the burst duration.

[0029] In an example, each of the plurality of first sub-bursts and second sub-bursts extends a sub-burst duration of about 2 ms that includes a sub-burst on duration of about 1 ms followed by a sub-burst off duration of about 1 ms.

[0030] In an example, each of the first and second plurality of square wave sub-bursts includes a plurality of pulses that extend a pulse duration of about 66.7 ms that includes a pulse on duration of about 33.3 ms followed by a pulse off duration of about 33.3 ms.

DESCRIPTION OF DRAWINGS

[0031] These and other features will be more readily understood from the following detailed description taken in conjunction with the accompanying drawings, in which:

[0032] FIG. 1 is a diagram illustrating one exemplary embodiment of a treatment environment in which a transcranial alternating current stimulation (tACS) device including a controller and a stimulator is employed to deliver electrical stimulation to a patient's head;

[0033] FIG. 2A is a rear-facing perspective view of the stimulator of FIG. 1;

[0034] FIG. 2B is a top-down view of the stimulator of FIG. 1;

[0035] FIG. 3A is a schematic diagram of an exterior of the controller of FIG. 1;

[0036] FIG. 3B is a block diagram illustrating components of the controller of FIG. 1;

[0037] FIGS. 4A-4B are schematic illustrations of a constant current waveform generated by the controller for tACS treatment; and

[0038] FIG. 5 is a flow diagram illustrating a method of treatment using the tACS device of FIG. 1.

[0039] It is noted that the drawings are not necessarily to scale. The drawings are intended to depict only typical aspects of the subject matter disclosed herein, and therefore should not be considered as limiting the scope of the disclosure.

DETAILED DESCRIPTION

[0040] As used herein, a "patient" is a vertebrate, preferably a mammal, more preferably a human. Mammals include, but are not limited to, murines, simians, humans, farm animals, sport animals, and pets.

[0041] As used herein, "treating" or "treatment" of a condition, disease or disorder or symptoms associated with a condition, disease or disorder refers to an approach for obtaining