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Subset 1 ("GO")
(142-1)

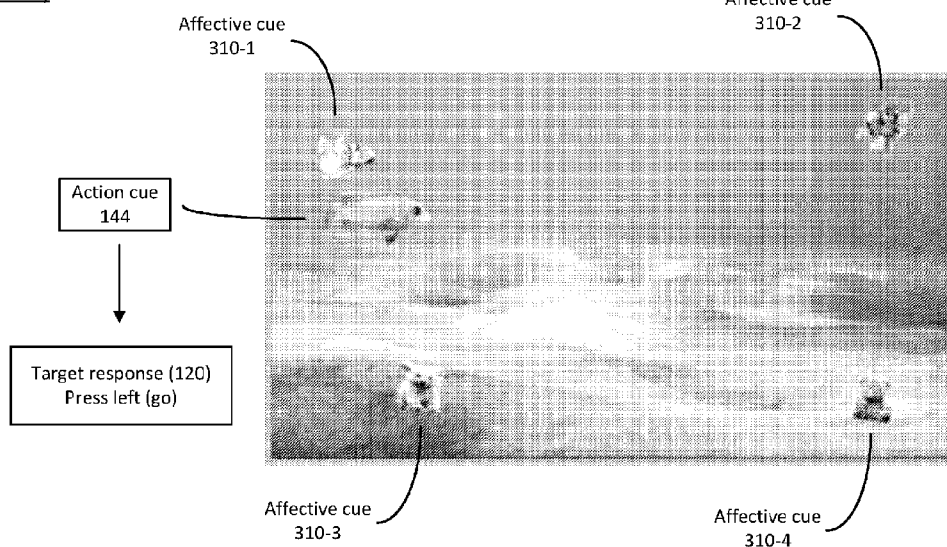


FIG. 3A

(57) Abstract: Systems and methods for improving a symptom of post-traumatic stress disorder in a subject are provided. An evaluation session is performed for a plurality of trials, including displaying images generating target cues, receiving responses to target cues, and generating outcome cues when the responses satisfy or fail to satisfy a response threshold. For a first subset of trials, target cues include action cues and a response satisfies the threshold when a reaction time satisfies a reference action time. For a second subset of trials, target cues include control cues and a response satisfies the threshold when a delay time satisfies a reference control time. For a third subset of trials, target cues include action and control cues, and a response satisfies the threshold when a delay time satisfies the reference control time. A measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder is determined.

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GAMIFIED APPROACH TO MAXIMIZING BIOBEHAVIORAL INHIBITION IN TRAUMA-RELATED CONDITIONS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] The present Application claims priority to United States Provisional Patent Application No.: 63/618,040, entitled “Gamified Approach to Maximizing Biobehavioral Inhibition in Trauma-related Conditions,” filed January 5, 2024, which is hereby incorporated by reference in its entirety for all purposes.

TECHNICAL FIELD

[0002] The present disclosure relates generally to systems and methods for improved treatment of trauma-related conditions, particularly by altering brain networks in subjects using visual inhibitory control regimens.

BACKGROUND

[0003] Post-traumatic stress disorder (PTSD) has a 6% lifetime prevalence in epidemiological studies in the United States, collapsing across many trauma types and demographic groups, with double the prevalence in women compared to men. Prevalence rates are higher when examining specific trauma exposures. For example, it is estimated that 23% of war survivors globally are affected by PTSD, which extrapolates to 242 million people. See, *e.g.*, Hoppen, T. H., and Morina, N. (2019), “The prevalence of PTSD and major depression in the global population of adult war survivors: A meta-analytically informed estimate in absolute numbers,” *European Journal of Psychotraumatology*, 10(1), 1578637.

[0004] The current standard of care for patients with PTSD are pharmacological and non-pharmacological treatments. Pharmacological treatments for PTSD include the use of selective serotonin reuptake inhibitors (SSRIs). While two SSRIs are FDA approved for PTSD, they are classified as “low efficacy” interventions due to yielded small effect sizes (relative to placebo) for PTSD symptom reduction. Well-validated non-pharmacological treatments for PTSD, including cognitive-behavioral therapies, involve working with a trained therapist to identify negative thoughts and address excessive fear in a systematic manner. While these interventions yield reliably moderate effect sizes, they have high drop-out (up to 30%) both in clinical trials and in “real-world” treatment contexts as they require direct and upsetting engagement with traumatic material. These interventions also require

specialized training for therapists, which limits reach. In settings where substantial financial investments are made in clinician training, dissemination of these treatments remains suboptimal.

[0005] Existing “gold standard” pharmacological and non-pharmacological treatments for PTSD have limitations in terms of reach, efficacy, and retention, creating opportunities for interventions that address these concerns. Multiple studies are exploring cognitive training to address PTSD symptoms. The advantages of the cognitive tasks are that they are self-guided (*e.g.*, do not require a trained therapist) and readily scalable, while allowing for innovation around user engagement. One existing approach is to “re-train” attention in the context of threat, termed “attention bias modification,” to address hyper-vigilance to threatening information in those with PTSD. Yet, the reach of this intervention is limited because there is significant heterogeneity in baseline attention bias in PTSD.

SUMMARY

[0006] Given the above background, what is needed in the art are systems and methods for improved access, engagement, and training of brain networks to improve cognitive control and to improve treatment of trauma-related conditions in subjects. In particular, given the above background, there is a need for developing systems and methods to improve neural flexibility and ability to adaptively respond to emotional internal and/or external events within the context of affective and/or emotional information processing.

[0007] The present disclosure addresses the need in the art for systems and methods for improved access, engagement, and training of brain networks by providing systems and methods that include a range of inhibitory control training elements (*e.g.*, go, no-go, stopping, and/or proactive anticipation of stopping). Advantageously, in some embodiments, the presently disclosed systems and methods incorporate and combine these multiple inhibitory control training elements (*e.g.*, cues), optionally with affective information processing elements (*e.g.*, positive and/or negative cues), to address the above-identified need in the art. In some embodiments, the presently disclosed systems and methods improve treatment of trauma-related conditions by altering a brain network (*e.g.*, to increase flexibility and/or adaptability) and/or communication between brain networks in a subject.

[0008] One aspect of the present disclosure provides a method for improving a symptom of post-traumatic stress disorder in a subject. In some embodiments, the method is performed

at an electronic device comprising a display, an input device, one or more processors, and memory storing one or more programs for execution by the one or more processors.

[0009] In some embodiments, the method includes performing a first evaluation session comprising, for each respective trial in a corresponding first plurality of trials, displaying, on the display, a respective user-interactive series of images generating one or more respective target cues, receiving, responsive to the one or more respective target cues, a corresponding target response from the subject using the input device, and generating a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial. In some embodiments, the respective outcome cue comprises, when the corresponding target response satisfies the respective response threshold, a first performance indicator, and when the corresponding target response fails to satisfy the respective response threshold, a second performance indicator.

[0010] For each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time. For each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time. For each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue and a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time.

[0011] In some embodiments, the method further includes determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder.

[0012] Another aspect of the present disclosure is directed to providing a method for improving a symptom of post-traumatic stress disorder in a subject. In some embodiments, the method is performed at an electronic device comprising a display, an input device, one or more processors, and memory storing one or more programs for execution by the one or more processors.

[0013] In some embodiments, the method includes executing a first evaluation session module that includes a corresponding first plurality of trials. For each respective trial in the corresponding first plurality of trials, the executing includes displaying, on the display, for a period of time, a respective user-interactive series of images, which generates one or more respective target cues associated with the respective user-interactive series of images during the period of time. Moreover, the executing includes receiving, responsive to the one or more respective target cues, during the period of time, a corresponding target response from the subject using the input device. Furthermore, the executing includes generating, by the one or more processors, during the period of time, a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial. The respective outcome cue includes a first performance indicator in accordance with a determination the corresponding target response satisfies the respective response threshold, and a second performance indicator in accordance with a determination the corresponding target response fails to satisfy the respective response threshold. For each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues includes a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time. For each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues includes a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time. Additionally, for each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises the respective action cue and the respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time. The executing further includes maintaining, via the memory, responsive to the generating, during the period of time, a record of performance indicators associated with the subject. Furthermore, the method includes applying, at least in part, the record of performance indicators associated with the subject to an assessment module. From this, the method determines a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder in the subject.

[0014] Another aspect of the present disclosure includes a system for improving a symptom of post-traumatic stress disorder in a subject, including a display; an input device; one or more processors; and memory storing one or more programs that, when executed by the one or more processors, cause the processors to perform any of the methods disclosed above.

[0015] Another aspect of the present disclosure includes a non-transitory computer readable storage medium having stored thereon program code instructions for improving a symptom of post-traumatic stress disorder in a subject that, when executed by a processor, cause the processor to perform any of the methods disclosed above.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Figures 1A, 1B, and 1C illustrates an exemplary system topology for improving a symptom of post-traumatic stress disorder in a subject, in accordance with some embodiments of the present disclosure.

[0017] Figures 2A, 2B, 2C, and 2D collectively provide a flow chart of processes and features for improving a symptom of post-traumatic stress disorder in a subject, in which optional steps are indicated by dashed lines, in accordance with some embodiments of the present disclosure.

[0018] Figures 3A, 3B, 3C, and 3D collectively illustrate example trials in an example evaluation session for improving a symptom of post-traumatic stress disorder in a subject, in accordance with an embodiment of the present disclosure.

[0019] Figures 4A, 4B, 4C, and 4D collectively illustrate example trails in various example evaluation sessions for improving a symptom of post-traumatic stress disorder in subjects, in accordance with an embodiment of the present disclosure.

[0020] Figures 5A, 5B, 5C, 5D, 5E, 5F, 5G, 5H, 5I, and 5J collectively illustrate example trails in additional example evaluation sessions for improving a symptom of post-traumatic stress disorder in subjects.

[0021] Figures 6A, 6B, 6C, and 6D collectively illustrate example trails in yet additional example evaluation sessions for improving a symptom of post-traumatic stress disorder in subjects.

[0022] Like reference numerals refer to corresponding parts throughout the several views of the drawings.

DETAILED DESCRIPTION

[0023] Given the above background, what is needed in the art are systems and methods for improved access, engagement, and training of brain networks to improve cognitive control and to improve treatment of trauma-related conditions in subjects. In particular, given the above background, there is a need for developing systems and methods to improve neural flexibility and ability to adaptively respond to emotional internal and/or external events within the context of affective and/or emotional information processing.

[0024] Advantageously, the presently disclosed subject matter addresses the above-identified need in the art by providing systems and methods for improving a symptom of post-traumatic stress disorder in a subject. In some embodiments, methods are performed at an electronic device comprising a display, an input device, one or more processors, and memory storing one or more programs for execution by the one or more processors. In some embodiments, methods include performing a first evaluation session. In some embodiments, the performing the first evaluation session includes executing a first evaluation session module at the electronic device. In some embodiments, the first evaluation session includes a corresponding first plurality of trials. In some embodiments, for each respective trial in a corresponding first plurality of trials of the first evaluation session, there is displayed, on the display, a respective user-interactive series of images generating one or more respective target cues. Responsive to the one or more respective target cues, a corresponding target response is received from the subject using the input device. A respective outcome cue is generated based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial. The outcome cue comprises, when the corresponding target response satisfies the respective response threshold, a first performance indicator, and, when the corresponding target response fails to satisfy the respective response threshold, a second performance indicator. For each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time. For each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time. For each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective

target cues comprises a respective action cue and a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time. In some embodiments, methods further include determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder.

[0025] Reference will now be made in detail to embodiments, examples of which are illustrated in the accompanying drawings. In the following detailed description, numerous specific details are set forth in order to provide a thorough understanding of the present disclosure. However, it will be apparent to one of ordinary skill in the art that the present disclosure may be practiced without these specific details. In other instances, well-known methods, procedures, components, circuits, and networks have not been described in detail so as not to unnecessarily obscure aspects of the embodiments.

[0026] *Definitions*

[0027] Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. As used herein, the following terms have the meanings ascribed to them below, unless specified otherwise.

[0028] As used herein, the term “about” or “approximately” means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, *i.e.*, the limitations of the measurement system. For example, “about” can mean within 3 or more than 3 standard deviations, per the practice in the art. Alternatively, “about” can mean a range of up to 20%, *e.g.*, up to 10%, up to 5%, or up to 1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, *e.g.*, within 5-fold, or within 2-fold, of a value.

[0029] As used herein, the term “subject” refers to any animal (*e.g.*, a mammal), including, but not limited to, humans, and non-human animals (including, but not limited to, non-human primates, dogs, cats, rodents, horses, cows, pigs, mice, rats, hamsters, rabbits, and the like (*e.g.*, which is to be the recipient of a particular treatment, or from whom cells are harvested). In certain embodiments, the subject is a human.

[0030] As used herein, the term “treating” or “treatment” refers to clinical intervention in an attempt to alter the disease course of the individual or cell being treated and can be

performed either for prophylaxis or during the course of clinical pathology. Therapeutic effects of treatment include, without limitation, preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastases, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. By preventing progression of a disease or disorder, a treatment can prevent deterioration due to a disorder in an affected or diagnosed subject or a subject suspected of having the disorder, but also a treatment may prevent the onset of the disorder or a symptom of the disorder in a subject at risk for the disorder or suspected of having the disorder.

[0031] As used herein, an “effective amount” or “therapeutically effective amount” is an amount sufficient to affect a beneficial or desired clinical result upon treatment. An effective amount can be administered to a subject in one or more doses. In terms of treatment, an effective amount is an amount that is sufficient to palliate, ameliorate, stabilize, reverse, or slow the progression of the disease, or otherwise reduce the pathological consequences of the disease. The effective amount is generally determined by the physician on a case-by-case basis and is within the skill of one in the art. Several factors are typically taken into account when determining an appropriate dosage to achieve an effective amount. These factors include age, sex and weight of the subject, the condition being treated, the severity of the condition and the form and effective concentration of the immunoresponsive cells administered.

[0032] As used herein, the term “diagnosis” or “diagnosed” refers to a determination as to whether a subject is likely affected by a given disease, disorder or dysfunction. The skilled artisan will appreciate that a diagnosis can be made on the basis of one or more diagnostic indicators including but not limited to, for example, biomarkers, images, and/or symptoms, the presence, absence, or amount of which is indicative of the presence or absence of the disease, disorder or dysfunction.

[0033] As used herein, the term “sensitivity,” “recall,” or “true positive rate” (TPR) refers to the number of true positives divided by the sum of the number of true positives and false negatives. Sensitivity can characterize the ability of a subject to correctly identify the proportion of a set that is positive for a particular cue. For example, sensitivity can characterize the ability of a subject to correctly perform a target response associated with an action cue (*e.g.*, a “go” response) in trials that include an action cue. In another example,

sensitivity can characterize the ability of a subject to correctly perform a target response associated with a control cue (*e.g.*, a “no-go” response) in trials that include a control cue.

[0034] As used herein, the term “specificity” or “true negative rate” (TNR) refers to the number of true negatives divided by the sum of the number of true negatives and false positives. Specificity can characterize the ability of a subject to correctly identify the proportion of a set that is not positive for a particular cue. For example, specificity can characterize the ability of a subject to correctly withhold a target response that is not associated with a control cue (*e.g.*, the “go” response) in trials that include a control cue. In another example, specificity can characterize the ability of a subject to correctly withhold a target response that is not associated with an action cue (*e.g.*, the “no-go” response) in trials that include an action cue. In other words, in some implementations, specificity characterizes a subject’s ability to discriminate between types of trials and to respond appropriately.

[0035] It will also be understood that, although the terms first, second, *etc.* may be used herein to describe various elements, these elements should not be limited by these terms. These terms are only used to distinguish one element from another. For example, a first subject could be termed a second subject, and, similarly, a second subject could be termed a first subject, without departing from the scope of the present disclosure. The first subject and the second subject are both subjects, but they are not the same subject. Furthermore, the terms “subject,” “user,” and “patient” are used interchangeably herein.

[0036] The terminology used in the present disclosure is for the purpose of describing particular embodiments only and is not intended to be limiting of the invention. As used in the description of the invention and the appended claims, the singular forms “a,” “an,” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. It will also be understood that the term “and/or” as used herein refers to and encompasses any and all possible combinations of one or more of the associated listed items. It will be further understood that the terms “comprises” and/or “comprising,” when used in this specification, specify the presence of stated features, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, integers, steps, operations, elements, components, and/or groups thereof.

[0037] As used herein, the term “if” may be construed to mean “when” or “upon” or “in response to determining” or “in response to detecting,” depending on the context. Similarly, the phrase “if it is determined” or “if [a stated condition or event] is detected” may be

construed to mean “upon determining” or “in response to determining” or “upon detecting [the stated condition or event]” or “in response to detecting [the stated condition or event],” depending on the context.

[0038] *Example Systems for Improving a Symptom of Post-Traumatic Stress Disorder in a Subject*

[0039] One aspect of the present disclosure provides systems for improving a symptom of post-traumatic stress disorder in a subject.

[0040] A detailed description of a system 100 for improving a symptom of post-traumatic stress disorder in a subject in accordance with the present disclosure is described in conjunction with Figures 1A-1C. As such, Figures 1A-1C collectively illustrate the topology of the system in accordance with the present disclosure. In the topology, there is a system 100 for improving a symptom of post-traumatic stress disorder in a subject.

[0041] Referring to Figures 1A-1C, in some embodiments, the system 100 receives data directly or indirectly through radio-frequency signals. In some embodiments such signals are in accordance with an 802.11 (WiFi), Bluetooth, or ZigBee standard. In some embodiments the system 100 receives data across one or more communications networks 16.

[0042] Examples of networks 16 include, but are not limited to, the World Wide Web (WWW), an intranet and/or a wireless network, such as a cellular telephone network, a wireless local area network (LAN) and/or a metropolitan area network (MAN), and other devices by wireless communication. The wireless communication optionally uses any of a plurality of communications standards, protocols and technologies, including but not limited to Global System for Mobile Communications (GSM), Enhanced Data GSM Environment (EDGE), high-speed downlink packet access (HSDPA), high-speed uplink packet access (HSUPA), Evolution, Data-Only (EV-DO), HSPA, HSPA+, Dual-Cell HSPA (DC-HSPDA), long term evolution (LTE), near field communication (NFC), wideband code division multiple access (W-CDMA), code division multiple access (CDMA), time division multiple access (TDMA), Bluetooth, Wireless Fidelity (Wi-Fi) (*e.g.*, IEEE 802.11a, IEEE 802.11ac, IEEE 802.11ax, IEEE 802.11b, IEEE 802.11g and/or IEEE 802.11n), voice over Internet Protocol (VoIP), Wi-MAX, a protocol for e-mail (*e.g.*, Internet message access protocol (IMAP) and/or post office protocol (POP)), instant messaging (*e.g.*, extensible messaging and presence protocol (XMPP), Session Initiation Protocol for Instant Messaging and Presence Leveraging Extensions (SIMPLE), Instant Messaging and Presence Service (IMPS)), and/or

Short Message Service (SMS), or any other suitable communication protocol, including communication protocols not yet developed as of the filing date of the present disclosure.

[0043] Of course, other topologies of the system 100 of Figures 1A-1C are possible. For instance, rather than relying on a communications network 16, information may be sent directly to the system 100. Further, the system 100 may constitute a portable electronic device, a server computer, or in fact constitute several computers that are linked together in a network or be a virtual machine in a cloud computing context. As such, the exemplary topology shown in Figures 1A-1C merely serves to describe the features of an embodiment of the present disclosure in a manner that will be readily understood to one of skill in the art.

[0044] Referring to Figures 1A-1C, in typical embodiments, the system 100 comprises one or more computers. For purposes of illustration in Figures 1A-1C, the system 100 is represented as a single computer that includes all of the functionality for improving a symptom of post-traumatic stress disorder in a subject. However, the disclosure is not so limited. In some embodiments, the functionality for improving a symptom of post-traumatic stress disorder in a subject is spread across any number of networked computers and/or resides on each of several networked computers and/or is hosted on one or more virtual machines at a remote location accessible across the communications network 16. One of skill in the art will appreciate that any of a wide array of different computer topologies are used for the application and all such topologies are within the scope of the present disclosure.

[0045] With the foregoing in mind, in some embodiments, an exemplary system 100 for improving a symptom of post-traumatic stress disorder in a subject comprises one or more processing units (CPU's) 74, a network or other communications interface 84, a memory 192 (*e.g.*, random access memory), one or more magnetic disk storage and/or persistent devices 90 optionally accessed by one or more controllers 288, one or more communication busses 13 for interconnecting the aforementioned components, a user interface 78, the user interface 78 including a display 82 and input 80 (*e.g.*, keyboard, keypad, touch screen, mouse, joystick, controller, *etc.*), and a power supply 76 for powering the aforementioned components. In some embodiments, the input 80 is a touch-sensitive display, such as a touch-sensitive surface. In some embodiments, the user interface 78 includes one or more soft keyboard embodiments. The soft keyboard embodiments may include standard (QWERTY) and/or non-standard configurations of symbols on the displayed icons. In some embodiments, data in memory 92 is seamlessly shared with non-volatile memory 90 using known computing techniques such as caching. In some embodiments, memory 92 and/or memory 90 includes

mass storage that is remotely located with respect to the central processing unit(s) 74. In other words, some data stored in memory 92 and/or memory 90 may in fact be hosted on computers that are external to the system 100 but that can be electronically accessed by the system 100 over an Internet, intranet, or other form of network or electronic cable (*e.g.*, illustrated as element 16) using network interface 84.

[0046] In some embodiments, the memory 92 of the system 100 for improving a symptom of post-traumatic stress disorder in a subject includes:

- an optional operating system 102 that includes procedures for handling various basic system services;
- an evaluation session module 110, optionally including:
 - one or more evaluation sessions 112 (*e.g.*, 112-1...112-K) comprising a plurality of trials 114 (*e.g.*, 114-1-1...114-1-L), and, for each respective trial 114 in the plurality of trials:
 - a user-interactive series of images 116 (*e.g.*, 116-1-1-1...116-1-1-M) that causes generating one or more target cues 118 (*e.g.*, 118-1-1-1...118-1-1-N),
 - a target response 120 (*e.g.*, 120-1-1) received from the subject responsive to the one or more target cues 118,
 - a response threshold 124 (*e.g.*, 124-1-1), and
 - an outcome cue 122 (*e.g.*, 122-1-1) generated based on a corresponding target response 120 relative to the response threshold 124;
- an outcome cue generation construct 130, optionally including, for each respective trial 114 in the plurality of trials:
 - when the corresponding target response 120 satisfies the response threshold 124, a respective outcome cue includes a first performance indicator 132 (*e.g.*, 132-1), and
 - when the corresponding target response 120 fails to satisfy the response threshold 124, the respective outcome cue includes a second performance indicator 132 (*e.g.*, 132-2);
- a trial data store 140, optionally including:
 - for each trial in a first subset 142 (*e.g.*, 142-1) of the plurality of trials 114, the one or more target cues 118 comprises an action cue 144 (*e.g.*, 144-1-1...144-

- 1-A), and the corresponding target response 120 satisfies the response threshold 124 when a reaction time for the corresponding target response satisfies a reference action time 146,
- for each trial in a second subset 142 (*e.g.*, 142-2) of the plurality of trials 114, the one or more target cues 118 comprises a control cue 148 (*e.g.*, 148-2-1...148-2-B), and the corresponding target response 120 satisfies the response threshold 124 when a delay time for the corresponding target response satisfies a reference control time 150, and
- for each trial in a third subset 142 (*e.g.*, 142-3) of the plurality of trials 114, the one or more target cues 118 comprises a respective action cue 144 (*e.g.*, 144-3-C...144-3-D) and a respective control cue 148 (*e.g.*, 148-3-E...148-3-F), and the corresponding target response 120 satisfies the response threshold 124 when a delay time for the corresponding target response satisfies the reference control time 150; and
- a determination module 160, optionally including a measure of inhibition control 162 that represents an improvement in the symptom of post-traumatic stress disorder.

[0047] In some embodiments, the evaluation session module 110 is accessible within any browser (phone, tablet, laptop/desktop) displayed at the system 100. However, the present disclosure is not limited thereto. In some embodiments the evaluation session module 110 is executed (*e.g.*, runs) on native device frameworks, and is available for download onto the system 100 running an operating system 102 such as Android or iOS.

[0048] In some implementations, one or more of the above identified data elements or modules of the system 100 for improving a symptom of post-traumatic stress disorder in a subject are stored in one or more of the previously described memory devices, and correspond to a set of instructions for performing a function described above. The above-identified data, modules, or programs (*e.g.*, sets of instructions) need not be implemented as separate software programs, procedures or modules, and thus various subsets of these modules may be combined or otherwise re-arranged in various implementations. In some implementations, the memory 92 and/or 90 optionally stores a subset of the modules and data structures identified above. Furthermore, in some embodiments the memory 92 and/or 90 stores additional modules and data structures not described above. Further still, in some embodiments, the system 100 stores data for improving a symptom of post-traumatic stress

disorder in a subject for two or more subjects, five or more subjects, one hundred or more subjects, or 1000 or more subjects.

[0049] In some embodiments, a system 100 for improving a symptom of post-traumatic stress disorder in a subject is a smart phone (*e.g.*, an iPhone), laptop, tablet computer, desktop computer, or other form of electronic device (*e.g.*, a gaming console). In some embodiments, the system 100 is not mobile. In some embodiments, the system 100 is mobile.

[0050] It should be appreciated that the system 100 illustrated in Figures 1A-1C is only one example of a multifunction device that may be used for improving a symptom of post-traumatic stress disorder in a subject, and that the system 100 optionally has more or fewer components than shown, optionally combines two or more components, or optionally has a different configuration or arrangement of the components. The various components shown in Figures 1A-1C are implemented in hardware, software, firmware, or a combination thereof, including one or more signal processing and/or application specific integrated circuits.

[0051] In some embodiments, the system 100 has any or all of the circuitry, hardware components, and software components found in the system 100 depicted in Figures 1A-1C. In the interest of brevity and clarity, only a few of the possible components of the system 100 are shown in order to better emphasize the additional software modules that are installed on the system 100.

[0052] While the system 100 disclosed in Figures 1A-1C can work standalone, in some embodiments it can also be linked with electronic medical records to exchange information in any way.

[0053] *Example Embodiments for Improving a Symptom of Post-Traumatic Stress Disorder in a Subject*

[0054] Now that details of a system 100 for improving a symptom of post-traumatic stress disorder in a subject have been disclosed, details regarding a flow chart of processes and features of the system, in accordance with an embodiment of the present disclosure, are disclosed with reference to Figures 2A-2D. In some embodiments, such processes and features of the system are conducted by the system 100 illustrated in Figures 1A-1C.

[0055] Figures 2A-2D collectively illustrate a method 200 for improving a symptom of post-traumatic stress disorder in a subject. In some embodiments, the method 200 is performed at an electronic device comprising a display, an input device, one or more processors, and memory storing one or more programs for execution by the one or more

processors. In some embodiments, the method 200 is performed at the system 100. However, the present disclosure is not limited thereto.

[0056] As noted above, individuals with trauma-related conditions, including post-traumatic stress disorder (PTSD), have difficulty with controlling intrusive negative memories and thoughts, and have a general problem with learning to control behavioral or physiological responses to affective information (*e.g.*, positive or negative events). Patients with PTSD often experience intrusive memories that are recurrent, distressing, and often cued by stimuli in the natural environment. Patients with PTSD can also exhibit difficulties with inhibitory control, which is defined as the inability to stop, change, or delay behaviors that are not appropriate for the context. See, *e.g.*, Logan, G. D. (1988). Toward an instance theory of automatization. *Psychological Review*, 95(4), 492–527; doi: 10.1037/0033-295X.95.4.492, which is hereby incorporated herein by reference in its entirety for all purposes.

[0057] Healthy, adaptable suppression of intrusive negative memories is linked to higher activity in the “executive control” brain network (lateral fronto-parietal), and lower activity of a “memory-control network” (hippocampus-dlpfc). Healthy, adaptable control of behavior more generally relies on “inhibitory control” networks, including those that ensure a response is not initiated, *i.e.* *no-go* (lateral PFC), those that are important for *stopping* a behavior that has already started (right IFC, pre-SMA, STN), and those that mediate the *anticipation of stopping* and proactively preparing to stop (striatum, SMA). People with PTSD do not show these healthy patterns of brain activity or behaviors. On the other hand, many studies show that people with PTSD have brain networks that are “stuck” or do not change or adapt to the environment or internal signals like they should.

[0058] Multiple studies have shown that the inhibitory control deficiencies in PTSD patients can take many forms, including deficits in fear inhibition, response inhibition, memory suppression, and behavioral and emotional control. Deficiencies in inhibitory control, especially as it relates to suppressing and regulating intrusive memories, can slow or halt PTSD symptom recovery. See, *e.g.*, Moores, *et al.* (2008). Abnormal recruitment of working memory updating networks during maintenance of trauma-neutral information in post-traumatic stress disorder. *Psychiatry Research: Neuroimaging*, 163(2), 156–170; doi: 10.1016/j.psychresns.2007.08.011; Rauch, *et al.* (2003). Neuroimaging Studies of Amygdala Function in Anxiety Disorders. *Annals of the New York Academy of Sciences*, 985(1), 389–410; doi:10.1111/j.1749-6632.2003.tb07096.x; and Rauch, *et al.* (2006). Neurocircuitry Models of Posttraumatic Stress Disorder and Extinction: Human Neuroimaging Research—

Past, Present, and Future. *Biological Psychiatry*, 60(4), 376–382; doi: 10.1016/j.biopsych.2006.06.004, each of which is hereby incorporated herein by reference in its entirety for all purposes. See also, *e.g.*, Mary *et al.* (2020). Resilience after trauma: The role of memory suppression. *Science* 367(6479); and Rooij *et al.* (2014). Impaired right inferior frontal gyrus response to contextual cues in male veterans with PTSD during response inhibition. *J Psychiatry Neurosci.* 39(5): 330–338, each of which is hereby incorporated herein by reference in its entirety for all purposes.

[0059] The presently disclosed systems and methods advantageously provide improved access, engagement, and training of brain networks to improve cognitive control and treatment of trauma-related conditions in subjects. In particular, within the context of affective and/or emotional information processing, the presently disclosed systems and methods advantageously prepare the subject's brain to adaptively respond to emotional internal and/or external events, thus improving neural flexibility and adaptability.

[0060] The presently disclosed systems and methods include a range of inhibitory control training elements (*e.g.*, go, no-go, stopping, reactive inhibition, and/or proactive inhibition or anticipation of stopping) resulting in an advantageous combination of multiple inhibitory control training elements (*e.g.*, cues), optionally, with affective information processing elements (*e.g.*, positive and/or negative cues). Without being limited to any one theory of operation, this advantageous combination facilitates at least the following: 1) inhibitory control networks are trained to improve functioning, enabling the brain to be more adaptive to environment changes and/or internal signals such as intrusive memories or stressful events; 2) inhibitory control networks are engaged and/or primed in the same context of or before the processing of affective or emotional information, so that the brain can adapt better and difficult or salient information does not trigger stuck neural networks; and 3) all brain networks can flexibly switch within and between each other in general (*e.g.*, they are no longer stuck in one state, or no longer have one state dominating mental function).

[0061] The main idea about the “active ingredient,” and without being limited to any one theory of operation, is that training on a mix of behavioral control paradigms, including affective processing or distractors, trains the neural circuits to flexibly adapt and shift within functions (*e.g.*, different types of inhibitory control) and between functions (*e.g.*, inhibitory control vs. affective processing). More flexible neural circuits foster resilience, allow buffering, release neural-cognitive processes from “stuck” negative thought cycles or intrusive memories. A complementary novel idea would be that by training a combination of

inhibitory control networks, alongside emotional information, incongruency, or distractor elements, prefrontal neural circuits would be recruited proactively and preceding emotional conflict.

[0062] In some embodiments, the presently disclosed systems and methods improve treatment of trauma-related conditions by altering a brain network (*e.g.*, to increase flexibility and/or adaptability) and/or communication between brain networks in a subject.

[0063] Trauma-focused treatments, such as cognitive behavioral therapy (CBT), have failed to demonstrate effectiveness among military samples; 60-72% of military subjects continued to meet diagnostic criteria for PTSD following treatment. See, *e.g.*, Steenkamp, *et al.* (2015). Psychotherapy for Military-Related PTSD: A Review of Randomized Clinical Trials. JAMA 314(5):489-500. doi: 10.1001/jama.2015.8370, which is hereby incorporated herein by reference in its entirety for all purposes. It has also been found that many individuals with PTSD do not properly respond to treatment, in addition to there being a high dropout rate across treatment types. See, *e.g.*, Watkins, *et al.* (2018). Treating PTSD: A Review of Evidence-Based Psychotherapy Interventions. Front Behav Neurosci. 2018; 12: 258, which is hereby incorporated herein by reference in its entirety for all purposes.

[0064] There is a clear dissemination gap with evidence-based treatments, including a lack of highly trained providers (particularly for patients in remote/rural areas) to deliver weekly one-to-one evidence-based therapies, that a digital therapeutic may address treatment gaps with minimal clinician support or in combination with standard of care.

[0065] Most documented clinical trials (available, for example, on the Internet at clinicaltrials.gov) for PTSD involve modifications of standard-of-care psychotherapy or novel drug studies. However, there are several comparable trials employing cognitive training tasks. NCT03316196 seeks to test a cognitive control task in the treatment of PTSD in veterans, targeting working memory deficits. Similarly, several clinical trials (*e.g.*, NCT04185155) involve a visuospatial task involving manipulating rapidly moving blocks, played one or more times to address specific symptoms of PTSD. By contrast to ongoing studies/existing technologies, in some embodiments, the presently disclosed systems and methods involve a distinct cognitive mechanism – inhibitory control – and, advantageously, explicitly integrates emotional information and “gamified” components to boost user engagement.

[0066] In some embodiments, the presently disclosed systems and methods are advantageously individualized to each subject (*e.g.*, participant) and adapt over time to fit to the subject's journey through improvement in one or more symptoms exhibited by the subject, such as a first symptom of PTSD exhibited by the subject. In some embodiments, through administering the systems and methods of the present disclosure, individualized scores are generated and provided to participants, doctors and the care team, that inform on individual abilities. In some embodiments, the systems and methods of the present disclosure maintain (*e.g.*, using memory 92 of Figures 1A-1C, *etc.*) a record of the subject's performance when executing the evaluation session module 110, such as a record of performance indicators achieved by the subject when performing the evaluation session. However, the present disclosure is not limited thereto.

[0067] In some embodiments, the presently disclosed systems and methods have applications in PTSD, anxiety, depression, addiction, craving, OCD, and/or eating disorders, as well as neurodegenerative disorders due to widespread engagement and trainings of large scale cognitive neural networks that are "stuck" in a range of disorders. For instance, in some embodiments, administering the systems and methods of the present disclosure to a population of subjects improves a symptom of PTSD, anxiety, depression, addiction, craving, OCD, eating disorders, neurodegenerative disorders, or a combination thereof exhibited by the subject. However, the present disclosure is not limited thereto.

[0068] *Disorders.*

[0069] Referring to Block 202, in some embodiments, the subject suffers from post-traumatic stress disorder, or a symptom thereof.

[0070] In some embodiments, the subject suffers from a condition selected from the group consisting of PTSD, anxiety, depression, addiction, craving, OCD, eating disorders, and neurodegenerative disorders, and any symptom thereof.

[0071] In some embodiments, the subject suffers from a psychiatric or mental condition.

[0072] In some embodiments, the suffering from post-traumatic stress disorder, or a first symptom thereof causes the subject to exhibit a second symptom thereof. However, the present disclosure is not limited thereto.

[0073] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Moreover, the clinically diagnosed mental disorder is an anxiety disorder, a mood disorder, a psychotic disorder, an eating disorder, an impulse control

disorder, an addiction disorder, a personality disorder, an obsessive-compulsive disorder, or a post-traumatic stress disorder.

[0074] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Furthermore, the clinically diagnosed mental disorder is an anxiety disorder. In some such embodiments, the anxiety disorder includes a separation anxiety disorder, a selective mutism, a specific phobia, a social anxiety disorder, a panic disorder, an agoraphobia, a generalized anxiety disorder, a substance-induced anxiety disorder, or an anxiety disorder due to a medical condition of the subject.

[0075] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. In some such embodiments, the clinically diagnosed mental disorder is a mood disorder, in which the mood disorder includes a depression disorder, a bipolar disorder, or a cyclothymic disorder.

[0076] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Moreover, the clinically diagnosed mental disorder is a psychotic disorder. In some such embodiments, the psychotic disorder includes a schizophrenia disorder, a delusion disorder, or a hallucination disorder.

[0077] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Moreover, the clinically diagnosed mental disorder is an eating disorder, in which the eating disorder includes anorexia nervosa, bulimia nervosa, or binge eating disorder.

[0078] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Moreover, the clinically diagnosed mental disorder is an impulse control disorder, and in which impulse control disorder includes a pyromania disorder, a kleptomania disorder, or a compulsive gambling disorder.

[0079] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Furthermore, the clinically diagnosed mental disorder is an addiction disorder, in which the addiction disorder includes an alcohol disorder or a substance abuse disorder.

[0080] In some embodiments, the psychiatric or mental condition is a clinically diagnosed mental disorder. Moreover, the clinically diagnosed mental disorder is a personality disorder, in which the personality disorder includes an antisocial personality disorder, an obsessive-compulsive personality disorder, or a paranoid personality disorder.

[0081] Referring to Block 204, in some embodiments, the symptom of post-traumatic stress disorder is impaired inhibition control or flexibility of a neural pathway of the subject.

[0082] In some embodiments, the subject exhibits a symptom selected from the group consisting of: deficits in fear inhibition, response inhibition, memory suppression, and behavioral and emotional control. In some embodiments, the method improves a symptom selected from the group consisting of deficits in fear inhibition, response inhibition, memory suppression, and behavioral and emotional control.

[0083] In some embodiments, the method alters an inhibitory control network or a neural pathway of the subject (*e.g.*, as noted above, by altering a brain network to increase flexibility, adaptability, and/or communication between brain networks in the subject).

[0084] *Evaluation session.*

[0085] Referring to Block 206, the method 200 includes, in some embodiments, performing a first evaluation session 112 comprising a corresponding first plurality of trials 114.

[0086] In some embodiments, the performing the first evaluation session 112 is conducted by executing a first evaluation session module at the electronic device 100, which causes the subject to perform the first evaluation session 112.

[0087] In some embodiments, the corresponding first plurality of trials comprises at least 300 trials.

[0088] In some embodiments, the first plurality of trials includes at least 20, at least 40, at least 50, at least 80, at least 100, at least 150, at least 200, at least 300, at least 400, at least 500, at least 600, at least 700, at least 800, at least 900, at least 1000 trials, at least 2000, or at least 5000 trials. In some embodiments, the first plurality of trials includes no more than 10,000, no more than 5000, no more than 2000, no more than 1000, no more than 800, no more than 500, no more than 200, no more than 100, or no more than 50 trials. In some embodiments, the first plurality of trials consists of from 20 to 50, from 40 to 200, from 100 to 500, from 200 to 800, from 500 to 2000, or from 1000 to 10,000 trials. In some embodiments, the first plurality of trials falls within another range starting no lower than 20 trials and ending no higher than 10,000 trials.

[0089] In some embodiments, the first evaluation session is performed for a period of time. For instance, in some embodiments, the period of time performing the first evaluation

session by the subject is in a duration of at least 2 minutes, at least 5 minutes, at least 10 minutes, at least 30 minutes, at least 1 hour, at least 2 hours, or at least 6 hours. In some embodiments, the first evaluation session is performed over a duration of no more than 12 hours, no more than 6 hours, no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 10 minutes, or no more than 5 minutes. In some embodiments, the first evaluation session is performed over a duration of from 2 minutes to 30 minutes, from 10 minutes to 1 hour, from 1 hour to 6 hours, or from 3 hours to 12 hours. In some embodiments, the first evaluation session has a duration that falls within another range starting no lower than 2 minutes and ending no higher than 12 hours. In some embodiments, the first evaluation session does not have a fixed duration.

[0090] In some embodiments, the method 200 further includes repeating the performing (A) for each iteration in a plurality of iterations. In other words, in some embodiments, the method includes performing additional evaluation sessions, subsequent to the first evaluation session, for a plurality of iterations. In some such embodiments, each repeating of the performing of the evaluation session causes the electronic device to execute the evaluation session module 112. However, the present disclosure is not limited thereto. In some embodiments, the repeating of the performing of the evaluation session is conducted during a single execution of the evaluation session module 112 at the electronic device 100.

[0091] In some embodiments, the plurality of iterations is repeated at regular or irregular intervals. In some embodiments, the plurality of iterations comprises performing additional evaluation sessions at intervals separated by at least 1 day, at least 2 days, at least 3 weeks, at least 1 week, at least 2 weeks, at least 3 weeks, at least 1 month, at least 2 months, or at least 6 months. In some embodiments, the additional evaluation sessions are performed at intervals of no more than 1 year, no more than 6 months, no more than 3 months, no more than 1 month, no more than 3 weeks, no more than 2 weeks, no more than 1 week, or no more than 3 days. In some embodiments, the additional evaluation sessions are performed at intervals of from 1 day to 3 days, from 3 days to 1 week, from 1 week to 1 month, or from 1 month to 1 year. In some embodiments, the additional evaluation sessions are performed at intervals falling within another range starting no lower than 1 day and ending no higher than 1 year.

[0092] For instance, in an example embodiment, the plurality of iterations comprises performing, after the first evaluation sessions, a plurality of additional evaluation sessions (*e.g.*, repeats) at regular intervals of three times per week, every week.

[0093] In some embodiments, the plurality of iterations (*e.g.*, repeated sessions) comprises at least 2, at least 3, at least 5, at least 10, at least 20, at least 30, at least 50, at least 100, or at least 200 iterations. In some embodiments, the plurality of iterations comprises no more than 500, no more than 200, no more than 100, no more than 50, no more than 10, or no more than 5 iterations. In some embodiments, the plurality of iterations consists of from 2 to 10, from 5 to 30, from 20 to 100, or from 80 to 500 iterations. In some embodiments, the plurality of iterations falls within another range starting no lower than 2 iterations and ending no higher than 500 iterations.

[0094] In some embodiments, the plurality of iterations comprises at least 5 iterations. For instance, in an example embodiment, the plurality of iterations comprises of 18 evaluation sessions, performed at intervals of three times per week for six weeks.

[0095] In some embodiments, the method 200 further includes performing evaluation sessions for a plurality of iterations until an improvement in a symptom of a trauma-related condition is determined. In some embodiments, the method further includes performing evaluation sessions for a plurality of iterations until an improvement in a symptom of post-traumatic stress disorder is determined. In some embodiments, the improvement is determined using a measure of inhibition control and/or a secondary assessment tool, as described in further detail elsewhere herein (see, *e.g.*, the section entitled “Assessment and measure of inhibition control,” below). In some embodiments, an improvement in a symptom of the trauma-related condition (*e.g.*, PTSD) occurs after only one evaluation session (*e.g.*, the first evaluation session). In some embodiments, an improvement in a symptom of the trauma-related condition (*e.g.*, PTSD) occurs after 1 or more, 2 or more, 3 or more, 4 or more, 5 or more, 10 or more, 20 or more, or 50 or more iterations in the plurality of iterations. In some embodiments, an improvement in a symptom of the trauma-related condition (*e.g.*, PTSD) occurs after any number of iterations disclosed above.

[0096] In some embodiments, each respective evaluation session in a plurality of evaluation sessions comprises a corresponding plurality of trials (*e.g.*, each evaluation session includes a set of trials). Thus, in some embodiments, a second, third, fourth, and any subsequent evaluation session in a plurality of evaluation sessions comprises a corresponding second, third, fourth, and subsequent plurality of trials. In some embodiments, a first number of trials in the corresponding first plurality of trials is different from a second number of trials in the corresponding second, third, fourth, and subsequent plurality of trials. In some embodiments, the first number of trials in the corresponding first plurality of trials is the same

as the second number of trials in the corresponding second, third, fourth, and subsequent plurality of trials.

[0097] In some embodiments, an evaluation session in a respective iteration (*e.g.*, subsequent to the first evaluation session) is the same or different as any previous or subsequent evaluation session (*e.g.*, in the first evaluation session and/or in any previous or subsequent iteration). In some embodiments, a respective evaluation session in a plurality of evaluation sessions (*e.g.*, in a plurality of iterations) comprises the same or different number of trials, types of trials, composition of trials (*e.g.*, proportion or percentage of any type of trial relative to the total number of trials in the evaluation session) as any other evaluation session in the plurality of evaluation sessions. In some embodiments, a respective evaluation session in a plurality of evaluation sessions is performed at the same or different interval (*e.g.*, a regular or irregular interval) as any other evaluation session in the plurality of evaluation sessions.

[0098] Various modifications to evaluation sessions are contemplated in the present disclosure, as will be apparent to one skilled in the art. For instance, in some embodiments, any subsequent evaluation session in a plurality of evaluation sessions comprises any of the embodiments disclosed herein for a first evaluation session, a first plurality of trials, a respective trial or any subset, cue, or element thereof, or any substitutions, modifications, additions, deletions, and/or combinations thereof, as will be apparent to one skilled in the art.

[0099] In some embodiments, the method 200 comprises causing the subject to perform a practice session prior to the first evaluation session. In some embodiments, the practice session is used to initialize or establish a baseline for one or more parameters (*e.g.*, predetermined intervals for cues, delay times for cues, response thresholds, *etc.*) for the first evaluation session and/or for any subsequent evaluation sessions. In some embodiments, the practice session comprises the same or different number of trials, types of trials, composition of trials (*e.g.*, proportion or percentage of any type of trial relative to the total number of trials in the evaluation session) as the first evaluation session or any subsequent evaluation session in a plurality of evaluation sessions, as will be apparent to one skilled in the art. In some embodiments, the practice session comprises any of the embodiments disclosed herein for a first evaluation session or for any subsequent evaluation session, or any substitutions, modifications, additions, deletions, and/or combinations thereof, as will be apparent to one skilled in the art.

[00100] In some embodiments, the practice session is performed by executing the first evaluation session module 112 at the electronic device to cause the subject to perform the practice session at the electronic device 100. In some embodiments, the subject performs the practice session in a similar or same manner as the first evaluation session, but the method 200 fails to maintain the record of performance indicators associated with the subject during the practice session, so as to not bias the record of performance indicators during the evaluation sessions.

[00101] *Target cues.*

[00102] Referring again to Block 206, in some embodiments, the method 200 further comprises, for each respective trial 114 in the corresponding first plurality of trials, displaying, on the display, a respective series of images (*e.g.*, user-interactive series of images) 116 generating one or more respective target cues 118.

[00103] In some embodiments, the respective series of images 116 is interactive, allowing the subject to engage with one or more images in the respective series of images 116. For instance, in some embodiments, a portion of a respective image in the one or more images, or an object overlaid on one or more images in the respective series of images 116 is configured for interaction with the subject, such as by using the input (*e.g.*, input 80 of Figure 1A) of the electronic device 100.

[00104] In some embodiments, the respective series of images 116 is displayed for a period of time. In some embodiments, the period of time is at least 2 minutes, at least 5 minutes, at least 10 minutes, at least 30 minutes, at least 1 hour, at least 2 hours, or at least 6 hours. In some embodiments, the period of time is no more than 12 hours, no more than 6 hours, no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 10 minutes, or no more than 5 minutes. In some embodiments, the period of time is from 2 minutes to 30 minutes, from 10 minutes to 1 hour, from 1 hour to 6 hours, or from 3 hours to 12 hours. In some embodiments, the period of time falls within another range starting no lower than 2 minutes and ending no higher than 12 hours. In some embodiments, the period of time does not have a fixed duration.

[00105] For example, in some embodiments, the presently disclosed systems and methods provide a computerized or interactive digital game that causes subjects to perform actions using the input 80 of the electronic device, such as one or more individuals buttons presses in

response to a set of images or sounds (*e.g.*, a first cue) and withhold button presses to different set of images or sounds (*e.g.*, a second cue).

[00106] In some embodiments, the series of images (*e.g.*, user-interactive series of images) comprises a video or an animation. In some embodiments, the series of images comprises a series of frames (*e.g.*, in a video or an animation). In some embodiments, the series of images further comprises an animation (*e.g.*, overlaid on one or more images in the series of images). In some embodiments, the series of images comprises one or more static images. For instance, in some embodiments, the series of images comprises an initial image in the series of images, a terminal image in the series of images, and the period of time is defined as a duration elapsed between displaying of the initial image in the series of images and the displaying of the terminal image in the series of images. For instance, in some embodiments the displaying causes the display of a subset of images in the series of images per second, in which the subset of images includes approximately 12 images per second, approximately 60 images per second, approximately 48 frames per second of video, approximately 24 frames per second of video, or approximately 16 frames per second of video. In some embodiments, the video feed includes a dynamic number of frames per second of video (*e.g.*, in accordance with a bandwidth of network 16 and/or system 100). However, the present disclosure is not limited thereto.

[00107] In some embodiments, a respective trial in the corresponding first plurality of trials generates a respective target cue (*e.g.*, an action cue, control cue, *etc.*) that occurs concurrently with or within the duration of the series of images (*e.g.*, user-interactive series of images).

[00108] In some embodiments, each respective target cue in the one or more respective target cues is a visual, auditory, or physical cue. In some embodiments, visual cues include, but are not limited to, images, objects (*e.g.*, icons, geometric shapes) on a display, and/or animations. In some embodiments, visual cues comprise an animation overlaid on an image on a display. In some embodiments, auditory cues include, but are not limited to, a sound, a buzzer, a tone, and/or a spoken word. In some embodiments, physical cues include, but are not limited to, haptic feedback, a puff of air, a vibration, and/or a touch.

[00109] Consider, for instance, the example trial illustrated in Figure 3A. The series of images represents an underwater scene comprising one or more target cues (*e.g.*, action cue 144) as well as one or more affective cues (310-1, 310-2, 310-3, 310-4). Action cue 144 is

generated as an animation that is overlaid one or more static images of the underwater scene (*e.g.*, a fish swimming in place, a fish swimming towards the center of the display, a fish swimming away and off-screen).

[00110] Consider, for instance, another example trial in which the series of images comprises a series of static images, and where target cues are simple geometric shapes displayed at set intervals in the series of static images. In such a case, the series of images can include a plain solid color background, and an action cue can be a black bar or rectangle displayed on the left or right side of the display that appears at a predetermined interval after the start of the trial.

[00111] Example embodiments of target cues contemplated in the present disclosure further include, but are not limited to, images, objects, icons, geometric shapes, animations, arrows, indicia of emotions (*e.g.*, happy face or sad face), alphanumeric text, congruent or incongruent word pairs, colors, textures, and/or patterns.

[00112] In some embodiments, a respective target cue is positioned, visually, on at a particular position on the display (*e.g.*, on the right side or left side). In some embodiments, a respective target cue is randomly placed at any location on the display.

[00113] In some embodiments, the series of images (*e.g.*, user-interactive series of images) comprises at least 1, at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 500, or at least 1000 images. In some embodiments, the series of images comprises no more than 5000, no more than 1000, no more than 500, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 images. In some embodiments, the series of images consists of from 1 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 images. In some embodiments, the series of images falls within another range starting no lower than 1 image and ending no higher than 5000 images.

[00114] Referring to Block 208, in some embodiments, for each respective trial in the corresponding first plurality of trials, the one or more respective target cues are generated a first predetermined interval after the start of the respective trial.

[00115] For instance, in some embodiments, a respective target cue for a respective trial is set to appear on a display (*e.g.*, is generated) a predetermined time after the start of the trial. Returning, then, to the example trial illustrated in Figure 3A, the underwater scene would display on the display at trial start (*e.g.*, time $t = 0$), and action cue 144 (*e.g.*, an animation of

a fish swimming in place) would appear on the display at a predetermined time after the trial start (*e.g.*, time $t = 200$ milliseconds).

[00116] In some embodiments, the first predetermined interval is from about 100 milliseconds to about 1000 milliseconds.

[00117] In some embodiments, the first predetermined interval is at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the first predetermined interval is no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the first predetermined interval is from 10 milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the first predetermined interval falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00118] In some embodiments, the one or more target cues comprises one or more action cues and/or control cues. In some embodiments, an action cue signals a first type of target response to be entered by user interaction (*e.g.*, an affirmative target response, such as a button press). In some embodiments, a control cue signals a second type of target response to be entered by user interaction (*e.g.*, a negative target response, such as a withholding of a motor response). Target cues, including action cues and control cues, are further described elsewhere herein (see, *e.g.*, the sections entitled “Go trials,” “No-go trials,” and “Stop trials,” below).

[00119] *Target responses.*

[00120] Referring again to Block 206, in some embodiments, the method 200 further comprises, for each respective trial 114 in the corresponding first plurality of trials, receiving, responsive to the one or more respective target cues 118, a corresponding target response 120 from the subject using the input device.

[00121] In some embodiments, for each respective trial in the corresponding first plurality of trials, the corresponding target response comprises a presence or an absence of a motor

response. In some embodiments, the motor response is selected from the group consisting of: a user interaction with a user affordance, a user interaction with the input device, and a user response captured by the input device. For instance, in some embodiments, a target response is a button press, a keystroke, a mouse click, a toggle, a tap on a touchscreen display, a blink, an eye movement, a squeeze of a hand grip, and/or any voluntary or involuntary motor response that can be captured or recorded by a device, as will be apparent to one skilled in the art. In some embodiments, a target response is an affirmative or a negative response.

Accordingly, in some such embodiments, where an affirmative response is any of the voluntary or involuntary motor responses disclosed above, a negative response comprises the absence of any of the voluntary or involuntary motor responses. In some embodiments, a first target response is a keystroke or a button press, and a second target response is an absence or withholding of a keystroke or button press.

[00122] In some embodiments, the corresponding target response is captured or recorded by an input device. In some embodiments, the input device is part of or connected to system 100. Non-limiting example embodiments of input devices include a computer mouse, a keyboard, a button, a joystick, a smartphone, a touchscreen display, a camera, a hand grip, a pedal, and/or an accelerometer.

[00123] In some embodiments, a first type of target cue in the one or more target cues is associated with a corresponding first type of target response in a plurality of target responses, and a second type of target cue in the one or more target cues is associated with a corresponding second type of target response in the plurality of target responses. In some embodiments, the one or more target cues comprises a plurality of types of target cues, the corresponding target response is selected from a plurality of types of target responses, and each respective type of target cue in the plurality of types of target cues is associated with a corresponding type of target response in the plurality of types of target responses.

[00124] For example, as described above, in some embodiments, an action cue signals a first type of target response (*e.g.*, an affirmative target response, such as a button press), and a control cue signals a second type of target response (*e.g.*, a negative target response, such as a withholding of a button press).

[00125] In some embodiments, the one or more target cues comprises a plurality of candidate target cues, the corresponding target response is selected from a plurality of candidate target responses, and each respective candidate target cue in the plurality of

candidate target cues is associated with a respective candidate target response in the plurality of candidate target responses.

[00126] For instance, in an example embodiment, a respective action cue is selected from a pool of two possible candidate action cues (*e.g.*, an object that appears on the left side of the display, or an object that appears on the right side of the display). A corresponding target response is further selected from a pool of two possible candidate target responses (*e.g.*, a keystroke of the “A” key, or a keystroke of the “L” key). Each respective candidate action cue is associated with a respective candidate target response in that, when the action cue appears on the left side of the display, the corresponding target response is a first keystroke (*e.g.*, of the “A” key), and when the action cue appears on the right side of the display, the corresponding target response is a second keystroke (*e.g.*, of the “L” key).

[00127] In some embodiments, when a respective target cue is generated, the respective target cue signals the corresponding target response that is associated with the particular target cue (*e.g.*, target responses are assessed for accuracy relative to the particular target cue that is generated).

[00128] *Outcome cues.*

[00129] Referring again to Block 206, in some embodiments, the method 200 further comprises, for each respective trial 114 in the corresponding first plurality of trials generating a respective outcome cue 122 based on (i) the corresponding target response 120 relative to (ii) a respective response threshold 124 for the respective trial 114, comprising, when the corresponding target response 120 satisfies the respective response threshold 124, a first performance indicator 132, and when the corresponding target response 120 fails to satisfy the respective response threshold 124, a second performance indicator 132. In some embodiments, the respective outcome cue is generated during the period of time, such that the respective outcome cue is perceived or sensed by the subject during the period of time that the series of images is displayed. However, the present disclosure is not limited thereto.

[00130] In some embodiments, for each respective trial in the corresponding first plurality of trials, the respective outcome cue is a visual, auditory, or physical cue. In some embodiments, visual cues include, but are not limited to, images, objects (*e.g.*, icons, geometric shapes) on a display, and/or animations. In some embodiments, visual cues comprise an animation overlaid on an image on a display. In some embodiments, auditory cues include, but are not limited to, a sound, a buzzer, a tone, and/or a spoken word. In some

embodiments, physical cues include, but are not limited to, haptic feedback, a puff of air, a vibration, and/or a touch.

[00131] In some embodiments, the determination of whether the corresponding target response satisfies the respective response threshold varies is dependent on the type of trial, for each respective trial in the plurality of trials. For instance, in some embodiments, the corresponding target response is a motor response (*e.g.*, button press) that satisfies the response threshold when it is received within a response window. In some embodiments, the corresponding target response is a withholding of a motor response (*e.g.*, no button press) that satisfies the response threshold when it is successfully withheld or aborted for at least the duration of a delay period.

[00132] In some embodiments, the response threshold has a duration of at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the response threshold has a duration of no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the response threshold has a duration of from 10 milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the response threshold has a duration that falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00133] In some embodiments, the respective outcome cue is generated further based on a determination that the corresponding target response is accurately associated with the respective target cue. In some such embodiments, as described above, in which a respective target cue signals or is associated with a corresponding target response, the corresponding target response is assessed for accuracy relative to the particular target cue that is generated. Referring again to the example embodiment above, in which the “A” key is correctly entered in response to the action cue on the left side of the display, the outcome cue generates a first performance indicator, and where the “L” key is incorrectly entered in response to the action cue on the left side of the display, the outcome cue generates a second performance indicator. Similarly, in which the “L” key is correctly entered in response to the action cue on the right

side of the display, the outcome cue generates a first performance indicator, and where the “A” key is incorrectly entered in response to the action cue on the right side of the display, the outcome cue generates a second performance indicator.

[00134] In some embodiments, the method 200 maintains a record of performance indicators associated with the subject when performing the evaluation session, such as when executing the evaluation session module at the electronic device. In some embodiments, the record of performance indicators is stored transitorily in the memory 92 of the electronic device, and allows for the record of performance indicators to affect the current evaluation session. In some embodiments, the record of performance indicators is stored in a user profile associated with the subject, which allows for evaluating historical performance indicator trends associated with the subject and the like. However, the present disclosure is not limited thereto.

[00135] In some embodiments, the first performance indicator indicates a satisfactory performance. In some embodiments, the second performance indicator indicates an unsatisfactory performance. For example, in some embodiments, the first performance indicator is a positive feedback (*e.g.*, reward) and the second performance indicator is a negative feedback (*e.g.*, penalty).

[00136] In some embodiments, the first performance indicator is a positive feedback (*e.g.*, reward) and the second performance indicator is a neutral feedback (*e.g.*, no reward).

[00137] In some embodiments, the first performance indicator is a presence of feedback (*e.g.*, positive or neutral) and the second performance indicator is an absence of feedback (*e.g.*, no feedback).

[00138] Non-limiting example embodiments for the first and second performance indications include, for instance, a presence or absence of feedback, a positive or neutral feedback, a positive or negative feedback. In some embodiments, positive feedback includes, but is not limited to, awarding points, coins, or scores, and/or generating positive tones or images. For instance, Figure 3D illustrates an example outcome cue 122 that is generated as an image of a pot of coins together with a performance score. In some embodiments, negative feedback includes, but is not limited to, losing points, coins, or deducting from a score, and/or generating negative tones or images.

[00139] In some embodiments, the outcome cue further comprises a neutral indicator that occurs, or is generated, upon receiving the corresponding target response, independent of

whether the corresponding target response satisfies the response threshold. For instance, in some embodiments, the neutral indicated is overlaid over some or all of the series of images during the period of time in accordance with a determination the corresponding target response satisfies the response threshold. However, the present disclosure is not limited thereto.

[00140] In some embodiments, the neutral indicator is visual (*e.g.*, an animation, an image), auditory (*e.g.*, a sound), and/or physical (*e.g.*, a haptic feedback), *etc.*

[00141] For instance, in some embodiments, where a target cue is an animation of a fish on a display, a target response of a button press results in a subsequent animation of the fish swimming towards the center of the display and away. In some embodiments, the neutral indicator occurs regardless of whether or not the corresponding target response was received within the response window, and/or whether or not the corresponding target response was accurate relative to the type of target cue presented (*e.g.*, on the left or right side of the display).

[00142] *Go trials.*

[00143] Referring to Block 210, in some embodiments, for each respective trial 114 in a first subset 142-1 of trials in the corresponding first plurality of trials, the one or more respective target cues 118 comprises a respective action cue 144, and the corresponding target response 120 satisfies the respective response threshold 124 when a reaction time for the corresponding target response satisfies a reference action time 146.

[00144] A trial in the first subset of trials is alternately referred to herein as a “go” trial.

[00145] In some embodiments, the first subset of trials comprises at least 200 trials.

[00146] In some embodiments, the first subset of trials comprises at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, at least 300, at least 500, at least 1000, or at least 2000 trials. In some embodiments, the first subset of trials comprises no more than 5000, no more than 2000, no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 trials. In some embodiments, the first subset of trials consists of from 2 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 trials. In some embodiments, the first subset of trials falls within another range starting no lower than 2 trials and ending no higher than 5000 trials.

[00147] In some embodiments, the first subset of trials consists of from 30% to 80% of the first plurality of trials. For instance, in an example embodiment, at least 60% of the trials in the first evaluation session are “go” trials.

[00148] In some embodiments, the first subset of trials comprises at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the first plurality of trials. In some embodiments, the first subset of trials comprises no more than 95%, no more than 90%, no more than 80%, no more than 70%, no more than 60%, no more than 50%, or no more than 40% of the first plurality of trials. In some embodiments, the first subset of trials consists of from 20% to 60%, from 40% to 80%, from 50% to 90%, or from 70% to 95% of the first plurality of trials. In some embodiments, the first subset of trials falls within another range starting no lower than 20% of the first plurality of trials and ending no higher than 95% of the first plurality of trials.

[00149] In some embodiments, at least a majority of trials in the plurality of trials are “go” trials.

[00150] As noted above, in some embodiments, an action cue signals a first type of target response to be entered by user interaction (*e.g.*, an affirmative target response, such as a button press). In an illustrative example, a “go” trial includes an action cue that corresponds to an affirmative target response, such as the presence of a motor response (*e.g.*, a button press, a keystroke, a mouse click, a toggle, a tap on a touchscreen display, a blink, an eye movement, a squeeze of a hand grip, and/or any voluntary or involuntary motor response that can be captured or recorded by a device). In some embodiments, the “go” trial generates an outcome cue based on whether the corresponding target response is received within the reference action time (*e.g.*, quickly enough to satisfy a response window, as described below).

[00151] In some embodiments, the reference action time is at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the reference action time is no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the reference action time is from 10

milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the reference action time falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00152] In some embodiments, the reference action time is a response window for entry of the corresponding target response. In some embodiments, the reference action time is determined based on a process in which the subject's response time is measured and used to determine a baseline for the response window. In some embodiments, the reference action time is initialized, prior to the first evaluation session, using a practice session.

[00153] In some embodiments, the reaction time for the corresponding target response is measured between the generating of the one or more respective target cues and the receiving of the corresponding target response, and the reference action time is determined by a procedure prior to the performing (*e.g.*, prior to the first evaluation session). In some embodiments, the procedure includes performing a practice session comprising, for each respective practice trial in a corresponding plurality of practice trials: displaying, on the display, a respective user-interactive series of images generating one or more respective target cues, and receiving, responsive to the one or more respective target cues, a corresponding target response from the subject using the input device. In some embodiments, the procedure further includes determining a measure of central tendency using, for each respective practice trial in the plurality of practice trials, a reaction time for the corresponding target response.

[00154] Non-limiting examples of measures of central tendency contemplated for use in the present disclosure include an arithmetic mean, weighted mean, midrange, midhinge, trimean, geometric mean, geometric median, Winsorized mean, median, and mode of the distribution of values. In some embodiments, the measure of central tendency is modified by a scaling factor. In some embodiments, the measure of central tendency is the average reaction time multiplied by a factor of 2.

[00155] In some embodiments, the plurality of practice trials comprises at least 10 trials.

[00156] In some embodiments, the plurality of practice trials comprises at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, at least 300, at least 500, at least 1000, or at least 2000 trials. In some embodiments, the plurality of practice trials comprises no more than 5000, no more than 2000, no more than 1000, no more than 500, no

more than 200, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 trials. In some embodiments, the plurality of practice trials consists of from 2 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 trials. In some embodiments, the plurality of practice trials falls within another range starting no lower than 2 trials and ending no higher than 5000 trials.

[00157] In some embodiments, the practice session is performed only once (*e.g.*, prior to the first evaluation session). In some embodiments, the practice session is performed before each respective evaluation session in a plurality of evaluation sessions (*e.g.*, each iteration). In some embodiments, the practice session is performed prior to one or more evaluation sessions in a plurality of evaluation sessions.

[00158] In some embodiments, the reference action time is updated after at least the first evaluation session. In some embodiments, the reference action time is updated after each respective evaluation session in a plurality of evaluation sessions. In some embodiments, the reference action time is updated after one or more evaluation sessions in a plurality of evaluation sessions.

[00159] In some embodiments, for at least the first evaluation session, the reference action time is updated after each respective trial in the corresponding first plurality of trials. In some embodiments, for at least the first evaluation session, the reference action time is updated after each respective trial in the first subset of trials of the first plurality of trials (*e.g.*, after each “go” trial).

[00160] In some embodiments, for one or more evaluation sessions in a plurality of evaluation sessions, the reference action time is updated after each respective trial in the corresponding plurality of trials. In some embodiments, for one or more evaluation sessions in a plurality of evaluation sessions, the reference action time is updated after each respective trial in the first subset of trials of the corresponding plurality of trials (*e.g.*, after each “go” trial in each respective evaluation session).

[00161] Accordingly, in some embodiments, the reference action time is dynamically updated depending on the subject’s response times. In some embodiments, the dynamic updating of the reference action time (*e.g.*, the response window) occurs after each evaluation session or on a rolling basis during the evaluation session after each trial or each “go” trial. Advantageously, and without being limited to any one theory of operation, in some embodiments, the dynamic updating of the reference action time allows for a consistent level

of challenge by increasing or decreasing the difficulty of the response task according to the individual's ability (*e.g.*, by modulating the corresponding target speed for response based on previous response times).

[00162] Referring to Block 212, in some embodiments, the method further includes determining a measure of central tendency using, for each respective trial in at least the first subset of trials, a reaction time for the corresponding target response, and updating the reference action time with the measure of central tendency for the reaction time.

[00163] In some embodiments, the measure of central tendency is the average reaction time multiplied by a factor of 2.

[00164] In some embodiments, the reference action time is not initialized using subject responses but is set as a predetermined value.

[00165] In some embodiments, the reference action time is not dynamically updated, but is a fixed value.

[00166] In some embodiments, for each respective trial in the first subset of trials: the reaction time for the corresponding target response satisfies the reference action time when the reaction time is less than or equal to the reference action time, and the reaction time for the corresponding target response fails to satisfy the reference action time when the reaction time is greater than the reference action time.

[00167] In some embodiments, for each respective trial in the first subset of trials: the reaction time for the corresponding target response satisfies the reference action time when the reaction time is less than the reference action time, and the reaction time for the corresponding target response fails to satisfy the reference action time when the reaction time is greater than or equal to the reference action time.

[00168] Accordingly, a reaction time that is at least as fast as (or faster than) the response window will result in a first performance indicator (*e.g.*, a positive or neutral outcome cue), and a reaction time that is slower than the response window will result in a second performance indicator (*e.g.*, a neutral or negative outcome cue, or no outcome cue).

[00169] As noted above, in some embodiments, target responses are further assessed for accuracy relative to the particular target cue (*e.g.*, action cue) that is generated.

[00170] In some embodiments, for each respective trial in the first subset of trials: the respective action cue is selected from a plurality of candidate action cues, the corresponding

target response is selected from a plurality of candidate target responses, each respective candidate action cue in the plurality of candidate action cues is associated with a respective candidate target response in the plurality of candidate target responses, and the generating the respective outcome cue further comprises determining an accuracy of the corresponding target response relative to the respective action cue.

[00171] For instance, as described above, an action cue is selected from a pool of two possible candidate action cues including a first action cue comprising an object (*e.g.*, an animation of a fish) that appears on the left side of the display, and a second action cue comprising an object (*e.g.*, an animation of a fish) that appears on the right side of the display. Corresponding target responses are further selected from a pool of two possible candidate target responses including a first keystroke (*e.g.*, the “A” key) and a second keystroke (*e.g.*, the “L” key). The first action cue corresponds to the first keystroke, and the second action cue corresponds to the second keystroke. In some embodiments, the generation of the outcome cue is based on both the accuracy and the timeliness of the corresponding target response relative to the corresponding target cue.

[00172] Consider, for instance, an illustrative implementation of a “go” trial 142-1 in Figure 3A that includes an action cue 144 (*e.g.*, an animation of a fish) that appears either on the left or right sides of the display after 200 milliseconds of the scene or trial onset. A motor response 120 is required in response, depending on the position of the action cue (*e.g.*, left keystrokes for left position and right keystrokes for right position). The threshold for being fast or too slow is determined by the subject’s own performance (*e.g.*, as determined by an initial practice session). Performance accuracy is determined and presented with an outcome cue that can be an image or sound.

[00173] During the initial practice session, which is played just once the first time the subject starts the first session, the subject separately plays the same game for a number of practice trials (*e.g.*, 40 trials) and their average response time is recorded and averaged across that 40 trials (split between 50% left and 50% right positions). In the first evaluation session comprising 520 trials, their correct reference action time is their average practice response time multiplied by 2. Thus, if a user responded with a 0.5 second average response speed during the practice session, their response window for correct responses in the first evaluation session of 520 trials would be 1 second (*e.g.*, responses must be received in less than 1 second). This response window may be updated dynamically according to the subject’s performance, or alternately is carried on through all subsequent sessions.

[00174] *No-go trials.*

[00175] Referring to Block 214, in some embodiments, for each respective trial 114 in a second subset 142-2 of trials in the corresponding first plurality of trials, the one or more respective target cues 118 comprises a respective control cue 148, and the corresponding target response 120 satisfies the respective response threshold 124 when a delay time for the corresponding target response satisfies a reference control time 150.

[00176] A trial in the second subset of trials is alternately referred to herein as a “no-go” trial.

[00177] In some embodiments, the second subset of trials comprises at least 20 trials.

[00178] In some embodiments, the second subset of trials comprises at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, at least 300, at least 500, at least 1000, or at least 2000 trials. In some embodiments, the second subset of trials comprises no more than 5000, no more than 2000, no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 trials. In some embodiments, the second subset of trials consists of from 2 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 trials. In some embodiments, the second subset of trials falls within another range starting no lower than 2 trials and ending no higher than 5000 trials.

[00179] In some embodiments, the second subset of trials consists of from 5% to 30% of the first plurality of trials.

[00180] In some embodiments, the second subset of trials comprises at least 2%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, or at least 40% of the first plurality of trials. In some embodiments, the second subset of trials comprises no more than 50%, no more than 40%, no more than 30%, no more than 25%, no more than 20%, no more than 15%, or no more than 10% of the first plurality of trials. In some embodiments, the second subset of trials consists of from 20% to 60%, from 40% to 80%, from 50% to 90%, or from 70% to 95% of the first plurality of trials. In some embodiments, the second subset of trials falls within another range starting no lower than 2% of the first plurality of trials and ending no higher than 50% of the first plurality of trials.

[00181] As noted above, in some embodiments, a control cue signals a second type of target response (*e.g.*, a negative target response, such as a withholding of a button press). In an illustrative example, in contrast to “go” trials, a “no-go” trial includes a control cue that

corresponds to a negative target response, such as the absence or withholding of a motor response. In some embodiments, the “no-go” trial generates an outcome cue based on whether the corresponding target response is successfully withheld for a delay time that is at least as long as the duration of a reference control time (*e.g.*, successful ability to control or withhold a motor response).

[00182] In some embodiments, the reference control time is a period of time within which a subject’s ability to provide a corresponding target response (*e.g.*, delay or withhold an affirmative response) is assessed.

[00183] In some embodiments, the delay time refers to a length of time for which the subject is able to withhold an affirmative response.

[00184] In some embodiments, the “no-go” trial ends, or terminates, at the conclusion of the reference control time. In some embodiments, the “no-go” trial ends when the subject enters an affirmative response, if prior to the conclusion of the reference control time.

[00185] In some embodiments, for each respective trial in the second subset of trials, the delay time for the corresponding target response is measured between the generating of the respective control cue and one of: (i) the receiving of the corresponding target response or (ii) an expiration of the reference control time. In some embodiments, the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than or equal to the reference control time, and the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than the reference control time. In some embodiments, the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than the reference control time, and the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than or equal to the reference control time.

[00186] Thus, in some embodiments, the “delay time” refers to the subject’s ability to withhold an affirmative response, and the “reference control time” refers to the wait period given for assessment. In some embodiments, the outcome includes a first performance indicator (*e.g.*, a positive or neutral outcome cue) if the user can delay an affirmative response until the end of the wait period, or a second performance indicator (*e.g.*, a neutral or negative outcome cue, or no outcome cue) if the user cannot.

[00187] Consider, for instance, another illustrative evaluation session including an additional subset of “no-go” trials 142-2 (*e.g.*, a second subset of trials), in which an image

and/or a sound is introduced as a control cue 148. No action cues appear. The corresponding target response 120 is a withholding of a motor response (*e.g.*, the subject must withhold their button press response), and performance accuracy is determined based on delay times relative to a reference control time (*e.g.*, a wait period) and presented with an outcome cue that can be an image or sound.

[00188] In some embodiments, the reference control time is from about 100 milliseconds to about 2000 milliseconds.

[00189] In some embodiments, the reference control time is at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the reference control time is no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the reference control time is from 10 milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the reference control time falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00190] In some embodiments, the reference control time is determined based on the subject's delay time (*e.g.*, as a measure of central tendency for the subject's delay time over one or more "no-go" trials in the plurality of trials). In some embodiments, the reference control time is initialized, prior to the first evaluation session, using a practice session.

[00191] In some embodiments, the reference control time is dynamically updated depending on the subject's delay times. In some embodiments, the dynamic updating of the reference control time occurs after each evaluation session in a plurality of evaluation sessions or on a rolling basis, during a respective evaluation session, after each trial or each "no-go" trial in the corresponding plurality of trials.

[00192] In some embodiments, the reference control time is not initialized using subject delay times but is set as a predetermined value.

[00193] In some embodiments, the reference control time is not dynamically updated, but is a fixed value.

[00194] *Stop trials.*

[00195] Referring to Block 216, in some embodiments, for each respective trial 114 in a third subset 142-3 of trials in the corresponding first plurality of trials, the one or more respective target cues 118 comprises a respective action cue 144 and a respective control cue 148, and the corresponding target response 120 satisfies the respective response threshold 124 when a delay time for the corresponding target response satisfies the reference control time 150.

[00196] A trial in the third subset of trials is alternately referred to herein as a “stop” trial.

[00197] In some embodiments, the third subset of trials comprises at least 20 trials.

[00198] In some embodiments, the third subset of trials comprises at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, at least 300, at least 500, at least 1000, or at least 2000 trials. In some embodiments, the third subset of trials comprises no more than 5000, no more than 2000, no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 trials. In some embodiments, the third subset of trials consists of from 2 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 trials. In some embodiments, the third subset of trials falls within another range starting no lower than 2 trials and ending no higher than 5000 trials.

[00199] In some embodiments, the third subset of trials consists of from 5% to 30% of the first plurality of trials.

[00200] In some embodiments, the third subset of trials comprises at least 2%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, or at least 40% of the first plurality of trials. In some embodiments, the third subset of trials comprises no more than 50%, no more than 40%, no more than 30%, no more than 25%, no more than 20%, no more than 15%, or no more than 10% of the first plurality of trials. In some embodiments, the third subset of trials consists of from 20% to 60%, from 40% to 80%, from 50% to 90%, or from 70% to 95% of the first plurality of trials. In some embodiments, the third subset of trials falls within another range starting no lower than 2% of the first plurality of trials and ending no higher than 50% of the first plurality of trials.

[00201] In an illustrative example, in contrast to “go” trials and “no-go” trials, and “stop” trial includes at least an action cue and a control cue that follows the action cue, where the control cue indicates that the corresponding target response signaled by the action cue should be aborted or withheld. In some embodiments, the “stop” trial generates an outcome cue based on whether the corresponding target response corresponding to the action cue is successfully aborted or delayed for a delay time that is at least as long as the duration of a reference control time (*e.g.*, a successful ability to abort, control, or withhold a motor response).

[00202] In some embodiments, the control cue has a duration of from 2 milliseconds to 200 milliseconds (*e.g.*, a tone or image lasting 50 milliseconds).

[00203] In some embodiments, the control cue duration is at least 1, at least 2, at least 3, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, or at least 500 milliseconds. In some embodiments, the control cue duration is no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, or no more than 10 milliseconds. In some embodiments, the control cue duration is from 1 to 50, from 20 to 100, from 80 to 500, or from 200 to 1000 milliseconds. In some embodiments, the control cue duration falls within another range starting no lower than 1 millisecond and ending no higher than 1000 milliseconds.

[00204] In some embodiments, for each respective trial in the third subset of trials, the delay time for the corresponding target response is measured between the generating of the respective control cue and one of: (i) the receiving of the corresponding target response or (ii) an expiration of the reference control time.

[00205] In some embodiments, the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than or equal to the reference control time, and the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than the reference control time. In some embodiments, the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than the reference control time, and the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than or equal to the reference control time.

[00206] In some embodiments, the reference control time begins after the generation of the control cue. For instance, in an illustrative example of a trial, the action cue is generated 200

milliseconds after trial start at $t = 200$ milliseconds, the control cue is generated 200 milliseconds after the action cue at $t = 400$ milliseconds, and the reference control time is a period of 1 second beginning after the generation of the control cue. A corresponding target response for the example trial satisfies the respective response threshold when the subject successfully delays or aborts an affirmative response to the action cue for at least 1 second after the generation of the control cue.

[00207] Referring to Block 218, in some embodiments, for each respective trial in the third subset of trials, the respective control cue is generated a second predetermined interval after the generation of the respective action cue (*e.g.*, the control cue is generated 200 milliseconds after the action cue).

[00208] In some embodiments, the second predetermined interval is from about 100 milliseconds to about 1000 milliseconds.

[00209] In some embodiments, the second predetermined interval is at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the second predetermined interval is no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the second predetermined interval is from 10 milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the second predetermined interval falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00210] Referring to Block 220, in some embodiments, the method further includes, for each respective trial in the third subset of trials: in accordance with a determination the delay time for the corresponding target response satisfies the reference control time, increasing the second predetermined interval, and in accordance with a determination the delay time for the corresponding target response fails to satisfy the reference control time, decreasing the second predetermined interval.

[00211] Accordingly, in some embodiments, the trials in the third subset of trials (*e.g.*, “stop” trials) are dynamic in difficulty by modulating a “stop signal delay” represented by the second predetermined interval. In some embodiments, if the subject successfully withholds an affirmative response within the reference control time (*e.g.*, the wait period), the stop signal delay is increased, thus increasing the difficulty that the subject will successfully abort the affirmative response upon perceiving the control cue.

[00212] In some embodiments, if the subject fails to withhold an affirmative response within the reference control time (*e.g.*, the wait period), the stop signal delay is decreased, thus decreasing the difficulty that the subject will abort the affirmative response. In some embodiments, difficulty is modulated by the length of time between the action cue and the control cue, such that the subject may perceive the control cue at a shorter or longer delay after perceiving the action cue.

[00213] In some embodiments, the second predetermined interval is increased or decreased by an amount of at least 1, at least 2, at least 3, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, or at least 500 milliseconds. In some embodiments, the second predetermined interval is increased or decreased by an amount of no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, or no more than 10 milliseconds. In some embodiments, the second predetermined interval is increased or decreased by an amount of from 1 to 50, from 20 to 100, from 80 to 500, or from 200 to 1000 milliseconds. In some embodiments, the second predetermined interval is increased or decreased by an amount that falls within another range starting no lower than 1 millisecond and ending no higher than 1000 milliseconds.

[00214] In some embodiments, the second predetermined interval is increased or decreased at a fixed rate or at a dynamic rate (*e.g.*, by the same or different amount).

[00215] Referring to Block 222, in some embodiments, the method 200 further includes storing, after the performing the first evaluation session, the second predetermined interval. For instance, in some embodiments, the second predetermined interval is stored transitorily in the memory 92 of the electronic device, allowing for the second predetermined interval to affect the current evaluation session. In some embodiments, the second predetermined interval is stored in a user profile associated with the subject, which allows for evaluating historical interval trends associated with the subject and the like. However, the present disclosure is not limited thereto. For instance, in some embodiments, the stop signal delay

time is updated after each session and the updated stop signal delay time is used as a starting point for the subsequent evaluation session in a subsequent iteration.

[00216] In some embodiments, the stop signal delay time is updated after at least the first evaluation session. In some embodiments, the stop signal delay time is updated after each respective evaluation session in a plurality of evaluation sessions. In some embodiments, the stop signal delay time is updated after one or more evaluation sessions in a plurality of evaluation sessions. For instance, in some embodiments, the evaluation module and/or the assessment module updates the stop signal delay time during the period of time, such as when the subject is performing a respective evaluation session. However, the present disclosure is not limited thereto.

[00217] In some embodiments, for at least the first evaluation session, the stop signal delay time is updated after each respective trial in the corresponding first plurality of trials. In some embodiments, for at least the first evaluation session, the stop signal delay time is updated after each respective trial in the third subset of trials of the first plurality of trials (*e.g.*, after each “stop” trial).

[00218] In some embodiments, for one or more evaluation sessions in a plurality of evaluation sessions, the stop signal delay time is updated after each respective trial in the corresponding plurality of trials. In some embodiments, for one or more evaluation sessions in a plurality of evaluation sessions, the stop signal delay time is updated after each respective trial in the third subset of trials of the corresponding plurality of trials (*e.g.*, after each “stop” trial in each respective evaluation session).

[00219] Consider, for instance, an example embodiment of a “stop” trial, in which a control cue is generated a second predetermined interval (*e.g.*, a “stop signal delay of 200 milliseconds) after the action cue appears, where the control cue has a duration of 50 milliseconds. The control cue is a tone or sound that indicates that the subject must withhold their button press and therefore not press anything on this trial. Based on their performance accuracy, the second predetermined interval (*e.g.*, the stop signal delay) will increase or decrease, based on incorrect and correct responses, respectively, during “stop” trials. Performance accuracy is determined and presented with an outcome cue comprising an image or sound.

[00220] In some embodiments, the second predetermined interval is not dynamically updated, but is a fixed value.

[00221] In some embodiments, the reference control time is from about 100 milliseconds to about 2000 milliseconds.

[00222] In some embodiments, the reference control time is at least 10 milliseconds, at least 20 milliseconds, at least 50 milliseconds, at least 100 milliseconds, at least 200 milliseconds, at least 300 milliseconds, at least 500 milliseconds, at least 800 milliseconds, at least 1 second, at least 2 seconds, at least 3 seconds, at least 5 seconds, or at least 10 seconds. In some embodiments, the reference control time is no more than 30 seconds, no more than 10 seconds, no more than 5 seconds, no more than 1 seconds, no more than 500 milliseconds, no more than 200 milliseconds, no more than 100 milliseconds, no more than 50 milliseconds, or no more than 20 milliseconds. In some embodiments, the reference control time is from 10 milliseconds to 100 milliseconds, from 50 milliseconds to 500 milliseconds, from 300 milliseconds to 1 second, from 1 second to 5 seconds, from 2 seconds to 10 seconds, or from 5 seconds to 30 seconds. In some embodiments, the reference control time falls within another range starting no lower than 10 milliseconds and ending no higher than 30 seconds.

[00223] *Additional trials.*

[00224] Referring to Block 224, in some embodiments, the corresponding first plurality of trials further comprises a fourth subset of trials, where the displaying further comprises, for each respective trial in at least the fourth subset of trials: (i) generating a respective anticipation cue in the one or more respective target cues, and (ii) generating, after the generating (i), a respective action cue in the one or more respective target cues, where the anticipation cue indicates a probability of receiving a control cue after the action cue.

[00225] A trial in the fourth subset of trials is alternately referred to herein as an “anticipation” trial.

[00226] In some embodiments, for each respective trial in a first portion of the fourth subset of trials, the method further includes (iii) generating, after the generating (ii), a respective control cue in the one or more respective target cues, where the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time, and for each respective trial in a second portion of the fourth subset of trials, (iv) generating, after the generating (ii), no control cue, where the corresponding target response satisfies the respective response

threshold when a reaction time for the corresponding target response satisfies a reference action time.

[00227] Consider, for instance, an example anticipation trial illustrated in Figure 3C, in which an anticipation cue is introduced (*e.g.*, an image or sound) that is different from any action cues or control cues. For example, in Figure 3C, the anticipation cue is a background color, such as a color of the water in an underwater scene that is different relative to a background color of a “go,” “no-go,” or “stop” trial (green versus blue, represented in Figure 3C as dark gray versus light gray). In some embodiments, in the example anticipation trial, the anticipation cue is generated with or without a control cue. The anticipation trial is further associated with a probability that the control cue will occur. If the control cue occurs, the corresponding target response for the subject is a withholding of an affirmative or motor response (*e.g.*, subject must withhold their “go” response). Performance accuracy is determined and presented with an outcome cue (*e.g.*, an image or sound).

[00228] In some embodiments, the fourth subset of trials comprises at least 20 trials.

[00229] In some embodiments, the fourth subset of trials comprises at least 2, at least 5, at least 10, at least 20, at least 50, at least 100, at least 200, at least 300, at least 500, at least 1000, or at least 2000 trials. In some embodiments, the fourth subset of trials comprises no more than 5000, no more than 2000, no more than 1000, no more than 500, no more than 200, no more than 100, no more than 50, no more than 20, no more than 10, or no more than 5 trials. In some embodiments, the fourth subset of trials consists of from 2 to 10, from 5 to 30, from 20 to 100, from 80 to 500, from 200 to 2000, or from 1000 to 5000 trials. In some embodiments, the fourth subset of trials falls within another range starting no lower than 2 trials and ending no higher than 5000 trials.

[00230] In some embodiments, the fourth subset of trials consists of from 5% to 30% of the first plurality of trials.

[00231] In some embodiments, the fourth subset of trials comprises at least 2%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, or at least 40% of the first plurality of trials. In some embodiments, the fourth subset of trials comprises no more than 50%, no more than 40%, no more than 30%, no more than 25%, no more than 20%, no more than 15%, or no more than 10% of the first plurality of trials. In some embodiments, the fourth subset of trials consists of from 20% to 60%, from 40% to 80%, from 50% to 90%, or from 70% to 95% of the first plurality of trials. In some embodiments, the fourth subset of

trials falls within another range starting no lower than 2% of the first plurality of trials and ending no higher than 50% of the first plurality of trials.

[00232] In some embodiments, as noted above, a respective anticipation trial in the fourth subset of trials is further associated with a probability that the control cue will occur (*e.g.*, in the first portion of the fourth subset of trials).

[00233] In some embodiments, the first portion of the fourth subset of trials comprises no more than 50% of the fourth subset of trials (*e.g.*, that no more than 50% of anticipation trials will include the control cue). In some embodiments, the first portion of the fourth subset of trails comprises no more than 25% of the fourth subset of trials (*e.g.*, that no more than 25% of anticipation trials will include the control cue).

[00234] In some embodiments, the first plurality of trials comprises a plurality of subsets of anticipation trials (*e.g.*, in a fourth, fifth, sixth, and/or any subsequent subset of trials), and the probability that the control cue will occur in an anticipation trial varies between different subsets of anticipation trials. Accordingly, in an example implementation, a fourth subset of anticipation trials includes anticipation trials having a 25% probability that a control cue will occur, and a fifth subset of anticipation trials includes anticipation trials having a 50% probability that a control cue will occur.

[00235] In some embodiments, different subsets of anticipation trials include correspondingly different types of anticipation cues. For example, in some embodiments, a first anticipation cue signals a first probability, while a second anticipation cue signals a second probability. Consider again the example trial illustrated in Figure 3C, where the anticipation cue is a different background color in an underwater environment (*e.g.*, green water instead of blue). In some such embodiments, a light green background can indicate a 25% probability that a control cue will appear, while a dark green background may indicate a 50% probability that a control cue will appear. Any suitable variation or modification of cues is contemplated for use in the present disclosure, as will be apparent to one skilled in the art.

[00236] In some embodiments, a respective subset of anticipation trials comprises a probability that a control cue will occur in at least 10%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, or at least 60% of the respective subset of anticipation trials. In some embodiments, a respective subset of anticipation trials comprises a probability that a control cue will occur in no more than 70%, no more than 60%, no more than 50%, no more than 40%, no more than 30%, no more than

25%, no more than 20%, no more than 15%, or no more than 10% of the respective subset of anticipation trials. In some embodiments, a respective subset of anticipation trials comprises a probability that a control cue will occur in from 10% to 40%, from 20% to 50%, from 40% to 60%, or from 50% to 70% of the respective subset of anticipation trials. In some embodiments, a respective subset of anticipation trials comprises a probability that falls within another range starting no lower than 10% and ending no higher than 70%.

[00237] In some embodiments, a fourth subset of anticipation trials includes anticipation trials having a 33% probability that a control cue will occur, and a fifth subset of anticipation trials includes anticipation trials having a 66% probability that a control cue will occur.

[00238] In some embodiments, the plurality of subsets of trials comprises at least 2, at least 3, at least 5, at least 10, at least 20, or at least 30 subsets of trials. In some embodiments, the plurality of subsets of trials comprises no more than 50, no more than 30, no more than 20, no more than 10, or no more than 5 subsets of trials. In some embodiments, the plurality of subsets of trials consists of from 2 to 10, from 5 to 30, or from 20 to 50 subsets of trials. In some embodiments, the plurality of subsets of trials falls within another range starting no lower than 2 subsets of trials and ending no higher than 50 subsets of trials.

[00239] In some embodiments, the anticipation cue is visual (*e.g.*, an animation, an image), auditory (*e.g.*, a sound), and/or physical (*e.g.*, a haptic feedback), *etc.* In some embodiments, the respective anticipation cue comprises a color, an object, an image, and/or a sound. Example embodiments of anticipation cues contemplated in the present disclosure further include, but are not limited to, images, objects, icons, geometric shapes, animations, arrows, indicia of emotions (*e.g.*, happy face or sad face), alphanumeric text, congruent or incongruent word pairs, colors, textures, and/or patterns.

[00240] In some embodiments, one or more trials in the corresponding first plurality of trials further comprises one or more affective cues. In some embodiments, a respective affective cue in the one or more affective cues is selected from the group consisting of positive, negative, or neutral.

[00241] For example, as illustrated in Figures 3A-3D, a respective trial may also include affective cues 310 (*e.g.*, 310-1, 310-2, 310-3, 310-4, 310-5, 310-6, 310-7, or 310-8) as objects floating in the water, split into 4 categories: positive, negative, or neutral images, or none. Positive objects can include smiling starfish, trophies, *etc.* Negative objects can include guns, bloodied knives, *etc.* Neutral objects will include a book, a lamp, *etc.* In some

implementations, the “none” category has no affective cues generated (*e.g.*, no floating object in the trial). In some embodiments, affective cues and/or categories thereof are evenly or unevenly split across different subsets of trials.

[00242] In some embodiments, the plurality of subsets of trials are randomly mixed together in the plurality of trials.

[00243] *Assessment and measure of inhibition control.*

[00244] Referring to Block 225, in some embodiments, the method 200 further includes determining a first measure of inhibition control 162 that represents an improvement in the symptom of post-traumatic stress disorder. In some embodiments, the determining the first measure of inhibition control 162 includes applying some or all of the record of performance indicators associated with the subject to an assessment module (*e.g.*, determination module 160 in Figures 1A-1C) to receive as output from the assessment module the determination of the first measure of inhibition control.

[00245] In some embodiments, the first measure of inhibition control is selected from the group consisting of: a rate of omission, a rate of commission, a stop-signal reaction time (SSRT), a stop-signal anticipation task (SSAT) score, a reactive inhibition (RI), a proactive inhibition (PI), and an extra-proactive inhibition (EPI).

[00246] In some embodiments, the method 200 further includes determining a measure of inhibition control comprising a number of commission errors made during the second subset of trials (*e.g.*, “no-go” trials). For instance, in some embodiments, the assessment module 160 determines the measure of inhibition control that includes the number of commission errors made during the second subset of trials.

[00247] Generally, commission errors occur when the subject erroneously presses the button during a no-go trial (Meule, 2017) (*e.g.*, shouldn’t have been pressed but was). These commission errors are calculated as rates, where a higher error rate, also known as a higher false alarm rate, indicates less inhibitory control (Young *et al.*, 2018). Without being limited to any one theory of operation, commission errors indicate the extent to which the go/no-go tasks make the go task become habitual.

[00248] On a deeper level, in some implementations, sensitivity and response bias to stimuli during no/go trials can be analyzed using signal detection theory (SDT). See, *e.g.*, Young *et al.* (2018). This analysis includes separating responses into four categories: (a) responding in the presence of a go stimulus, (b) failing to respond in the presence of a

stimulus, (c) falsely responding to a no-go stimulus, and (d) not responding in the presence of a no-go stimulus. In some embodiments, high sensitivity indicates a large amount of hits or accurate rejections relative to misses or commission errors.

[00249] In some embodiments, the first measure of inhibition control comprises a number of omission errors (*e.g.*, should have been pressed but wasn't) made during the first subset of trials (*e.g.*, "go" trials).

[00250] In some embodiments, the first measure of inhibition control is stop-signal reaction time (SSRT).

[00251] Generally, it can be inferred that the stop process is initiated once a stop signal is presented. See, *e.g.*, Logan and Cowan (1984) and McMorris (2016). The "stop signal delay" (SSD) is defined as the time that passes between the presentation of the go-stimulus and the presentation of the stop signal. In some embodiments, SSRT is calculated using two common methods: the integration method and the mean method (Verbuggen *et al.*, 2013). The integration method asserts that the point in time the stop process ends (finishing time) can be predicted from the observed reaction times distribution in Go trials integrated with the observed likelihood of having to respond to a stop signal. SSRT can then be ascertained by subtracting SSD from the finishing time. In some embodiments, the stop-signal reaction time is calculated for "go" trials as: when $p(\text{respond} \mid \text{signal}) = .50 \rightarrow \text{SSRT} = \text{mean response time} - \text{observed mean SSD}$.

[00252] In some embodiments, the first measure of inhibition control is a stop-signal anticipation task (SSAT) score. In some embodiments, the calculated SSRT is further used to determine reactive inhibition and proactive inhibition, measured by SSAT. Proactive inhibition, the ability to modify ongoing responses based on the contextual stimuli presented, is assessed in SSAT (van Hulst *et al.*, 2018). Specifically, in SSAT, the visual cue presented is indicative of the likelihood a stop signal will occur (goal-driven). As the stop-signal probability increases, subjects respond by slowing down their response times. Proactive inhibition is measured by looking at the covariance between the slowing of RT and the increases of stop-signal probability using an ANCOVA. SSAT also measures reactive inhibition in that the signal immediately triggers action cancellation (stimulus-driven).

[00253] In some embodiments, the first measure of inhibition control is reactive inhibition, calculated as SSRT mean across 25%, 50%. In some embodiments, the first measure of inhibition control is proactive inhibition: calculated as 0% GoRT minus (mean of 25% and

50% GoRT). In some embodiments, the first measure of inhibition control is extra proactive inhibition, calculated from proactive inhibition as 25% mean GoRT minus 50% meanGoRT.

[00254] In some embodiments, the first measure of inhibition control is selected from the group consisting of false positive rate, true positive rate, false negative rate, true negative rate, sensitivity, and specificity.

[00255] Referring to Block 226, in some embodiments, the first measure of inhibition control is determined using (i) the corresponding target response and (ii) the respective response threshold for the respective trial, for each respective trial in the corresponding first plurality of trials for the subject.

[00256] In some embodiments, the method further includes determining a change in (i) the first measure of inhibition control relative to (ii) a second measure of inhibition control obtained from a second evaluation session for the subject.

[00257] Referring to Block 228, in some embodiments, the first measure of inhibition control is an alteration in an inhibitory control network or a neural pathway of the subject. In some embodiments, an alteration in an inhibitory control network or neural pathway is determined as a physiological or neural pathway change. In some embodiments, an alteration in an inhibitory control network or neural pathway is determined using an imaging technique (*e.g.*, magnetic resonance imaging (MRI)), clinical monitoring, and/or via patient feedback or questionnaires.

[00258] In some embodiments, the method 200 advantageously alters (*e.g.*, improves) a subject's performance in a respective evaluation session. In some embodiments, the method advantageously alters (*e.g.*, improves) a subject's performance on a secondary assessment tool. Moreover, in some embodiments, by using the system 100, the method 200 is capable of displaying the series of images to the subject that allows for interaction and engagement with the subject in the form of various ques generated during the period of time the series of images is displayed to the subject.

[00259] In some embodiments, the method 200 further includes administering a secondary assessment tool selected from the group consisting of: a Go/No-Go Task, an Incentive Flanker Task (IFT), a Hariri Task, a Think/No-Think Task, a Face-Stroop Task, and any similar task thereof.

[00260] Referring to Block 230, in some embodiments, the performing of the first evaluation session alters an inhibitory control network or a neural pathway of the subject.

[00261] Referring to Block 232, in some embodiments, the first measure of inhibition control is determined using one or more of physiological, clinical, and behavioral measures.

[00262] In some embodiments, the method further includes obtaining, prior to the performing of the first evaluation session, a diagnostic measure of inhibition control for the subject, and determining a change in (i) the first measure of inhibition control relative to (ii) the diagnostic measure of inhibition control for the subject.

[00263] In some embodiments, the measure of inhibition control is based on a Minimal Clinically Important Difference (MCID), a Clinical Global Impression Scale of Improvement (CGI), a Patient Global Impression Scale of Improvement (PGI), a Liebowitz Social Anxiety Scale (LSAS), or a combination thereof.

[00264] The MCID refers to the smallest benefit of value to the subject. It captures both the magnitude of the improvement and the value the subject places on the change. The MCID defines the smallest amount an outcome must change to be meaningful to the subject. Additional details and information regarding MCID assessments can be found at Kaplan, R., 2005, “The Minimally Clinically Important Difference in Generic Utility-based Measures,” COPD: Journal of Chronic Obstructive Pulmonary Disease, 2(1), pg. 91, which is hereby incorporated by reference in its entirety for all purposes.

[00265] The CGI evaluations a severity and/or changes in an ability of the subject to manage the psychiatric or mental condition. Additional details and information regarding CGI scale assessments can be found at Pérez *et al.*, 2007, “The Clinical Global Impression Scale for Borderline Personality Disorder Patients (CHI-BPD): A Scale Sensible to Detect Changes,” Actas Españolas de Psiquiatría, 35(4), pg. 229, which is hereby incorporated by reference in its entirety for all purposes.

[00266] The PGI provides a patient rated format, as opposed to a clinician rated format of the CGI scale assessment. Additional details and information regarding the PGI assessment can be found at Faith *et al.*, 2007, “Twelve Years-Experience with the Patient Generated Index (PGI) of Quality of Life: A Graded Structured Review,” Quality of Life Research, 16(4), pg. 705, which is hereby incorporated by reference in its entirety for all purposes.

[00267] The LSAS assesses social anxiety disorder in clinical research and practice. It includes a self-reported (LSAS-SR) and a clinician-administered (LSAS-CA). Additional details and information regarding an LSAS assessment is found at Rytwinski *et al.*, 2009, “Screening for Social Anxiety Disorder with the Self-Report Version of the Liebowitz Social

Anxiety Scale,” *Depression and Anxiety*, 26(1), pg. 34, which is hereby incorporated by reference in its entirety for all purposes.

[00268] In some embodiments, the measure of inhibition control comprises Clinical Interviews and Clinician-Administered Assessments (SCID-5, CAPS-5, MADRS, MoCA, WTAR).

[00269] Structured Clinical Interview for DSM-5 (SCID-5). The Structured Clinical Interview for DSM-5 (SCID-5; First *et al.*, 2015) is a semi-structured interview guide for making DSM-5 diagnoses. It is the most widely used structured diagnostic interview to determine psychiatric diagnoses in clinical research based on DSM-5 criteria. The SCID-5 is organized into diagnostic modules to assess mood, psychotic, substance use, anxiety, obsessive-compulsive and related, eating, trauma, and stressor-related disorders. This study will utilize the most comprehensive version of the SCID-5, the SCID-5-Research Version (RV), which contains more disorders than the Clinician Version and includes all the relevant subtypes, severity, and course specifiers. An important feature of the SCID-5-RV is its customizability, allowing the instrument to be tailored to meet the requirements of a particular study. The SCID-5-RV comes in a standard "core" configuration that includes the disorders most researchers are likely to assess routinely for most studies, as well as in an "enhanced" configuration that includes several optional disorders, in addition to the disorders from the "core" configuration.

[00270] Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). The Clinician-Administered PTSD Scale for DSM-5 (Weathers *et al.*, 2013a) is a 30-item, clinician-administered, structured interview that asks participants about the PTSD symptoms identified in the DSM-5. It is considered a "gold-standard" measure for PTSD and is often used in research and clinical practice to assess for current (past month and past week) changes in symptoms over time, and overall severity of PTSD. The questions assess the onset, duration, and severity of present PTSD symptoms, as well as social and occupational functioning, dissociation symptoms, and the validity of symptom reports. The CAPS-5 uses a singlepoint ordinal rating scale to measure symptom severity. Symptom severity ratings combine information about symptom frequency and intensity obtained by the interviewer.

[00271] Montgomery-Asberg Depression Rating Scale (MADRS). The Montgomery-Asberg Depression Rating Scale (Montgomery & Asberg, 1979) is a 10-item, clinician-administered measure used to evaluate depressive symptom in adults, and to assess changes

in depressive symptoms over time. The items are rated on a scale from 0-6, with differing descriptors for each item. The individual item scores are added together to form a total score, which can range from 0-60.

[00272] Montreal Cognitive Assessment (MoCA). The Montreal Cognitive Assessment is a widely used screening tool to differentiate mild cognitive impairment from cognitive changes associated with healthy aging (Nasreddine *et al.*, 2005). A recommended cutoff score of 23 will be used to determine study eligibility for this study, based on meta-analytic findings that suggest the original cutoff score for the MoCA (26/30) is associated with higher rates of false positives, especially among individuals of lower education and older age (Carson *et al.*, 2018).

[00273] Wechsler Test of Adult Reading (WTAR). The Wechsler Test of Adult Reading is a neuropsychological assessment measure used to derive a pre-morbid estimate of intelligence (Holdnack, 2001). The measure requires the participant to read a list of 50 words.

[00274] Columbia Suicide Severity Rating Scale (C-SSRS). The Columbia Suicide Severity Rating Scale (C-SSRS) is a semi-structured interview that measures the full spectrum of suicidality, including passive and active suicidal ideation, suicidal intent, and suicidal behaviors (Posner *et al.*, 2011). The C-SSRS is commonly employed in clinical trials.

[00275] In some embodiments, the measure of inhibition control comprises Clinical Self-Report Forms (PCL-5, CTQ, ACS, ERRI, ATQ-ER, TLEQ, QIDS-SR, SDS, RRS).

[00276] PTSD Checklist for DSM-5 (PCL-5). The PTSD Checklist for DSM-5 (PCL-5) is a widely used clinical self-report scale to evaluate current symptoms of PTSD. Each question on the 20-item checklist corresponds to a symptom for PTSD in the DSM-5. The PCL-5 is often used in research and clinical practice to screen subjects/patients for potential PTSD, as well as monitor PTSD symptoms and their severity over time (Weathers *et al.*, 2013b). The PCL-5 measure also has a Specific Version to assess PTSD symptom severity in relation to a participant's specific trauma.

[00277] Childhood Trauma Questionnaire (CTQ). The Childhood Trauma Questionnaire (CTQ) is a widely used, valid and reliable retrospective self-report scale to screen for history of childhood abuse and neglect (Bernstein *et al.*, 1994). The measure is 28 items and yields five subscale scores (emotional abuse and neglect, physical abuse and neglect, and sexual abuse) as well as a minimization-denial score.

[00278] The Traumatic Life Events Questionnaire (TLEQ). The Traumatic Life Events Questionnaire (TLEQ) is a widely used self-report scale to assess the frequency, severity, and timing of a wide range of traumatic events and experiences across an individual's lifetime (Kubany et al, 2000).

[00279] Quick Inventory of Depressive Symptomatology – Self Report (QIDS-SR). The Quick Inventory of Depressive Symptomatology – Self-Report (QIDS-SR) is a commonly used self-report scale to assess severity of depressive symptoms (Rush *et al.*, 2003). The total score of the QIDS-SR is based on the nine criterion symptom domains of major depressive disorder.

[00280] Sheehan Disability Scale (SDS). The Sheehan Disability Scale (SDS) is a 5-item self-report scale that assesses functional impairment in domains of work, school, social life, and family life (Sheehan *et al.*, 1996). Higher scores on this scale represent higher functional impairment.

[00281] Difficulties in Emotion Regulation Scale (DERS). The Difficulties in Emotion Regulation Scale (DERS) is a 36-item self-report measure that assesses clinically relevant domains of emotion regulation (Gatz & Roemer, 2004). The emotion regulation domains include awareness and understanding of emotions; acceptance of emotions; the ability to engage in goal-directed behavior, and refrain from impulsive behavior, when experiencing negative emotions; and access to effective emotion regulation strategies.

[00282] Attentional Control Scale (ACS). The Attentional Control Scale (ACS) is a 20-item self-report measure that assesses general capacity for attentional control, including the ability to focus attention, shift attention between tasks, and to flexibly control thought (Derryberry & Reed, 2002).

[00283] Adult Temperament Questionnaire – Effortful Control Scale (ATQ-EC). The Adult Temperament Questionnaire is a self-report questionnaire with numerous subscales that assess effortful control, negative affect, extraversion, and orienting sensitivity (Evans & Rothbart, 2007).

[00284] Event-Related Rumination Inventory (ERRI). The Event-Related Rumination Inventory (ERRI) is a self-report measure that assesses intrusive and deliberate repetitive thinking about a highly stressful life event (Cann *et al.*, 2011). The ERRI has two subscales: an intrusive item subscale and a deliberate item subscale.

[00285] Ruminative Response Scale (RRS). The Ruminative Response Scale (RRS) is a 22-item self-report measure that assesses the frequency of reflective, brooding, and depression-related ruminative behavior (Treyner *et al.*, 2003).

[00286] In some embodiments, the measure of inhibition control comprises neuroimaging methods (fMRI).

[00287] Resting State fMRI (R-fMRI). The 3T MRI scan will focus on capturing activity in the inhibitory control network. Following a standard 10-minute structural scan, approximately 10-minutes of resting state fMRI data will be collected. Subjects will be instructed to rest, eyes open and fixed on a central fixation cross, and to try to remain as still as possible.

[00288] Go/No-Go Paradigm. The Go/No-Go task is a straightforward and widely utilized measure of inhibitory control requiring withholding of a response based on a salient visual cue.

[00289] Incentive Flanker Task (IFT). The Incentive Flanker task (IFT) is a modified version of the widely used Eriksen Flanker Task (Eriksen & Eriksen, 1974), which assesses selective visual attention. The IFT asks participants to sort a target stimulus into a designated category while the corresponding target is surrounded by incongruent stimuli (*e.g.*, Huber & Schlosser, 2010).

[00290] Hariri Task. The Hariri paradigm (Hariri *et al.*, 2002) is a widely used task in which participants are presented with an affective image (stimulus) and neutral forms (control) and asked to match one of two simultaneously presented images with the identical target stimulus.

[00291] Behavioral Methods.

[00292] Combined Think/No-Think and Go/No-Go Paradigm. The combined Think/No-Think and Go/No-Go paradigm requires participants to learn 35 cue-target word pairs (for approximately 15 minutes) and then asked to alternatively suppress, recall, or think about the cue-target word pairs, when prompted (Herbert & Sullivan, 2012). Performance on this task will be an exploratory outcome, investigating its role as a “transfer of learning task” as it requires inhibitory control.

[00293] Face-Stroop Task. The Face-Stroop task is a modified version of the widely used Stroop task (Stroop, 1935) which assesses reaction time between congruent and incongruent

stimuli. During the Face-Stroop task, participants are simultaneously presented with images of emotional faces and emotional words (*e.g.*, “Happy”, “Sad”), with some trials presenting congruent stimuli (happy face + “Happy”) and other trials presenting incongruent stimuli (happy face + “Sad”) and asked to identify the faces and words separately (*e.g.*, Agusti *et al.*, 2017).

[00294] See, *e.g.*, Hirose *et al.* (2012). Efficiency of Go/No-go task Performance Implemented in the Left Hemisphere. *J Neurosci.*, 32(26): 9059–9065; Logan, G. D., and Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological review*, 91(3), 295; McMorris, T. (2016). History of research into the acute exercise–cognition interaction: A cognitive psychology approach. doi: 10.1016/B978-0-12-800778-5.00001-3; Logan, G. D., and Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological review*, 91(3), 295; Meule, A. (2017). Reporting and interpreting task performance in go/no-go affective shifting tasks. *Frontiers in Psychology*, 8, 701; van Hulst, B. M. *et al.* (2018). Children with ADHD symptoms show deficits in reactive but not proactive inhibition, irrespective of their formal diagnosis. *Psychological medicine*, 48(15), 2515-2521; Verbruggen, F. *et al.* “Fictitious inhibitory differences: how skewness and slowing distort the estimation of stopping latencies.” *Psychological science* vol. 24,3 (2013): 352-62. doi:10.1177/0956797612457390; and Young, M. E. *et al.* (2018). Optimal go/no-go ratios to maximize false alarms. *Behavior research methods*, 50(3), 1020-1029, each of which is hereby incorporated herein by reference in its entirety for all purposes.

[00295] See also, *e.g.*, First, M. B., *et al.* (2015). Structured clinical interview for DSM-5 – Research version (SCID-5 for DSM-5, research version; SCID-5-RV). Arlington, VA: American Psychiatric Association, 1-94; Weathers, F.W., *et al.* (2013a). The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5), available from the Internet at ptsd.va.gov; Montgomery and Åsberg. (1979). A new depression scale designed to be sensitive to change. *The British journal of psychiatry*, 134(4), 382-389; Nasreddine, Z. S., *et al.*, (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695-699; Carson, N., *et al.* (2018). A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. *International journal of geriatric psychiatry*, 33(2), 379-388; Holdnack, H.A. (2001). Wechsler Test of Adult Reading: WTAR. San Antonio. The Psychological Corporation; Posner, K., *et al.* (2011). The Columbia–Suicide Severity Rating Scale: initial validity and

internal consistency findings from three multisite studies with adolescents and adults.

American journal of psychiatry, 168(12), 1266-1277; Weathers, F.W., *et al.* (2013b). The PTSD Checklist for DSM-5 (PCL-5); Bernstein, D. P., *et al.* (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. The American Journal of Psychiatry, 151(8), 1132-1136; Kubany, E. S., *et al.* (2000). Development and preliminary validation of a brief broad-spectrum measure of trauma exposure: the Traumatic Life Events Questionnaire. Psychological assessment, 12(2), 210; Rush, A. J., *et al.* (2003). The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDSC), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biological psychiatry, 54(5), 573-583; Sheehan, D. V., *et al.* (1996). The measurement of disability. International clinical psychopharmacology; Gratz, K. L., and Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. Journal of psychopathology and behavioral assessment, 26(1), 41-54; Derryberry, D. and Reed, M.A. (2002). Anxiety-related attentional biases and their regulation by attentional control. Journal of Abnormal Psychiatry, 111(2), 225-236; Evans, D.E., and Rothbart, M.K. (2007). Development of a model for adult temperament. Journal of Research in Personality, 41, 868-888; Cann, A., *et al.* (2011). Assessing posttraumatic cognitive processes: The Event-Related Rumination Inventory. Anxiety, Stress, & Coping, 24(2), 137-156; Treynor, W., *et al.* (2003). Rumination reconsidered: A psychometric analysis. Cognitive Therapy and Research, 27(3), 247-259; Eriksen, B. A., and Eriksen, C. W. (1974). Effects of noise letters upon identification of a target letter in a non-search task. Perception and Psychophysics, 16, 143-149; Hubner, R., and Schlosser, J. (2010). Monetary reward increases attentional effort in the flanker task. Psychonomic Bulletin and Review, 17(6), 821-826; Hariri, A. R., *et al.* (2002). The amygdala response to emotional stimuli: A comparison of faces and scenes. NeuroImage, 17, 317-323; Herbert, C. and Sutterlin, S. (2012). Do not respond! Doing the think/no-think and go/no-go tasks concurrently leads to memory impairment of unpleasant items during later recall. Front. Psychol., 3(269), 1-6; Stroop, J.R. (1935). Studies of interference in serial verbal reactions. Journal of Experimental Psychology, 18(6), 643-662; and Agusti, A. I., *et al.* (2017). An emotional Stroop task with faces and words. A comparison of young and older adults. Consciousness and Cognition, 35, 99-104, each of which is hereby incorporated herein by reference in its entirety for all purposes.

[00296] In some embodiments, the method further includes reporting at least the first measure of inhibition control to the subject or to a medical provider.

[00297] In some embodiments, the method further includes administering the method to treat a trauma-related condition or a symptom thereof.

[00298] In some embodiments, the method further includes administering the method in conjunction with another therapeutic intervention, such as a psychotherapy regimen.

[00299] *Additional Embodiments*

[00300] Another aspect of the present disclosure includes a computer system comprising: a display; an input device; one or more processors; and memory storing one or more programs for improving a symptom of post-traumatic stress disorder in a subject that, when executed by the one or more processors, cause the processors to perform a method. In some embodiments, the method includes performing a first evaluation session comprising, for each respective trial in a corresponding first plurality of trials, displaying, on the display, a respective user-interactive series of images generating one or more respective target cues, receiving, responsive to the one or more respective target cues, a corresponding target response from the subject using the input device, and generating a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial. In some embodiments, the respective outcome cue comprises, when the corresponding target response satisfies the respective response threshold, a first performance indicator, and when the corresponding target response fails to satisfy the respective response threshold, a second performance indicator. For each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time. For each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time. For each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue and a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the

reference control time. In some embodiments, the method further includes determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder.

[00301] Another aspect of the present disclosure includes a non-transitory computer-readable storage medium having stored thereon program code instructions for improving a symptom of post-traumatic stress disorder in a subject that, when executed by a processor, cause the processor to perform a method. In some embodiments, the method includes performing a first evaluation session comprising, for each respective trial in a corresponding first plurality of trials, displaying, on the display, a respective user-interactive series of images generating one or more respective target cues, receiving, responsive to the one or more respective target cues, a corresponding target response from the subject using the input device, and generating a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial. In some embodiments, the respective outcome cue comprises, when the corresponding target response satisfies the respective response threshold, a first performance indicator, and when the corresponding target response fails to satisfy the respective response threshold, a second performance indicator. For each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time. For each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time. For each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue and a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time. In some embodiments, the method further includes determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder.

[00302] Yet another aspect of the present disclosure includes a system including a memory; one or more processors; and one or more modules stored in the memory and

configured for execution by the one or more processors, the one or more modules including instructions for performing any of the methods disclosed herein.

[00303] Still another aspect of the present disclosure includes a non-transitory computer readable storage medium, the non-transitory computer readable storage medium storing one or more programs for execution by one or more processors of a computer system, the one or more computer programs including instructions for performing any of the methods disclosed herein.

[00304] *Example 1 – Systems and Methods for Improving a Symptom of Post-traumatic Stress Disorder in a Subject*

[00305] Referring to Figures 4A through 4D, in this Example, the present disclosure implemented systems (*e.g.*, system 100 of Figures 1A-1C, *etc.*) and methods (*e.g.*, method 200 of Figures 2A-2D, *etc.*) for improving a symptom of post-traumatic stress disorder in a subject were used.

[00306] A plurality of trials were conducted on a population of subjects by having each subject in the population perform a first evaluation using a first evaluation session module executed at a client device.

[00307] In this example, there were 28 subjects in the population of subjects, eight of which were in-person (Figure 4A) and twenty of which were remote (Figure 4B).

[00308] The subjects made the fewest errors on “go” trials, and the most errors on the most difficult stop trials, which required inhibitory control by the subjects. In implementations that include an anticipation cue, which signaled a higher probability of a stop-signal, improved performance.

[00309] Referring to Figure 4C, over the course of multiple sessions (*e.g.*, multiple iterations of executing the evaluation session module, *etc.*), the population performed better and showed improved inhibitory control. Moreover, referring to Figure 4D, , the population further showed improvement in symptom severity related to negative outlook and inhibitory control over negative behaviors such as anger and/or frustration. In Figure 4D, ** is p less than 0.01, * is p is less than 0.05, and # is p is equal to 0.05.

[00310] *Example 2 – Systems and Methods for Improving a Symptom of Post-traumatic Stress Disorder in a Subject*

[00311] Referring to Figures 5A through 5J, in this Example, the present disclosure implemented systems (*e.g.*, system 100 of Figures 1A-1C, *etc.*) and methods (*e.g.*, method 200 of Figures 2A-2D, *etc.*) for improving a symptom of post-traumatic stress disorder in a subject were used.

[00312] A plurality of trials were conducted on a population of subjects by having each subject in the population of subjects perform a first evaluation using a first evaluation session module executed at a client device.

[00313] In this example, there were 28 subjects in the population, of which seventeen provided a complete data set, such as a plurality of responses to an assessment (*e.g.*, questionnaire) and one or more evaluation sessions performed using an evaluation session module executed at a client device. The mean age was 36 ± 8.99 years, and 10 of the subjects were male.

[00314] Each subject in the population of subjects was administered three evaluations session and two assessments, one assessment associated with the initial evaluation session in the three evaluation sessions and another assessment associated with the terminal evaluation session in the three evaluation sessions.

[00315] The assessment included a sociodemographic and general health questionnaire and a PROMIS questionnaire administered to each subject.

[00316] The population performed the same trial three times in a period of time of one week (*e.g.*, Monday, Wednesday, and Friday).

[00317] Figure 5A depicts the general performance of the population at the first trial of the initial evaluation session in the three evaluation sessions performed by each subject.

[00318] Figure 5B depicts the general performance of the population at the first trial of the second evaluation session in the three evaluation sessions performed by each subject.

[00319] Figure 5C depicts the general performance of the population at the first trial of the terminal evaluation session in the three evaluation sessions performed by each subject.

[00320] Referring to Figure 5D, each subject in the population of subjects performed a practice evaluation session prior to the initial session in the three evaluation sessions. The population performed the practice evaluation session (*e.g.*, session 1 of Figure 5D) and the

initial evaluation session (e.g., session 2 of Figure 5D) on the first day, the second evaluation session (e.g., session 3 of Figure 5D) and the terminal evaluation session (e.g., session 4 of Figure 5D) during the rest of the week, typically on Monday, Wednesday and Friday.

[00321] Figures 5E through 5J depict correlations of self-reported measures by the population during the trial.

[00322] Figures 5E-5F depict correlations with self-reported affective measures using the PROMIS questionnaire for Anhedonia. In Figure 5E, t is 3.1081 and the p -value is 0.0068. In Figure 5F, t is 3.4966, and the p -value is 0.0030.

[00323] Figures 5G-5H depict correlations with self-reported affective measures using the PROMIS questionnaire for anger. In Figure 5G, t is 2.2188 and the p -value is 0.0413. In Figure 5H, t is 2.5820, and the p -value is 0.0201.

[00324] Figure 5I depicts correlations with self-reported affective measures using the PROMIS questionnaire for anger. In Figure 5I, t is 2.2188 and the p -value is 0.0413.

[00325] Figure 5J depicts correlations with self-reported affective measures using the PROMIS questionnaire for positive mood. In Figure 5J, t is -2.0628, and the p -value is 0.0557.

[00326] *Example 3 – Systems and Methods for Improving a Symptom of Post-traumatic Stress Disorder in a Subject*

[00327] Referring to Figures 6A through 6D, in this Example, the present disclosure implemented systems (e.g., system 100 of Figures 1A-1C, etc.) and methods (e.g., method 200 of Figures 2A-2D, etc.) for improving a symptom of post-traumatic stress disorder in a subject.

[00328] A plurality of trials were conducted on a population of subjects by having each subject in the population perform a first evaluation using a first evaluation session module executed at a client device.

[00329] There were 90 subjects in the population of subjects in this example. Sixty-five of these 90 subjects were identified by including those that passed the attentional check and that had a mean accuracy at Go trials of greater than seventy-five percent. Two subjects were excluded by not having passed the attentional check.

[00330] The assessment included a sociodemographic and general health questionnaire and a PROMIS questionnaire administered to the subject.

[00331] Each subject in the population performed the evaluation session once, remotely.

[00332] Figure 6A depicts the general performance of the population at the first trial of the evaluation session performed by each subject in subset of the population of subjects.

[00333] Figure 6B depicts correlations with self-reported affective measures using the PROMIS questionnaire for negative mood.

[00334] Figure 6C depicts correlations with self-reported affective measures using the PROMIS questionnaire for positive mood. In Figure 6D, final SSd is an indirect metric of task performance, in which higher values of final SSD corresponded to better performance at Stop trials.

[00335] Figure 6D depicts correlations with self-reported affective measures using the PROMIS questionnaire for control of temper by the respective subject.

[00336] In Figures 6B-6D, final SSd represents an indirect metric of task performance, in which higher values of final SSD corresponded to better performance at Stop trials.

CONCLUSION

[00337] All references cited herein are incorporated herein by reference in their entirety and for all purposes to the same extent as if each individual publication or patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

[00338] The present invention can be implemented as a computer program product that comprises a computer program mechanism embedded in a non-transitory computer readable storage medium. For instance, the computer program product could contain the program modules shown in any combination of Figures 1A-1C or 2A-2D. These program modules can be stored on a CD-ROM, DVD, magnetic disk storage product, USB key, or any other non-transitory computer readable data or program storage product.

[00339] Many modifications and variations of this invention can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. The specific embodiments described herein are offered by way of example only. The embodiments were

chosen and described in order to best explain the principles of the invention and its practical applications, to thereby enable others skilled in the art to best utilize the invention and various embodiments with various modifications as are suited to the particular use contemplated. The invention is to be limited only by the terms of the appended claims, along with the full scope of equivalents to which such claims are entitled.

WHAT IS CLAIMED IS:

1. A method for improving a symptom of post-traumatic stress disorder in a subject, the method comprising:

at an electronic device comprising a display, an input device, one or more processors, and memory storing one or more programs for execution by the one or more processors:

(A) executing a first evaluation session module comprising a corresponding first plurality of trials, wherein the executing comprises, for each respective trial in the corresponding first plurality of trials:

displaying, on the display, for a period of time, a respective user-interactive series of images, thereby generating one or more respective target cues associated with the respective user-interactive series of images during the period of time,

receiving, responsive to the one or more respective target cues, during the period of time, a corresponding target response from the subject using the input device,

generating, by the one or more processors, during the period of time, a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial, the respective outcome cue comprising:

in accordance with a determination the corresponding target response satisfies the respective response threshold, a first performance indicator, and

in accordance with a determination the corresponding target response fails to satisfy the respective response threshold, a second performance indicator,

wherein:

for each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time,

for each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time, and

for each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises the respective action cue and the respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time, and

maintaining, via the memory, responsive to the generating, during the period of time, a record of performance indicators associated with the subject; and

(B) applying, at least in part, the record of performance indicators associated with the subject to an assessment module, thereby determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder in the subject.

2. The method of claim 1, wherein the symptom of post-traumatic stress disorder is impaired inhibition control or flexibility of a neural pathway of the subject.

3. The method of claim 1 or 2, wherein the corresponding first plurality of trials comprises at least 300 trials.

4. The method of any one of claims 1-3, further comprising repeating the executing (A) for each iteration in a plurality of iterations.

5. The method of claim 4, wherein the plurality of iterations is repeated at regular intervals.

6. The method of claim 4 or 5, wherein the plurality of iterations comprises at least 5 iterations.

7. The method of any one of claims 1-6, wherein the user-interactive series of images comprises a video or an animation.

8. The method of any one of claims 1-7, wherein each respective target cue in the one or more respective target cues is a visual, auditory, or physical cue.

9. The method of any one of claims 1-8, wherein, for each respective trial in the corresponding first plurality of trials, the one or more respective target cues are generated a first predetermined interval after a start of the respective trial.

10. The method of claim 9, wherein the first predetermined interval is from about 100 milliseconds to about 1000 milliseconds.
11. The method of any one of claims 1-10, wherein the first subset of trials comprises at least 200 trials.
12. The method of any one of claims 1-11, wherein the first subset of trials consists of from 30% to 80% of the first plurality of trials.
13. The method of any one of claims 1-12, wherein:
 - the reaction time for the corresponding target response is measured between the generating of the one or more respective target cues and the receiving of the corresponding target response, and
 - the reference action time is determined by a procedure comprising, prior to the executing (A):
 - performing a practice session comprising, for each respective practice trial in a corresponding plurality of practice trials:
 - displaying, on the display, a respective user-interactive series of images generating one or more respective target cues, and
 - receiving, responsive to the one or more respective target cues, a corresponding target response from the subject using the input device; and
 - determining a measure of central tendency using, for each respective practice trial in the plurality of practice trials, a reaction time for the corresponding target response.
14. The method of claim 13, wherein the plurality of practice trials comprises at least 10 trials.
15. The method of claim 13 or 14, wherein, for each respective trial in the first subset of trials:
 - the reaction time for the corresponding target response satisfies the reference action time when the reaction time is less than or equal to the reference action time, and
 - the reaction time for the corresponding target response fails to satisfy the reference action time when the reaction time is greater than the reference action time.
16. The method of any one of claims 13-15, wherein, for each respective trial in the first subset of trials:

the respective action cue is selected from a plurality of candidate action cues,
the corresponding target response is selected from a plurality of candidate target responses,

each respective candidate action cue in the plurality of candidate action cues is associated with a respective candidate target response in the plurality of candidate target responses, and

the generating the respective outcome cue further comprises determining an accuracy of the corresponding target response relative to the respective action cue.

17. The method of any one of claims 1-16, wherein the second subset of trials comprises at least 20 trials.

18. The method of any one of claims 1-17, wherein the second subset of trials consists of from 5% to 30% of the first plurality of trials.

19. The method of any one of claims 1-18, wherein, for each respective trial in the second subset of trials, the delay time for the corresponding target response is measured between the generating of the respective control cue and one of: (i) the receiving of the corresponding target response or (ii) an expiration of the reference control time.

20. The method of claim 19, wherein:

the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than or equal to the reference control time, and

the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than the reference control time.

21. The method of any one of claims 1-20, wherein the third subset of trials comprises at least 20 trials.

22. The method of any one of claims 1-21, wherein the third subset of trials consists of from 5% to 30% of the first plurality of trials.

23. The method of any one of claims 1-22, wherein the control cue has a duration of from 2 milliseconds to 200 milliseconds.

24. The method of any one of claims 1-23, wherein, for each respective trial in the third subset of trials, the delay time for the corresponding target response is measured between the

generating of the respective control cue and one of: (i) the receiving of the corresponding target response or (ii) an expiration of the reference control time.

25. The method of claim 24, wherein:

the delay time for the corresponding target response satisfies the reference control time when the delay time is greater than or equal to the reference control time, and

the delay time for the corresponding target response fails to satisfy the reference control time when the delay time is less than the reference control time.

26. The method of claim 24 or 25, wherein, for each respective trial in the third subset of trials, the respective control cue is generated a second predetermined interval after the generation of the respective action cue.

27. The method of claim 26, wherein the second predetermined interval is from about 100 milliseconds to about 1000 milliseconds.

28. The method of claim 26 or 27, further comprising, for each respective trial in the third subset of trials:

when the delay time for the corresponding target response satisfies the reference control time, increasing the second predetermined interval, and

when the delay time for the corresponding target response fails to satisfy the reference control time, decreasing the second predetermined interval.

29. The method of claim 28, further comprising storing, after the executing (A), the second predetermined interval.

30. The method of any one of claims 1-29, wherein the reference control time is from about 100 milliseconds to about 2000 milliseconds.

31. The method of any one of claims 1-30, wherein the corresponding first plurality of trials further comprises a fourth subset of trials, wherein:

the displaying further comprises, for each respective trial in at least the fourth subset of trials:

(i) generating a respective anticipation cue in the one or more respective target cues, and

(ii) generating, after the generating (i), a respective action cue in the one or more respective target cues, wherein the anticipation cue indicates a probability of receiving a control cue after the action cue.

32. The method of claim 31, further comprising:

for each respective trial in a first portion of the fourth subset of trials, (iii) generating, after the generating (ii), a respective control cue in the one or more respective target cues, wherein the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time, and

for each respective trial in a second portion of the fourth subset of trials, (iv) generating, after the generating (ii), no control cue, wherein the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time.

33. The method of claim 31 or 32, wherein the fourth subset of trials comprises at least 20 trials.

34. The method of any one of claims 31-33, wherein the fourth subset of trials consists of from 5% to 30% of the first plurality of trials.

35. The method of any one of claims 31-34, wherein the first portion of the fourth subset of trials comprises no more than 50% of the fourth subset of trials.

36. The method of any one of claims 31-35, wherein the first portion of the fourth subset of trails comprises no more than 25% of the fourth subset of trials.

37. The method of any one of claims 31-36, wherein the respective anticipation cue is a color, an object, an image, or a sound.

38. The method of any one of claims 1-37, wherein, for each respective trial in the corresponding first plurality of trials, the respective outcome cue is a visual, auditory, or physical cue.

39. The method of any one of claims 1-38, wherein for each respective trial in the corresponding first plurality of trials, the corresponding target response comprises a presence or an absence of a motor response.

40. The method of claim 39, wherein the motor response is selected from the group consisting of: a user interaction with a user affordance, a user interaction with the input device, and a user response captured by the input device.
41. The method of any one of claims 1-40, wherein one or more trials in the corresponding first plurality of trials further comprises one or more affective cues.
42. The method of claim 41, wherein a respective affective cue in the one or more affective cues is selected from the group consisting of: positive, negative, or neutral.
43. The method of any one of claims 1-42, wherein the first measure of inhibition control is selected from the group consisting of: a rate of omission, a rate of commission, a stop-signal reaction time (SSRT), a stop-signal anticipation task (SSAT) score, a reactive inhibition (RI), a proactive inhibition (PI), and an extra-proactive inhibition (EPI).
44. The method of any one of claims 1-43, wherein the first measure of inhibition control is determined using (i) the corresponding target response and (ii) the respective response threshold for the respective trial, for each respective trial in the corresponding first plurality of trials for the subject.
45. The method of any one of claims 1-44, further comprising determining a change in (i) the first measure of inhibition control relative to (ii) a second measure of inhibition control obtained from a second evaluation session for the subject.
46. The method of any one of claims 1-43, wherein the first measure of inhibition control is an alteration in an inhibitory control network or a neural pathway of the subject.
47. The method of any one of claims 1-46, further comprising administering a secondary assessment tool selected from the group consisting of: a Go/No-Go Task, an Incentive Flanker Task (IFT), a Hariri Task, a Think/No-Think Task, a Face-Stroop Task, and any similar task thereof.
48. The method of any one of claims 1-47, further comprising:
obtaining, prior to the executing (A), a diagnostic measure of inhibition control for the subject, and
determining a change in (i) the first measure of inhibition control relative to (ii) the diagnostic measure of inhibition control for the subject.

49. The method of any one of claims 1-48, further comprising:
determining a measure of central tendency using, for each respective trial in at least the first subset of trials, a reaction time for the corresponding target response, and
updating the reference action time with the measure of central tendency for the reaction time.
50. The method of any one of claims 1-49, wherein the executing (A) alters an inhibitory control network or a neural pathway of the subject.
51. The method of any one of claims 1-50, wherein the first measure of inhibition control is determined using one or more of physiological, clinical, and behavioral measures.
52. The method of any one of claims 1-51, wherein the subject suffers from post-traumatic stress disorder, or a symptom thereof.
53. A computer system comprising:
a display;
an input device;
one or more processors; and
memory storing one or more programs for improving a symptom of post-traumatic stress disorder in a subject that, when executed by the one or more processors, cause the processors to perform a method comprising:
(A) executing a first evaluation session module comprising a corresponding first plurality of trails, wherein the executing comprises, for each respective trial in the corresponding first plurality of trials:
displaying, on the display, for a period of time, a respective user-interactive series of images, thereby generating one or more respective target cues associated with the respective user-interactive series of images during the period of time,
receiving, responsive to the one or more respective target cues, during the period of time, a corresponding target response from the subject using the input device,
generating, by the one or more processors, during the period of time, a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial, the respective outcome cue comprising:
in accordance with a determination the corresponding target response satisfies the respective response threshold, a first performance indicator, and

in accordance with a determination the corresponding target response fails to satisfy the respective response threshold, a second performance indicator, wherein:

for each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time,

for each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time, and

for each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises the respective action cue and the respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time, and

maintaining, via the memory, responsive to the generating, during the period of time, a record of performance indicators associated with the subject; and

(B) applying, at least in part, the record of performance indicators associated with the subject to an assessment module, thereby determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder in the subject.

54. A non-transitory computer-readable storage medium having stored thereon program code instructions for improving a symptom of post-traumatic stress disorder in a subject that, when executed by a processor, cause the processor to perform a method comprising:

(A) executing a first evaluation session module comprising a corresponding first plurality of trials, wherein the executing comprises, for each respective trial in the corresponding first plurality of trials:

displaying, on the display, for a period of time, a respective user-interactive series of images, thereby generating one or more respective target cues associated with the respective user-interactive series of images during the period of time,

receiving, responsive to the one or more respective target cues, during the period of time, a corresponding target response from the subject using the input device, generating, by the one or more processors, during the period of time, a respective outcome cue based on (i) the corresponding target response relative to (ii) a respective response threshold for the respective trial, the respective outcome cue comprising:

in accordance with a determination the corresponding target response satisfies the respective response threshold, a first performance indicator, and

in accordance with a determination the corresponding target response fails to satisfy the respective response threshold, a second performance indicator,

wherein:

for each respective trial in a first subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective action cue, and the corresponding target response satisfies the respective response threshold when a reaction time for the corresponding target response satisfies a reference action time,

for each respective trial in a second subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises a respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies a reference control time, and

for each respective trial in a third subset of trials in the corresponding first plurality of trials, the one or more respective target cues comprises the respective action cue and the respective control cue, and the corresponding target response satisfies the respective response threshold when a delay time for the corresponding target response satisfies the reference control time, and

maintaining, via the memory, responsive to the generating, during the period of time, a record of performance indicators associated with the subject; and

(B) applying, at least in part, the record of performance indicators associated with the subject to an assessment module, thereby determining a first measure of inhibition control that represents an improvement in the symptom of post-traumatic stress disorder in the subject.

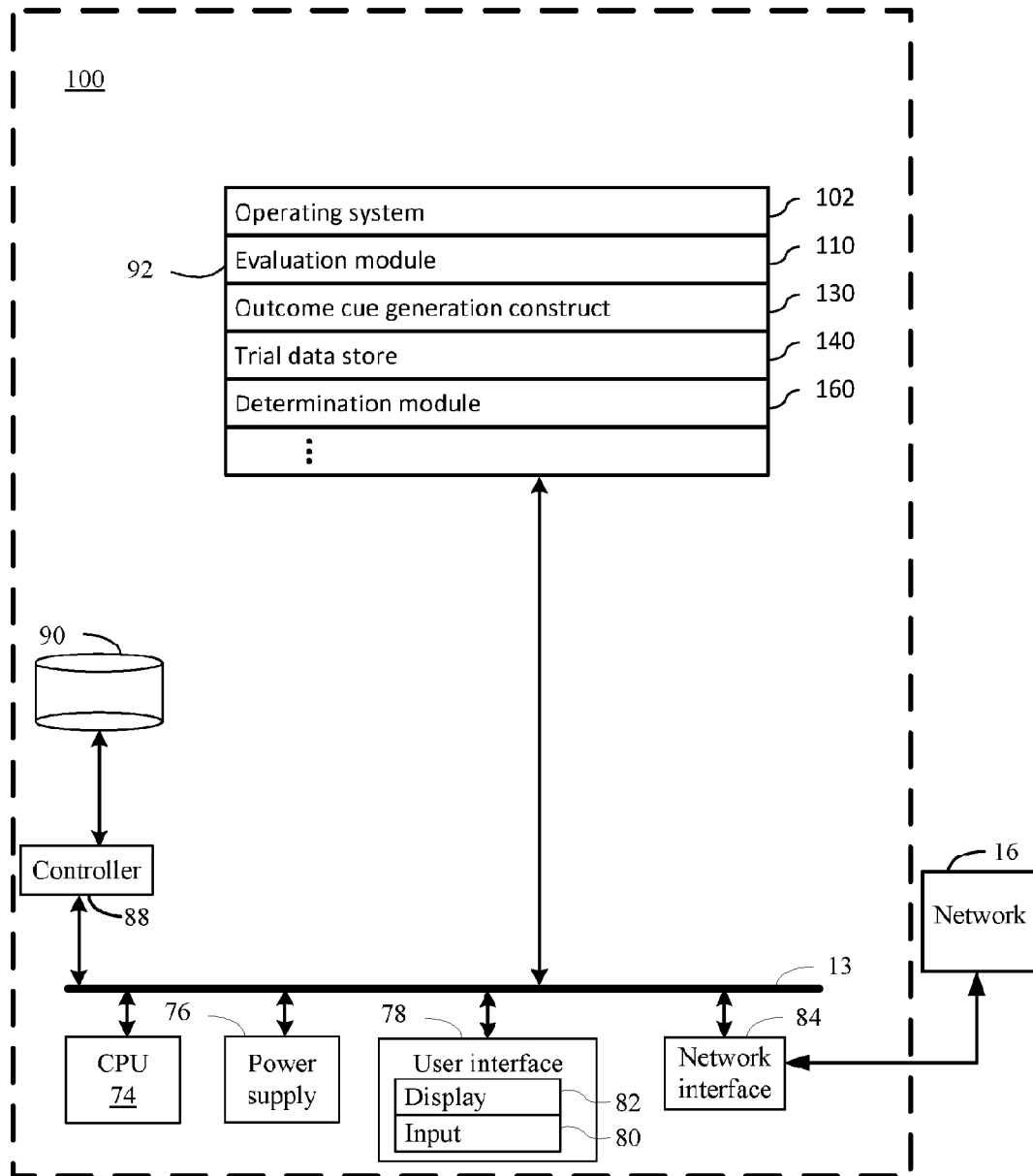


FIG. 1A

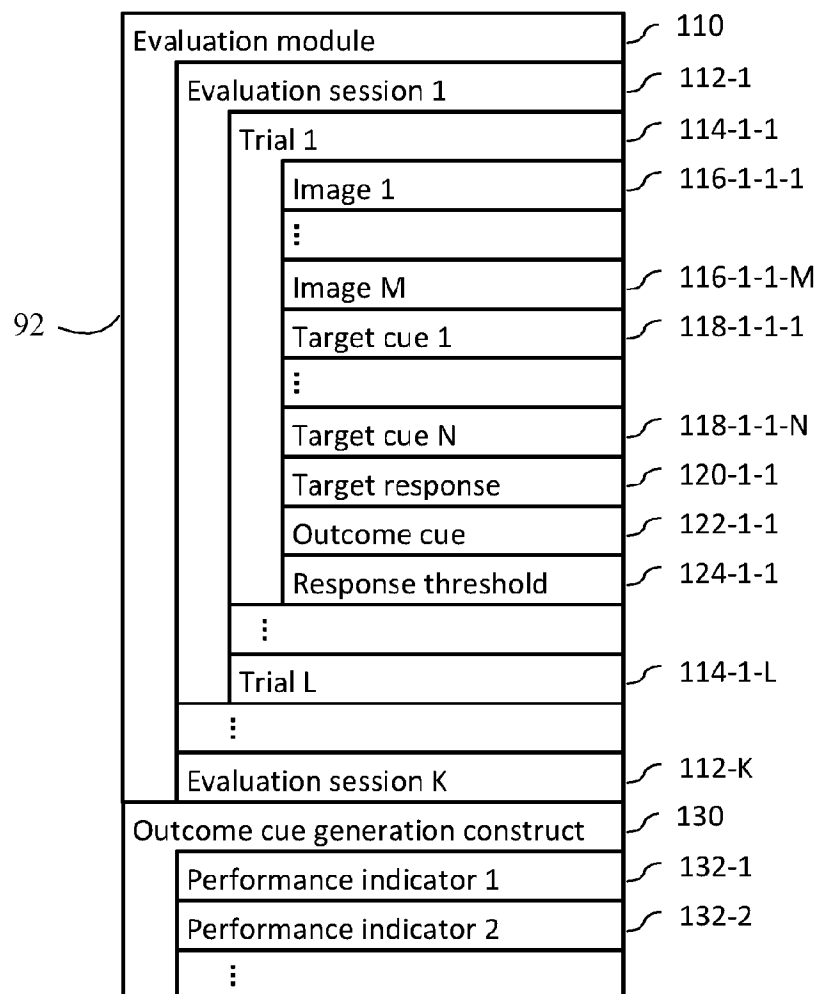


FIG. 1B

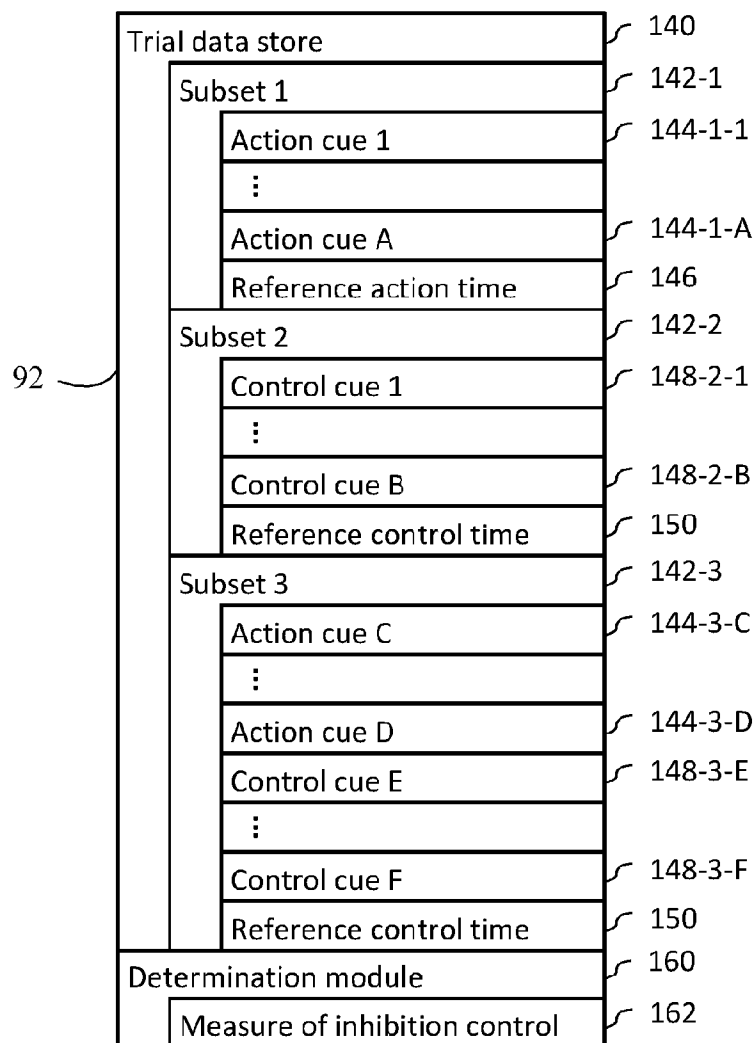


FIG. 1C

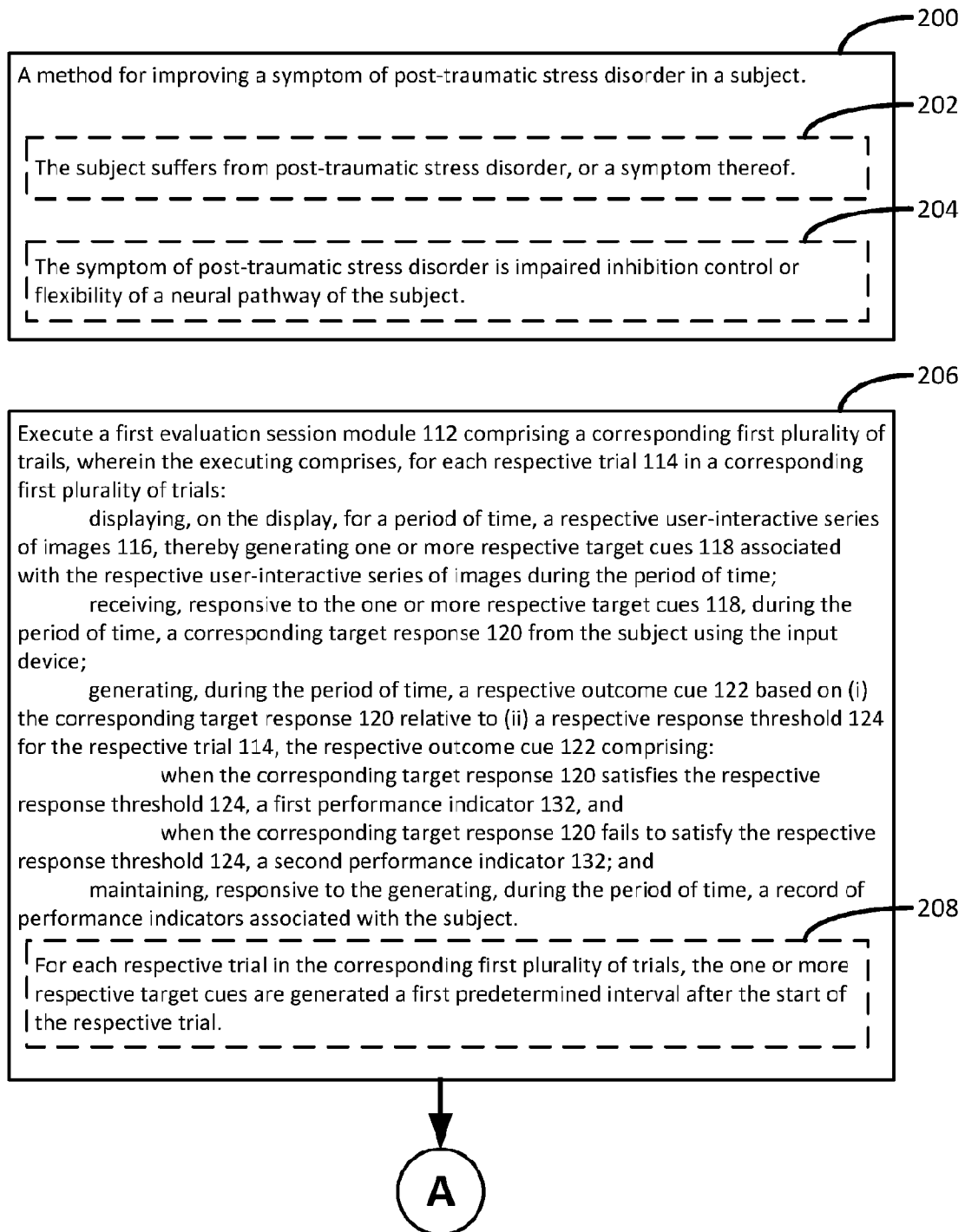


FIG. 2A

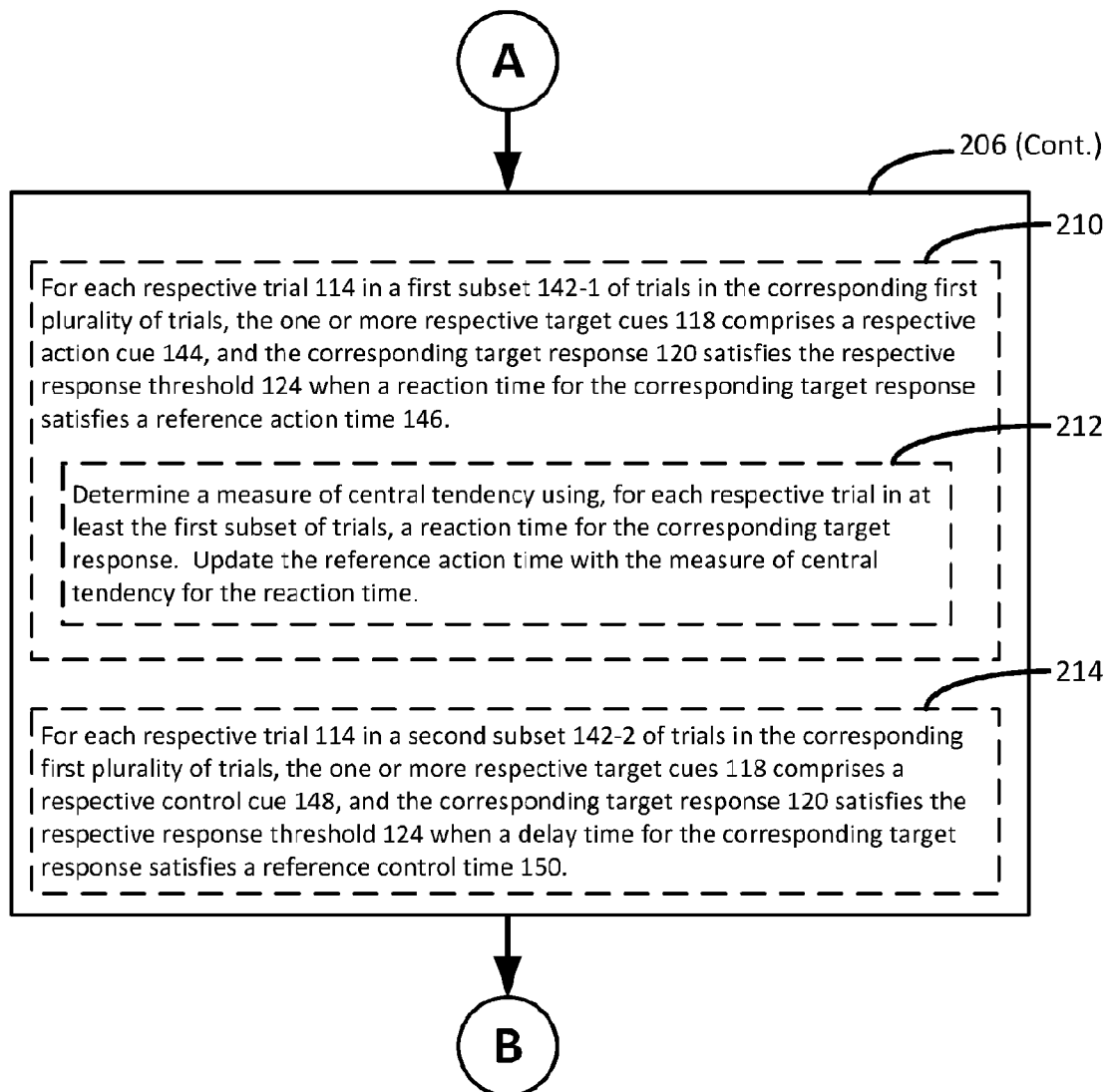


FIG. 2B

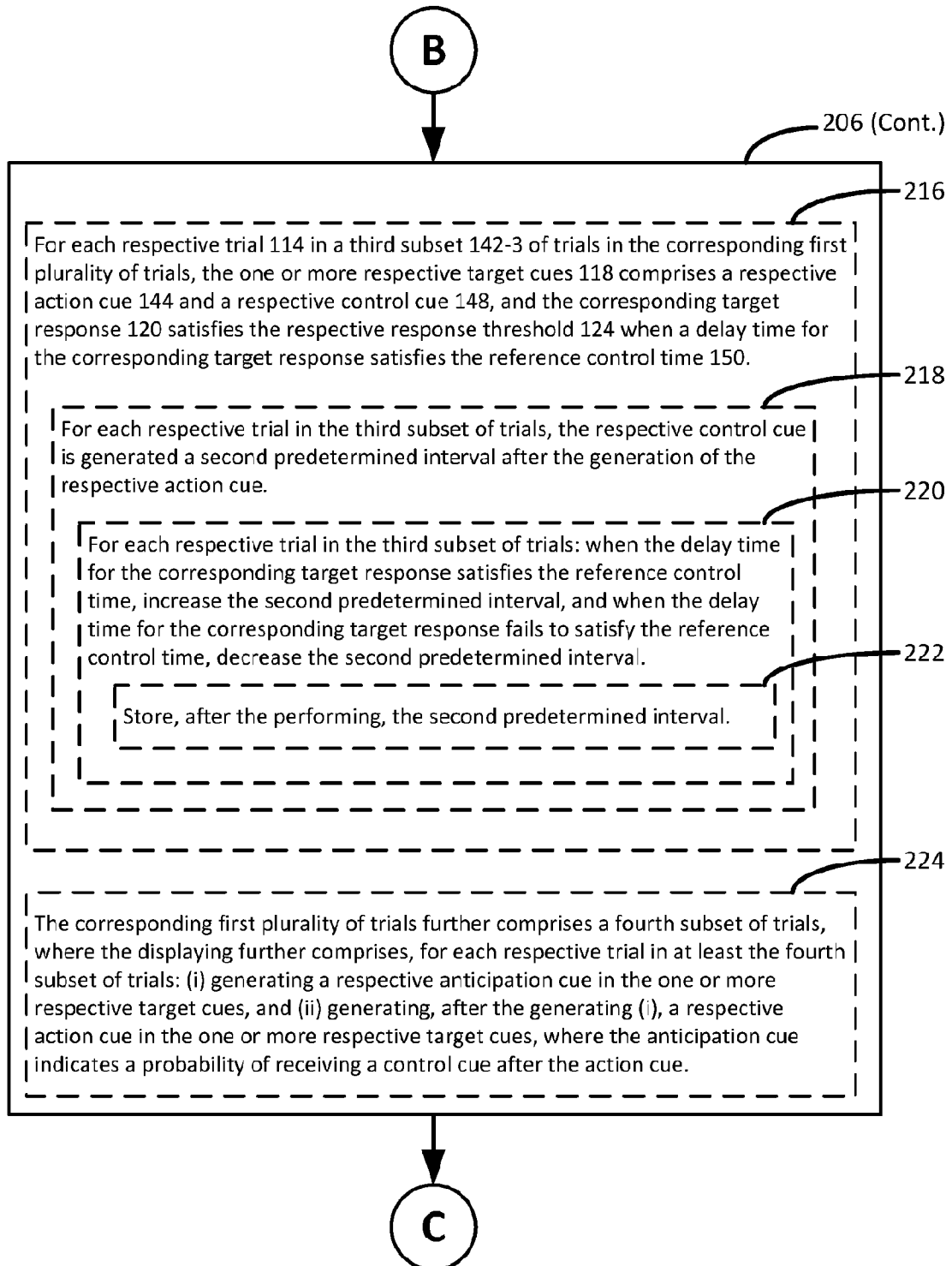


FIG. 2C

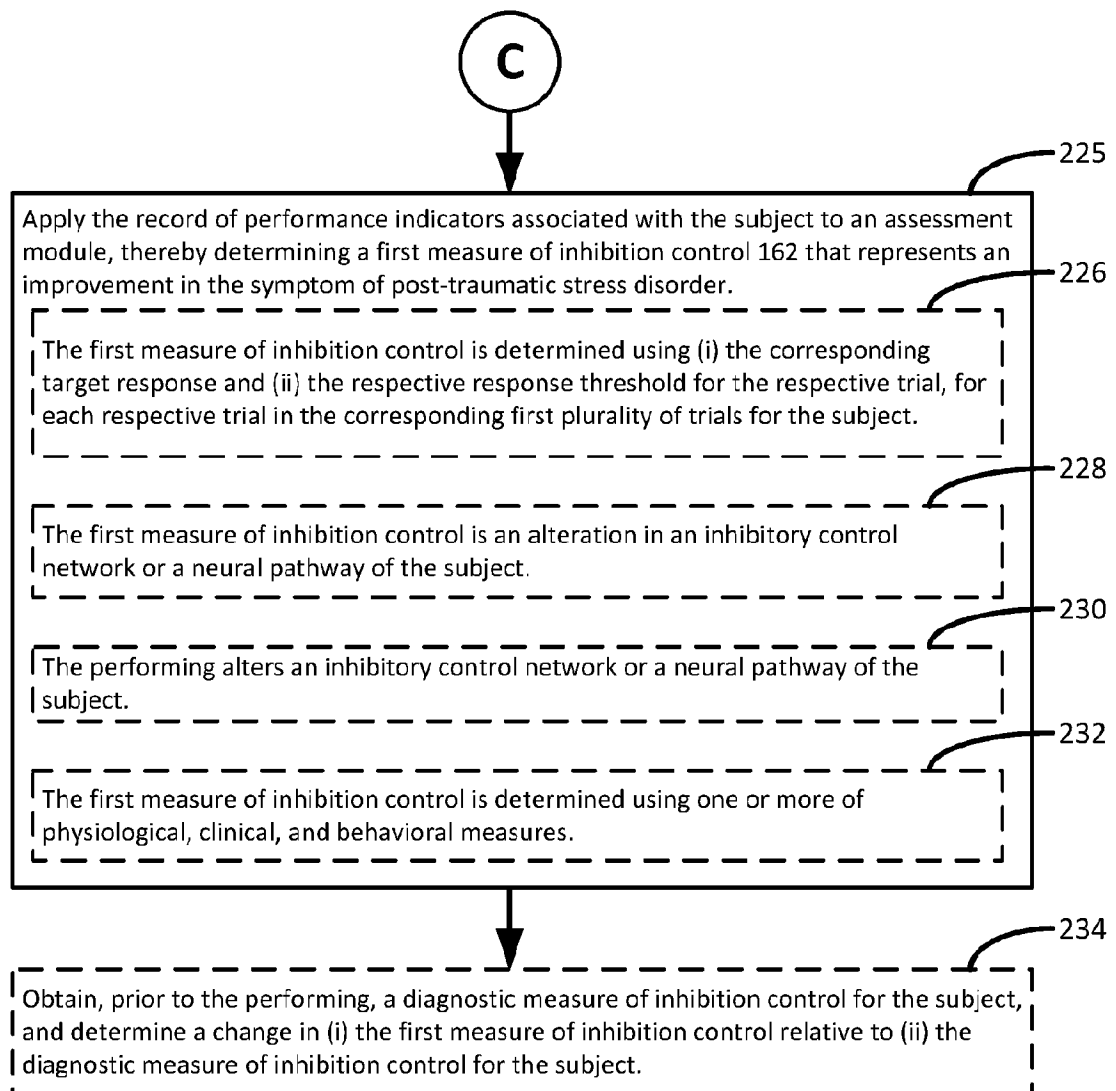


FIG. 2D

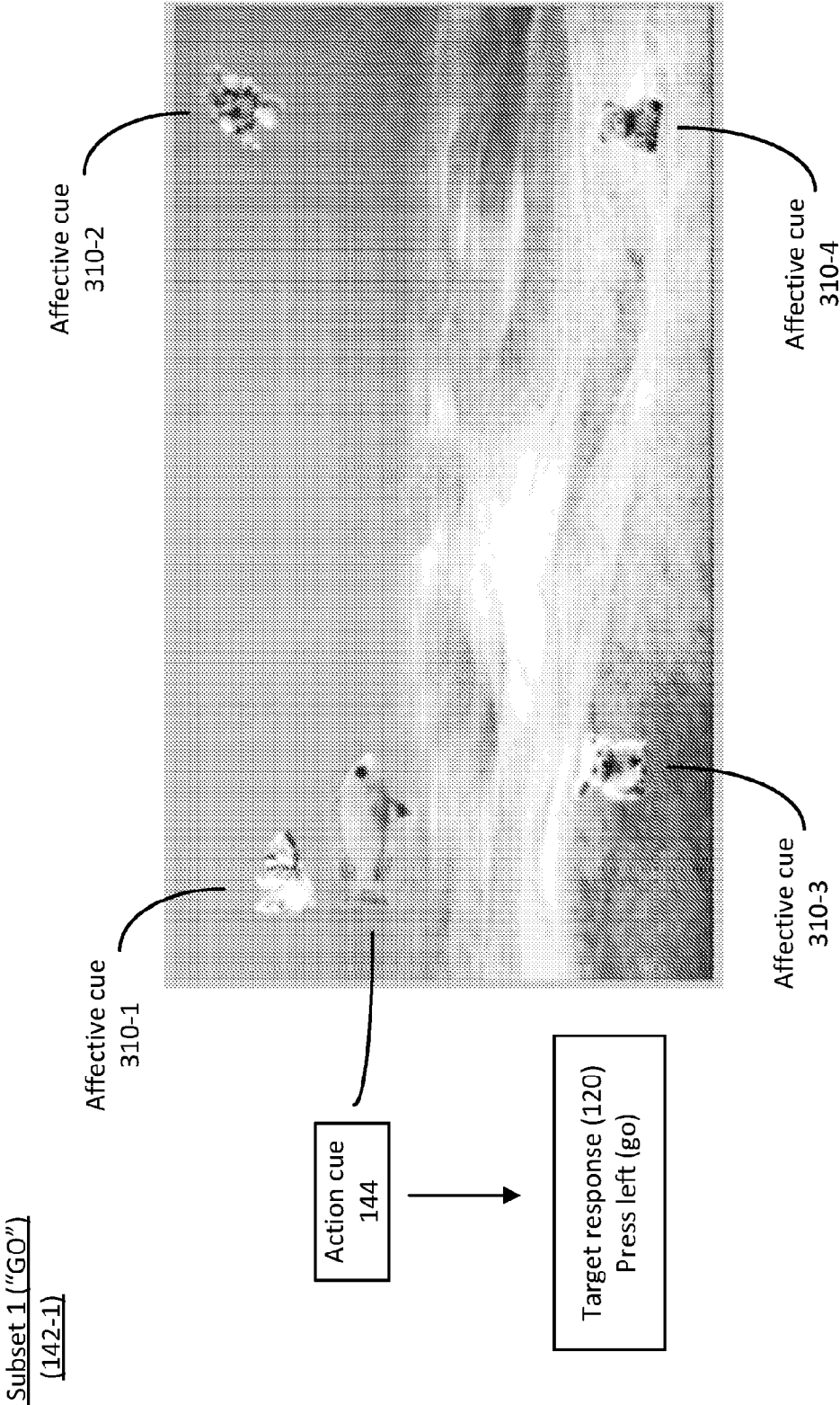


FIG. 3A

Subset 2 ("NO-GO")
(142-2)



FIG. 3B

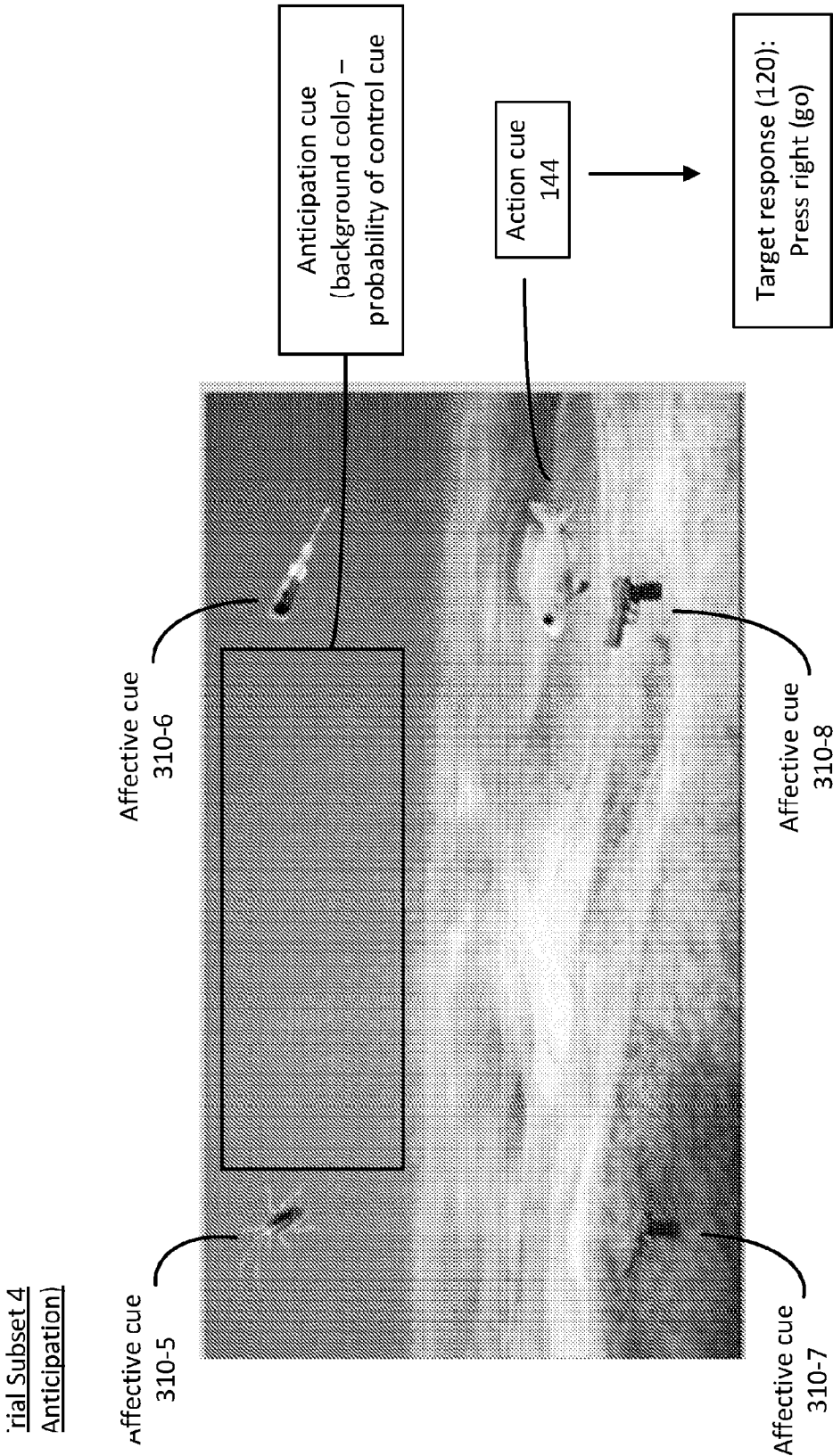


FIG. 3C

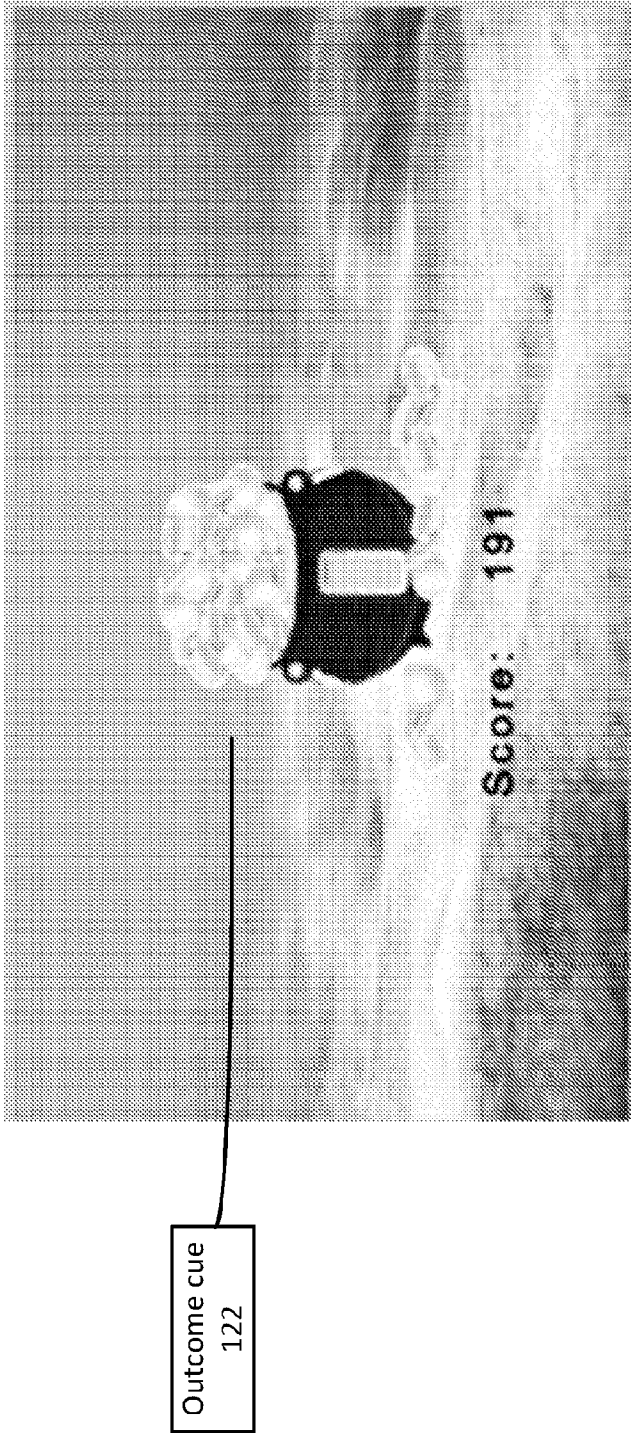


FIG. 3D

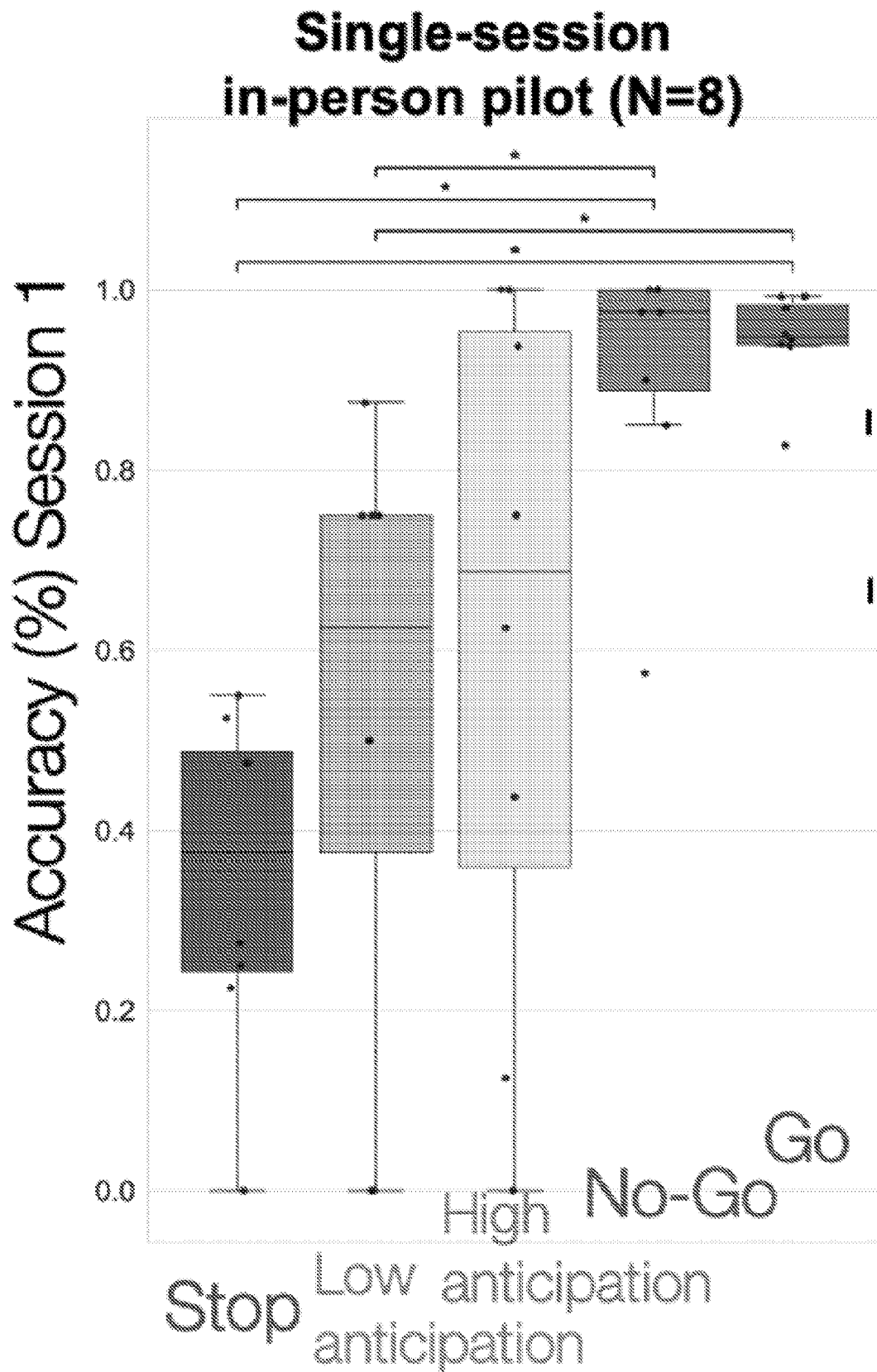


FIG. 4A

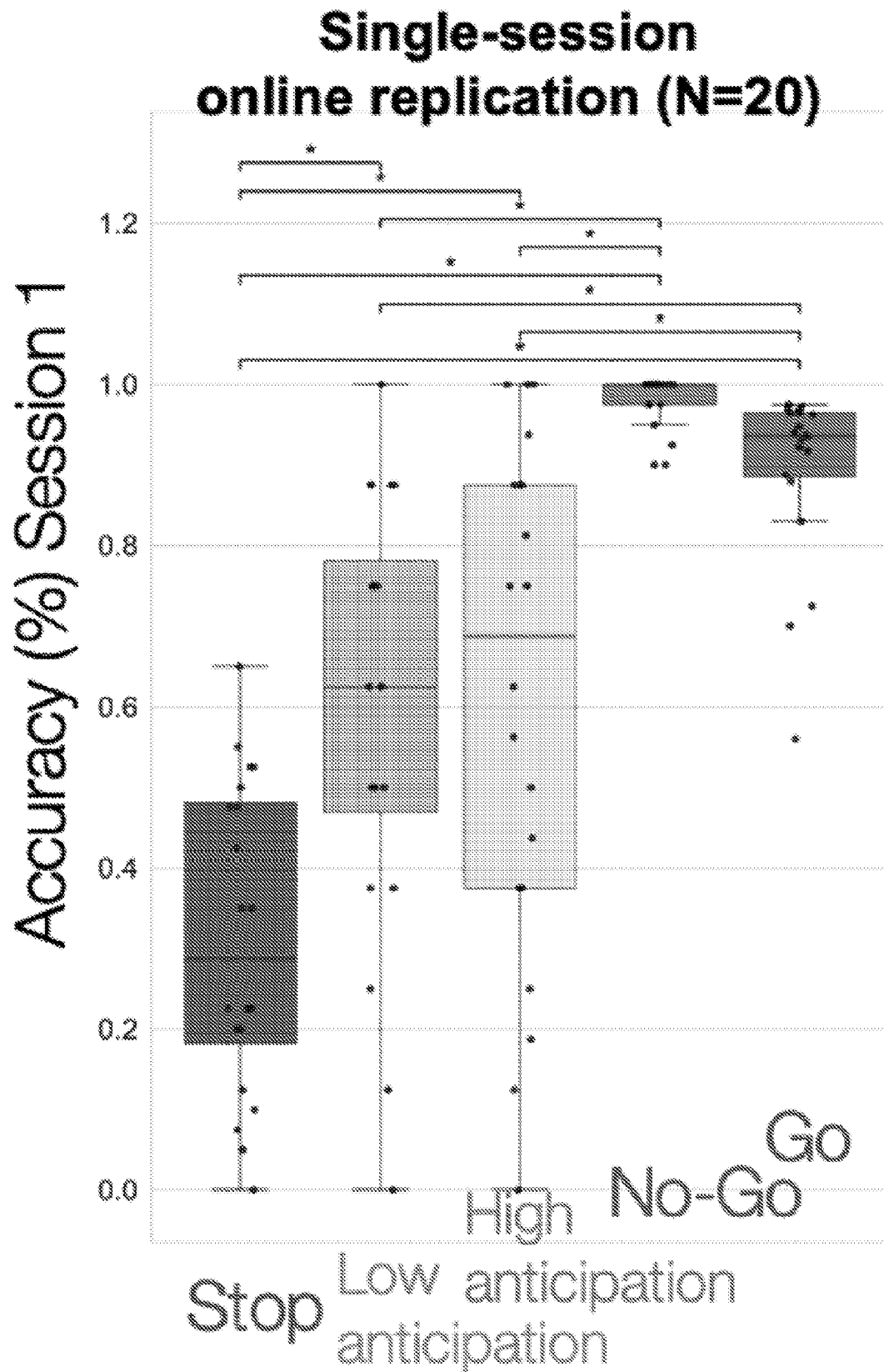


FIG. 4B

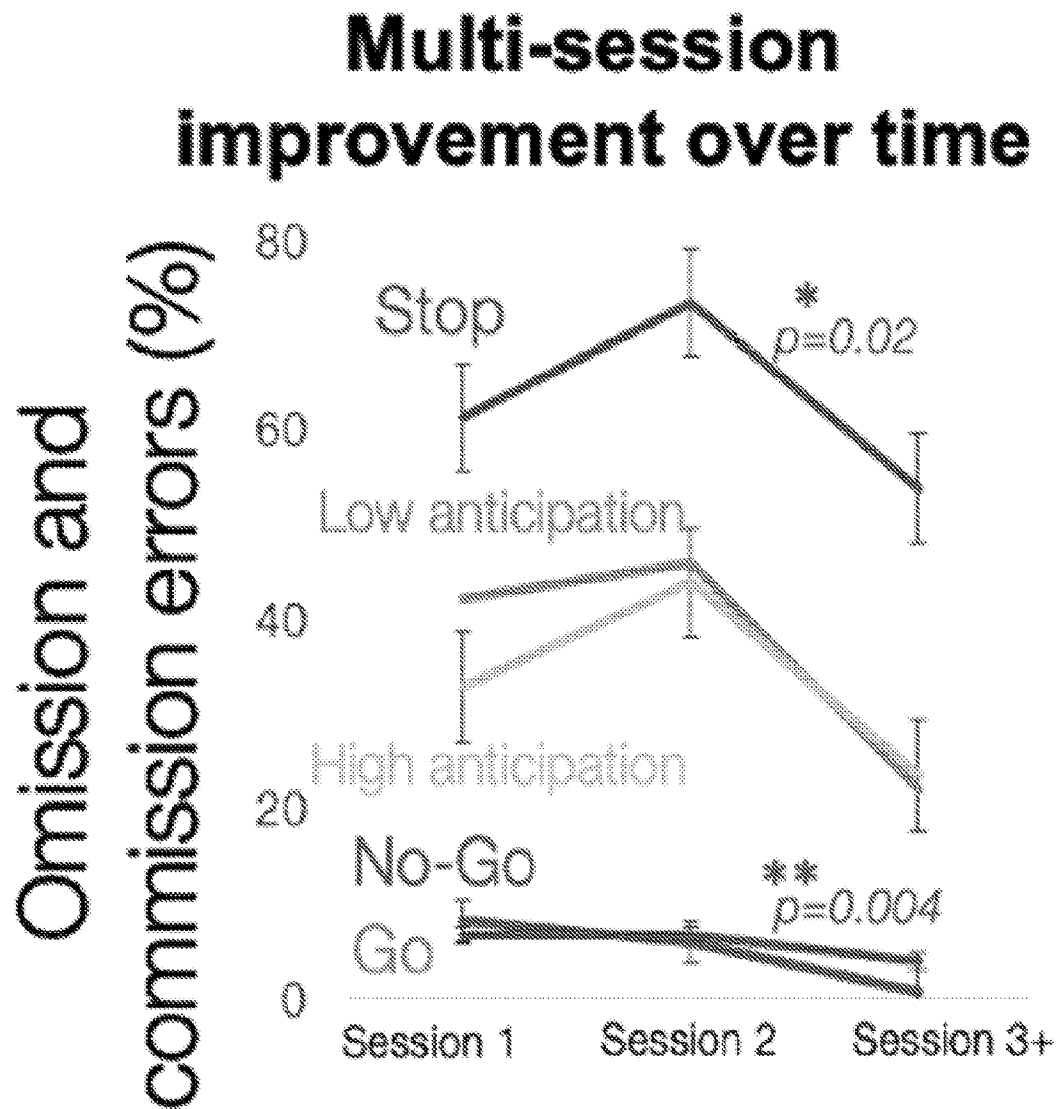


FIG. 4C

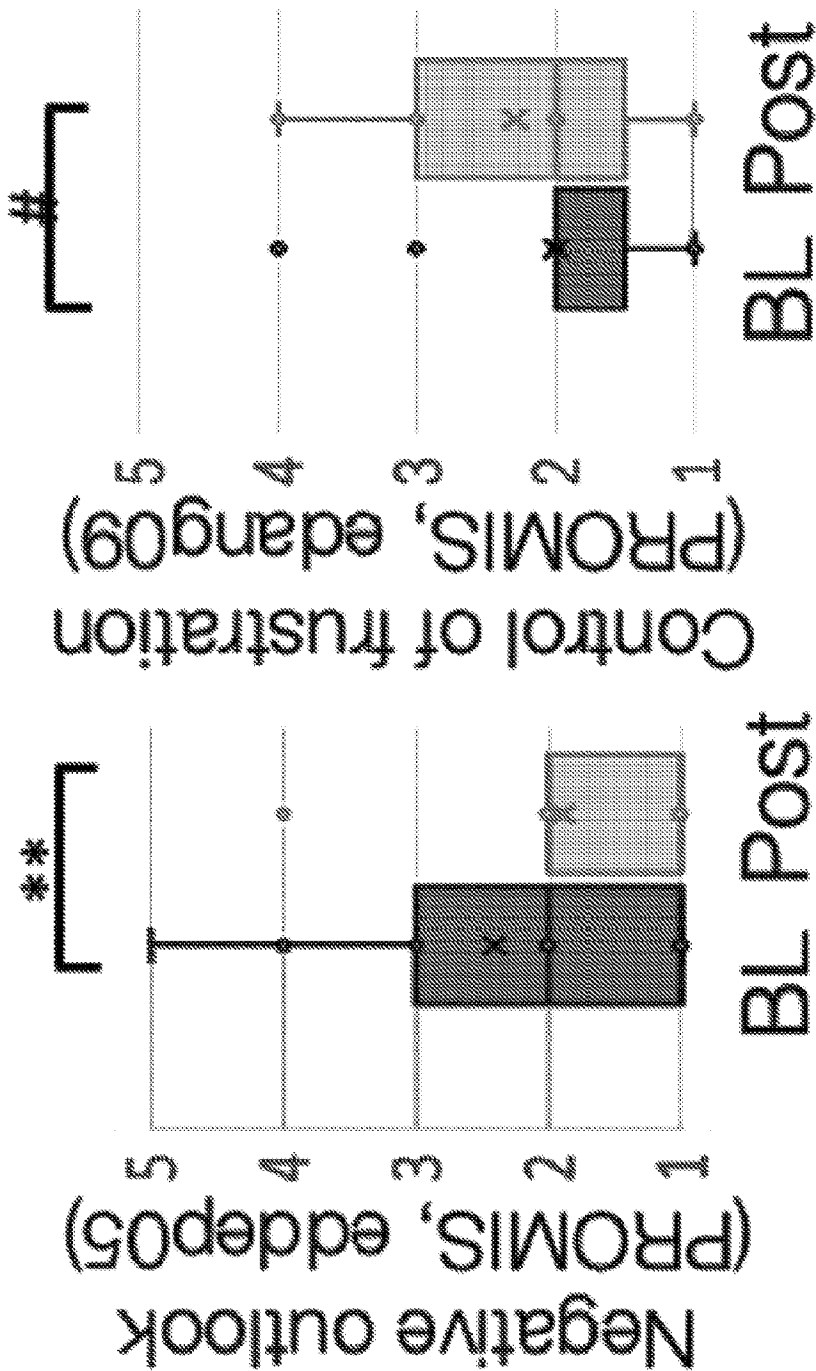


FIG. 4D

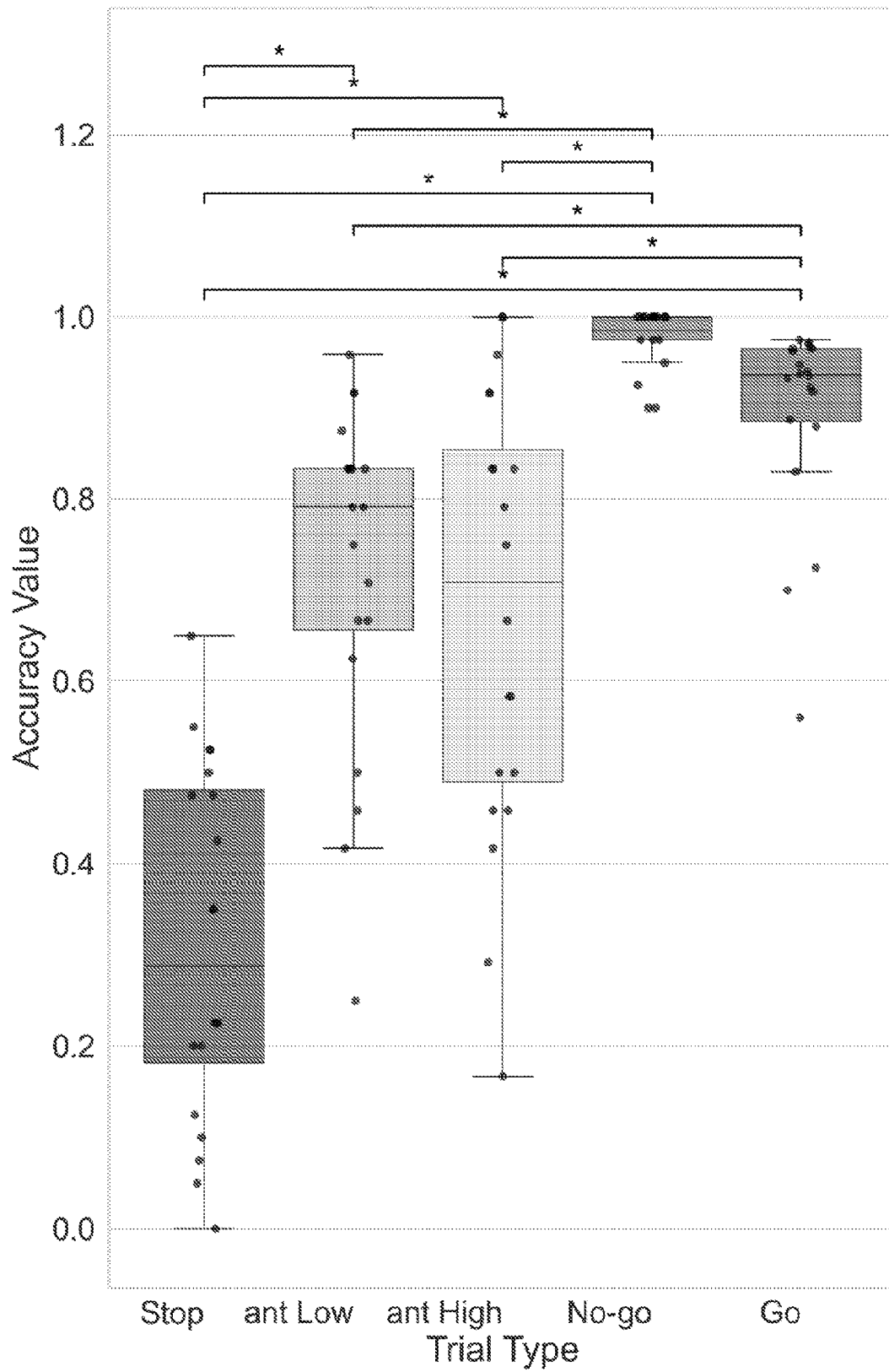


FIG. 5A

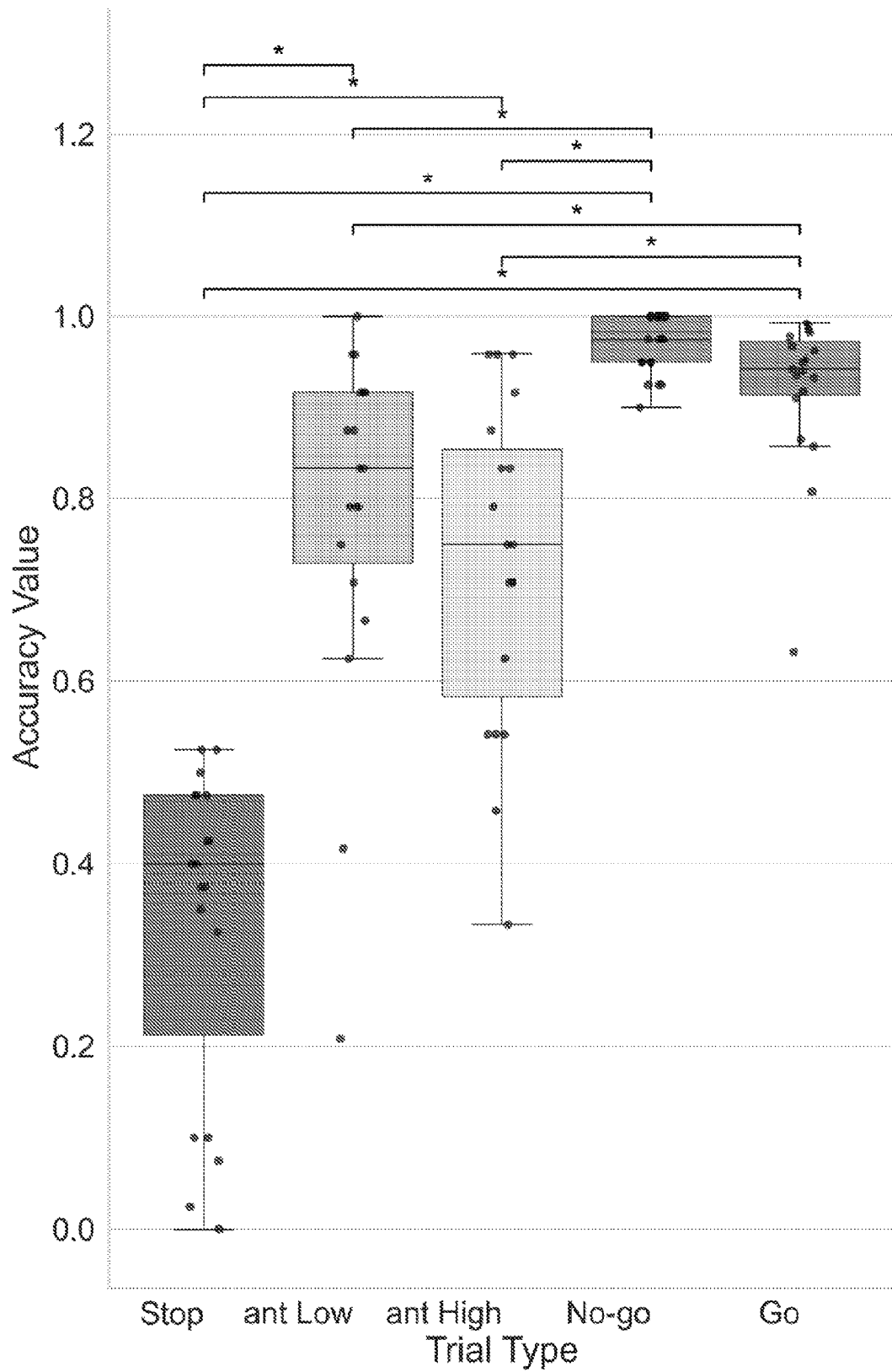


FIG. 5B

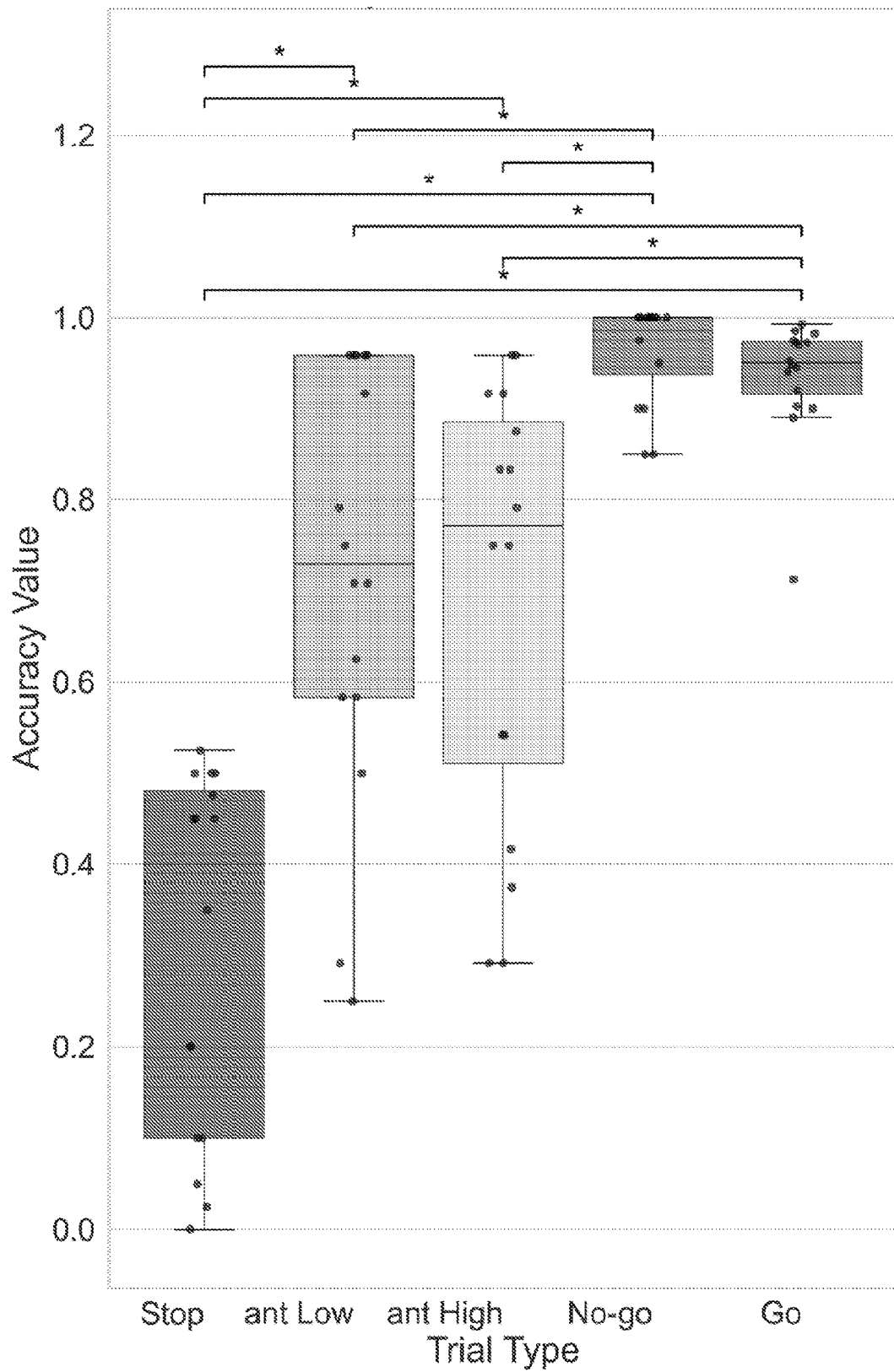


FIG. 5C

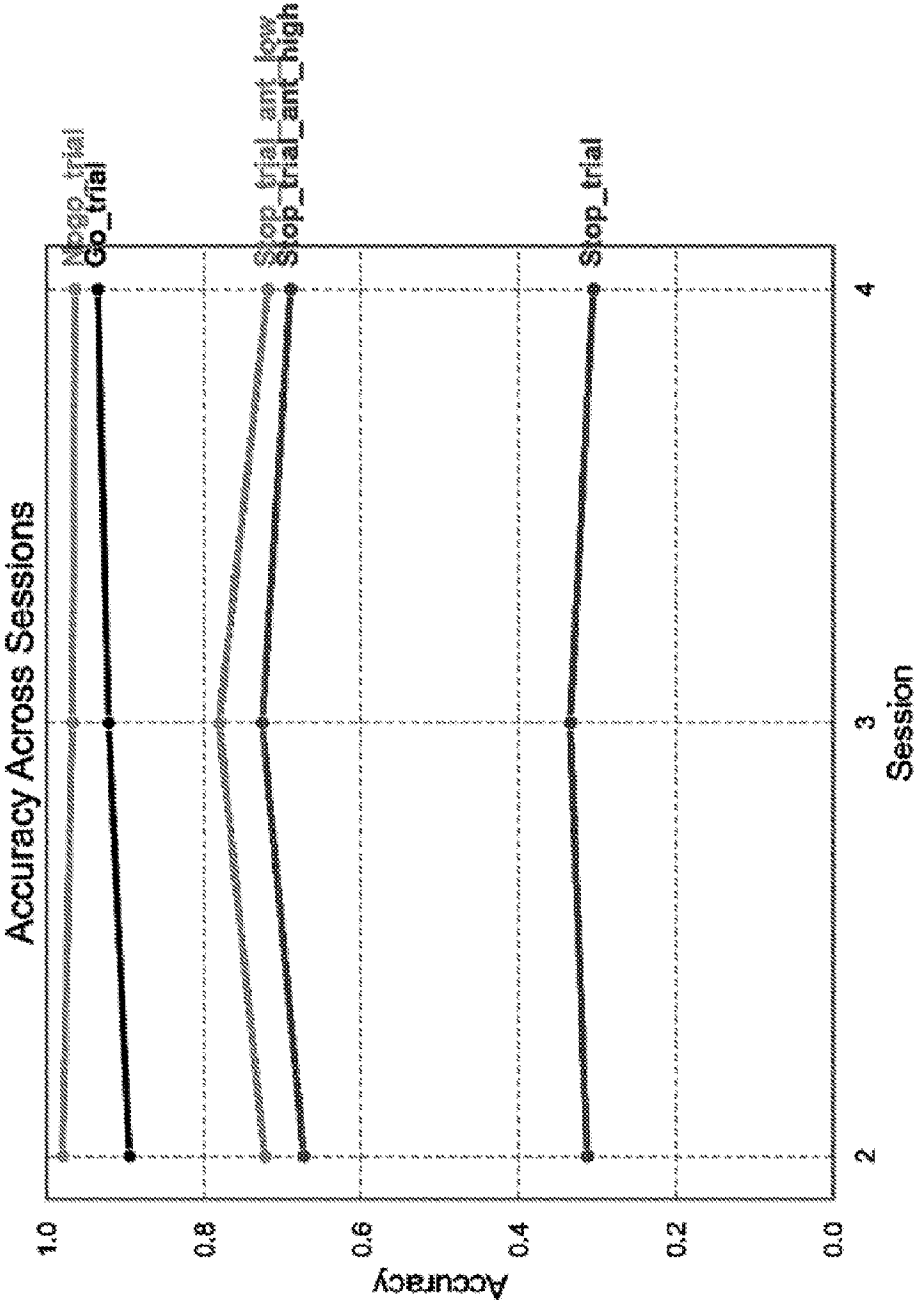


FIG. 5D

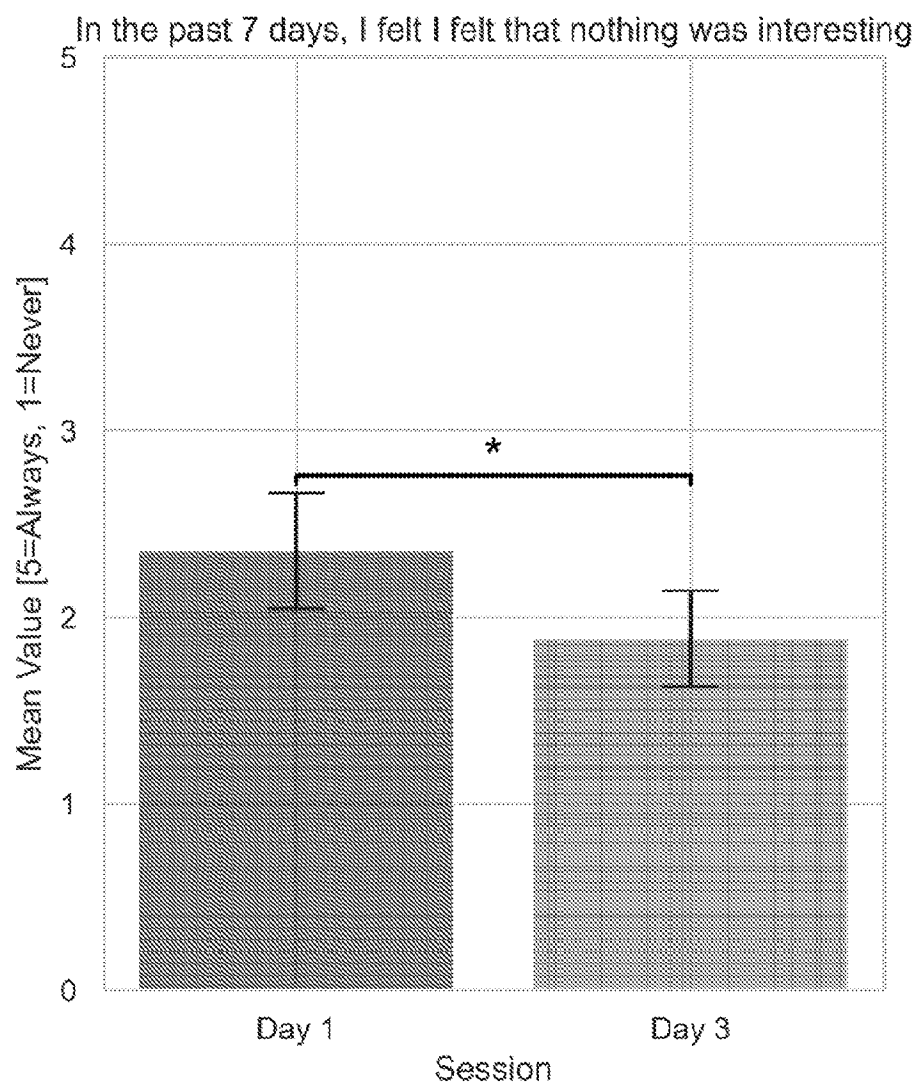


FIG. 5E

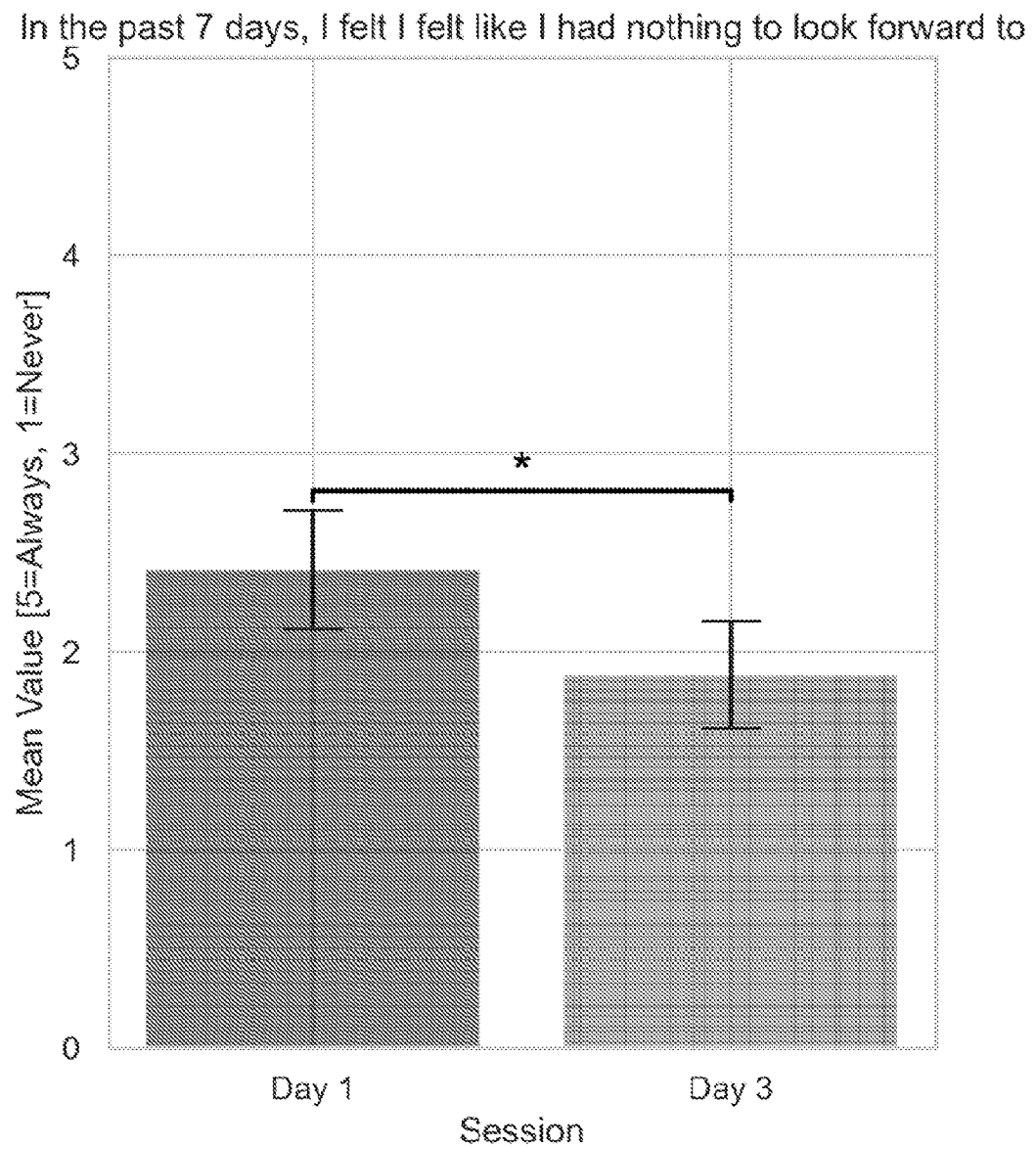


FIG. 5F

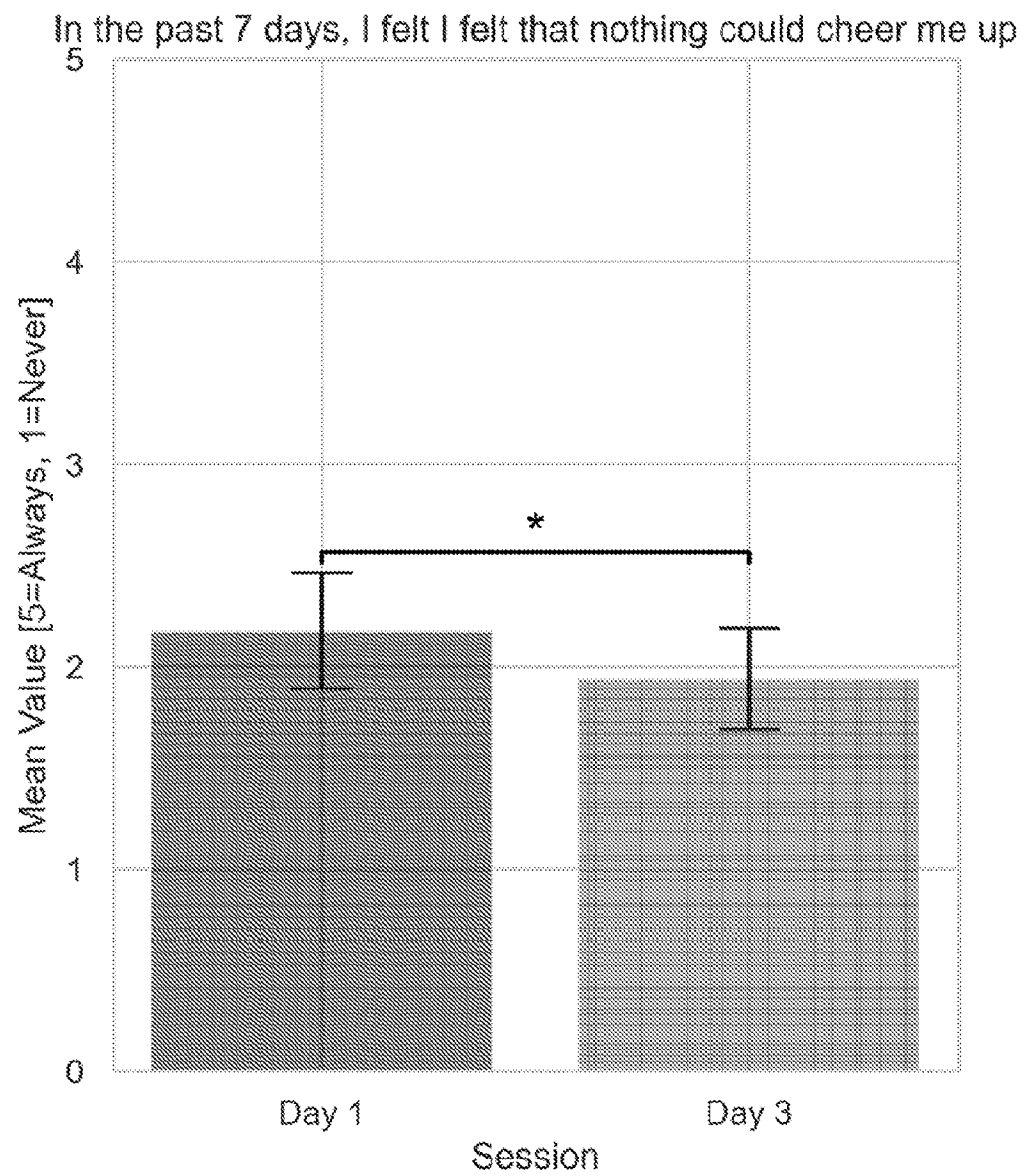


FIG. 5G

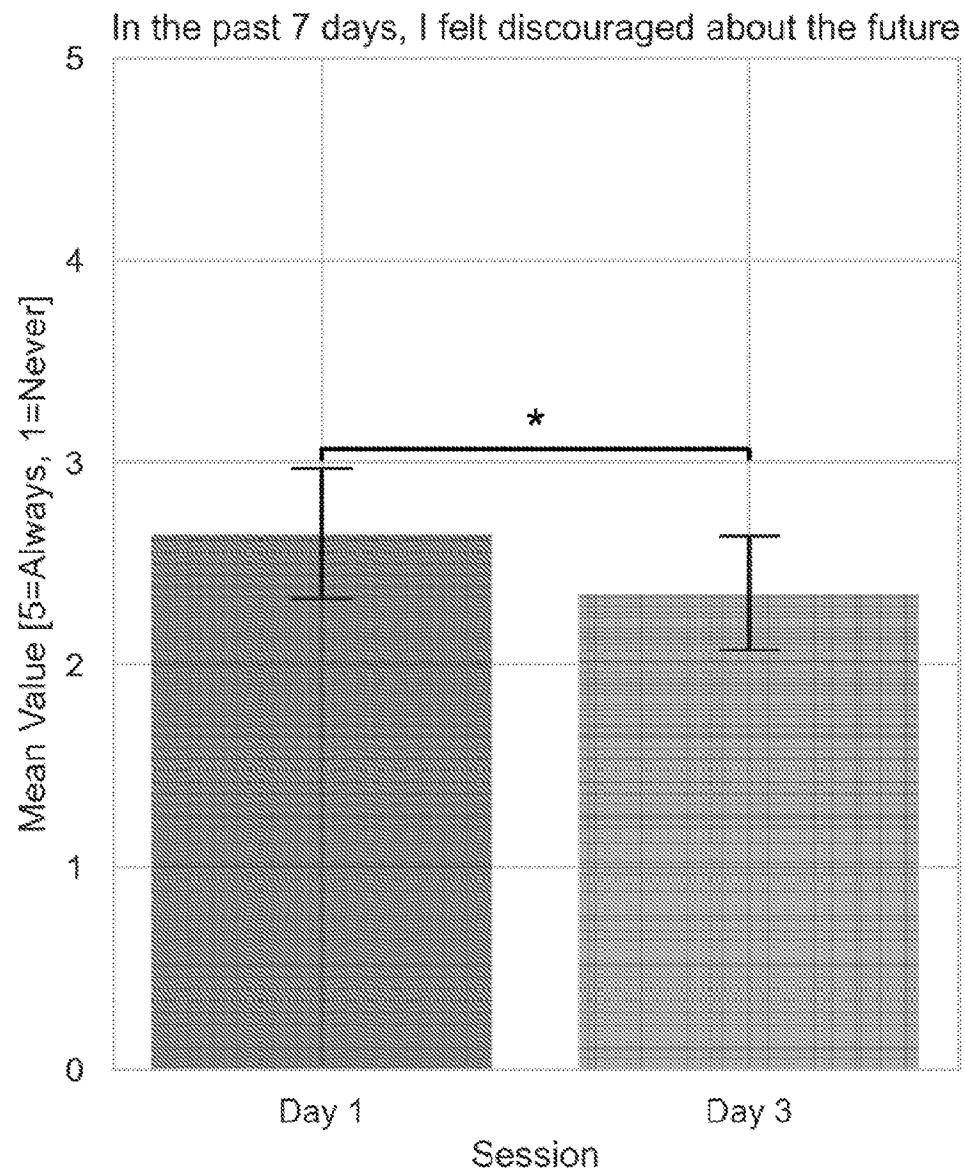


FIG. 5H

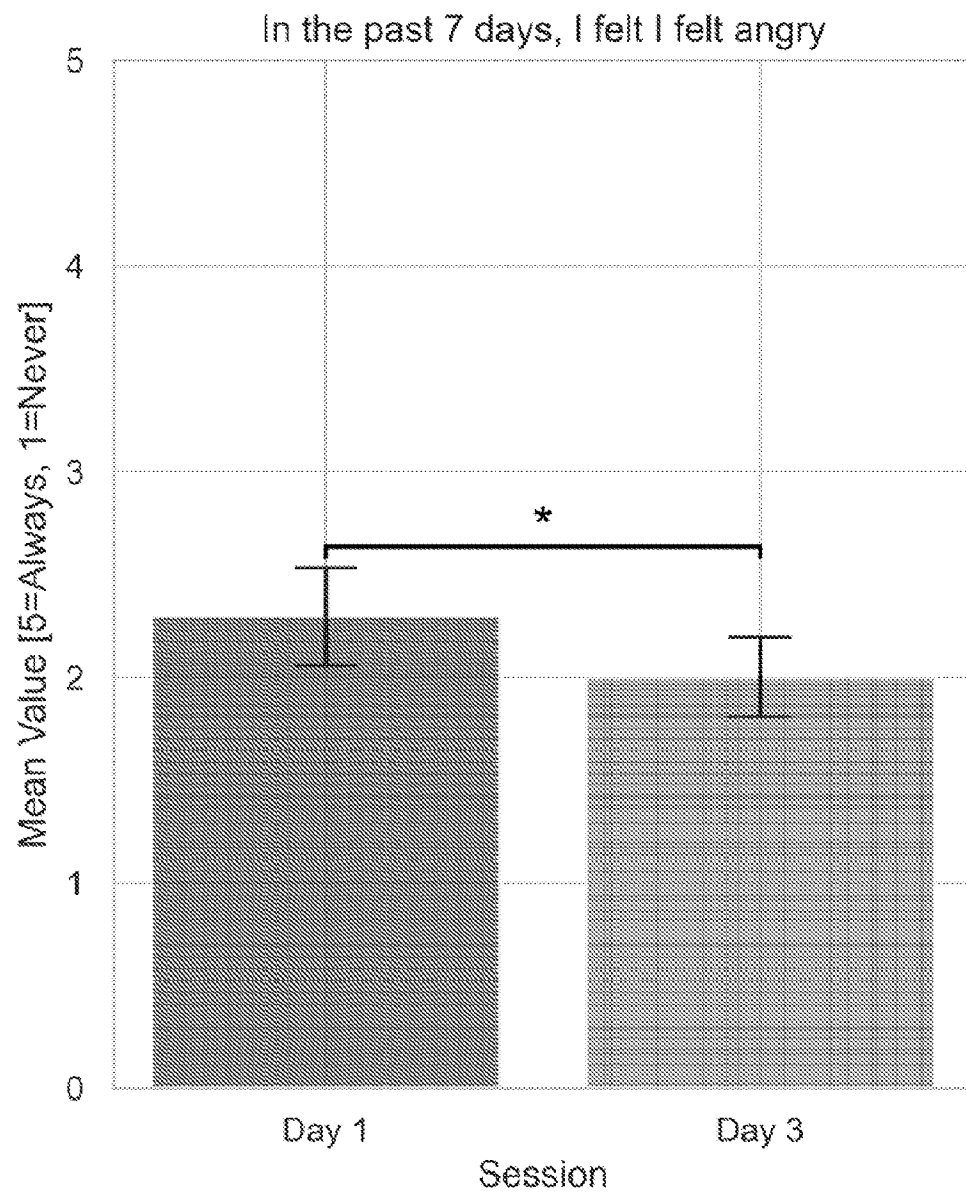


FIG. 5I

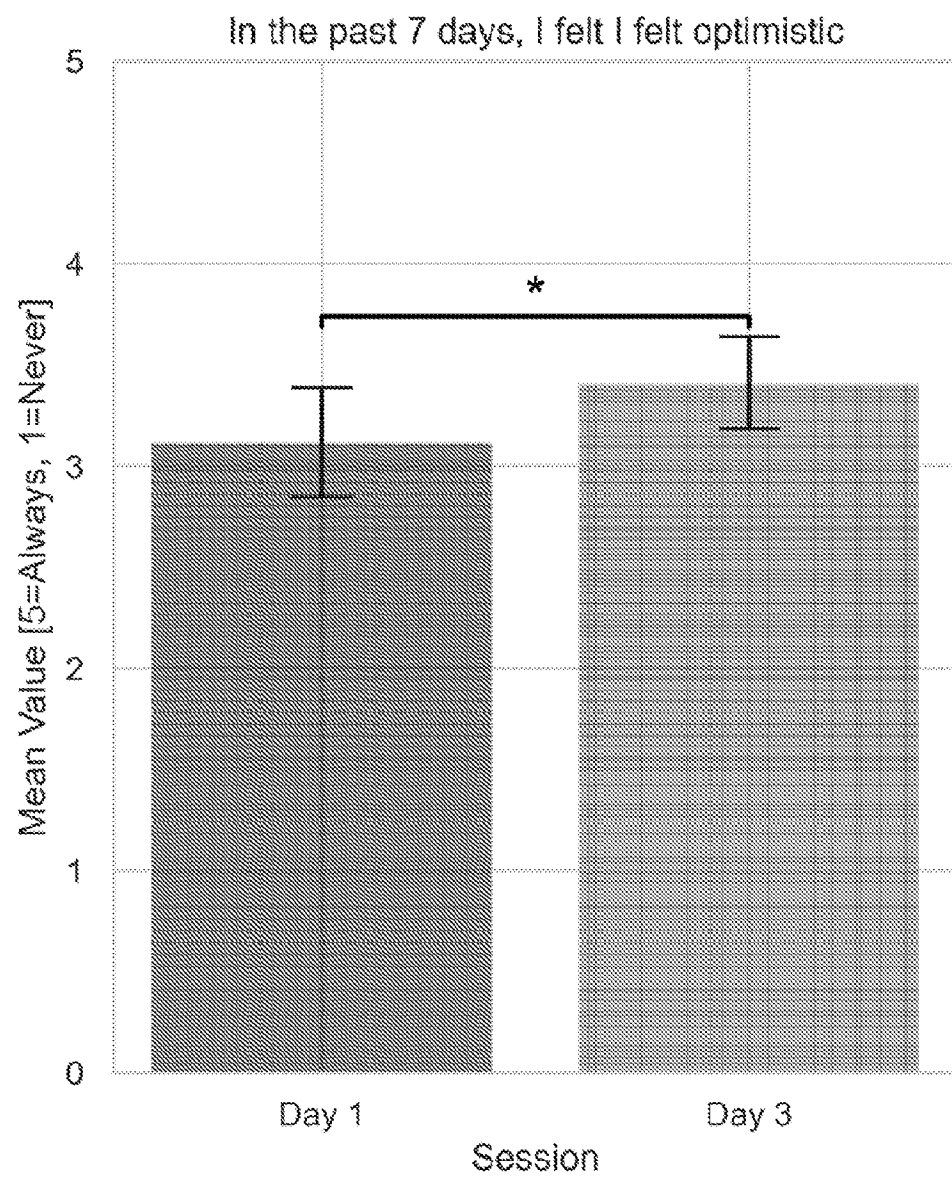


FIG 5J

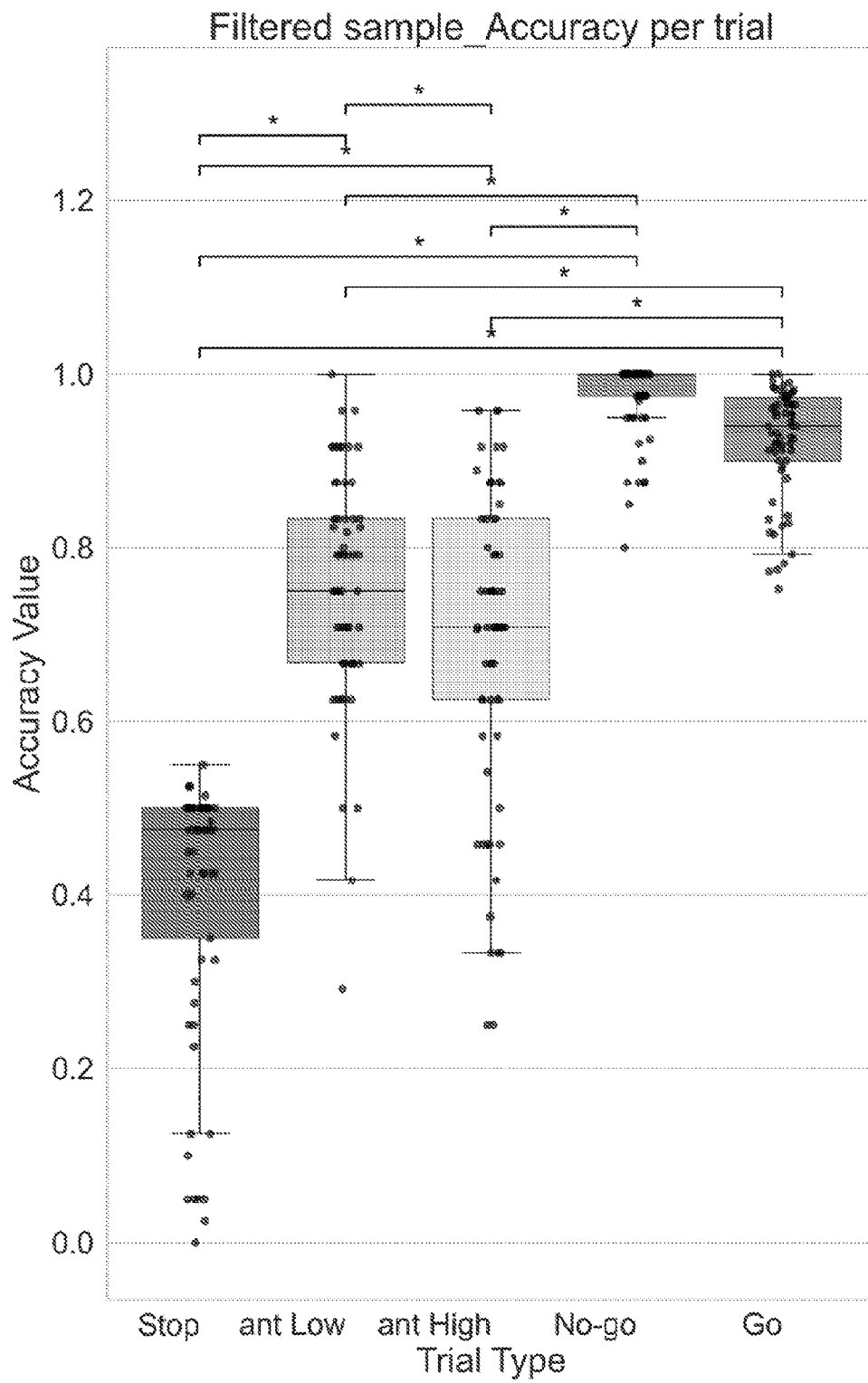


FIG. 6A

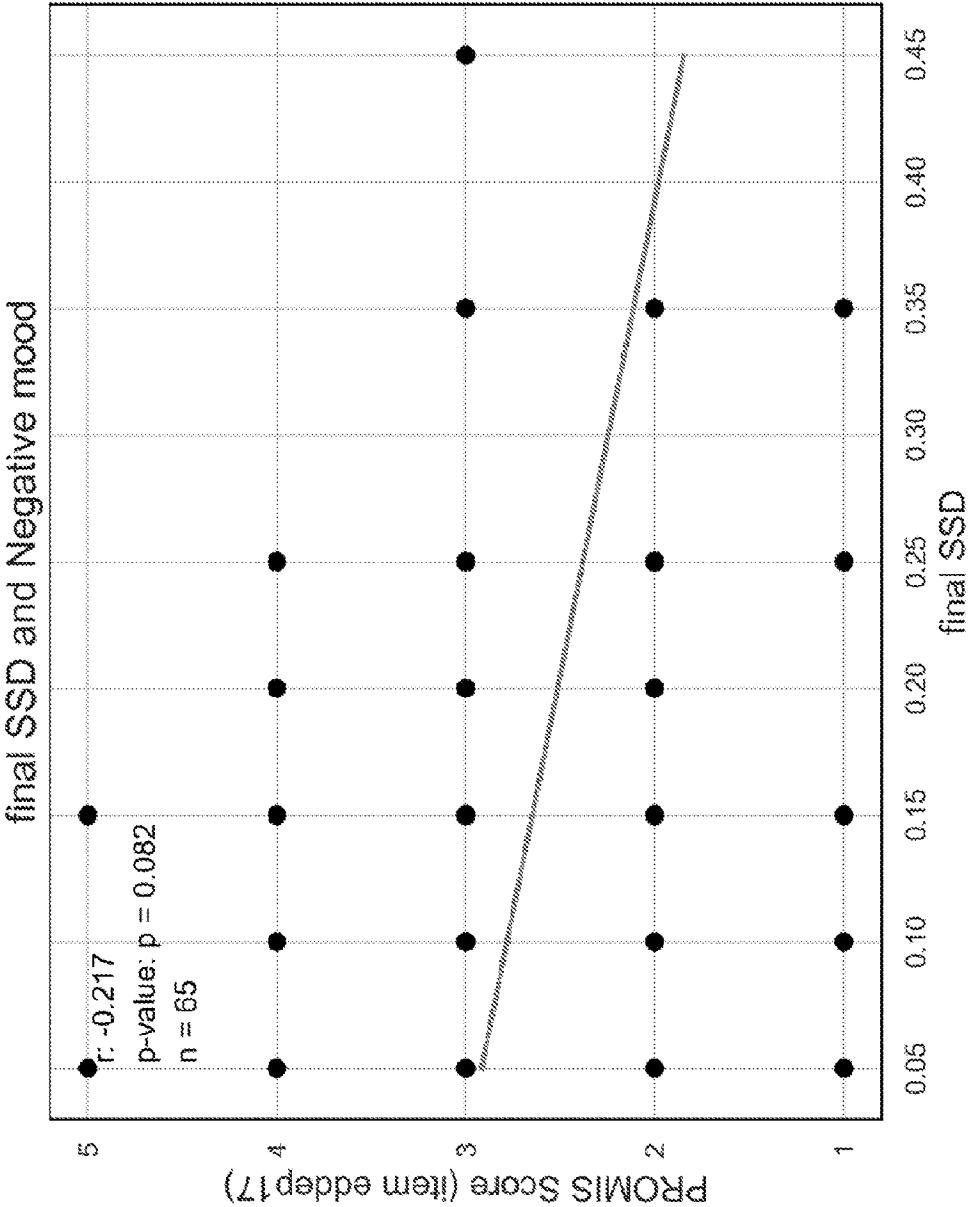


FIG. 6B

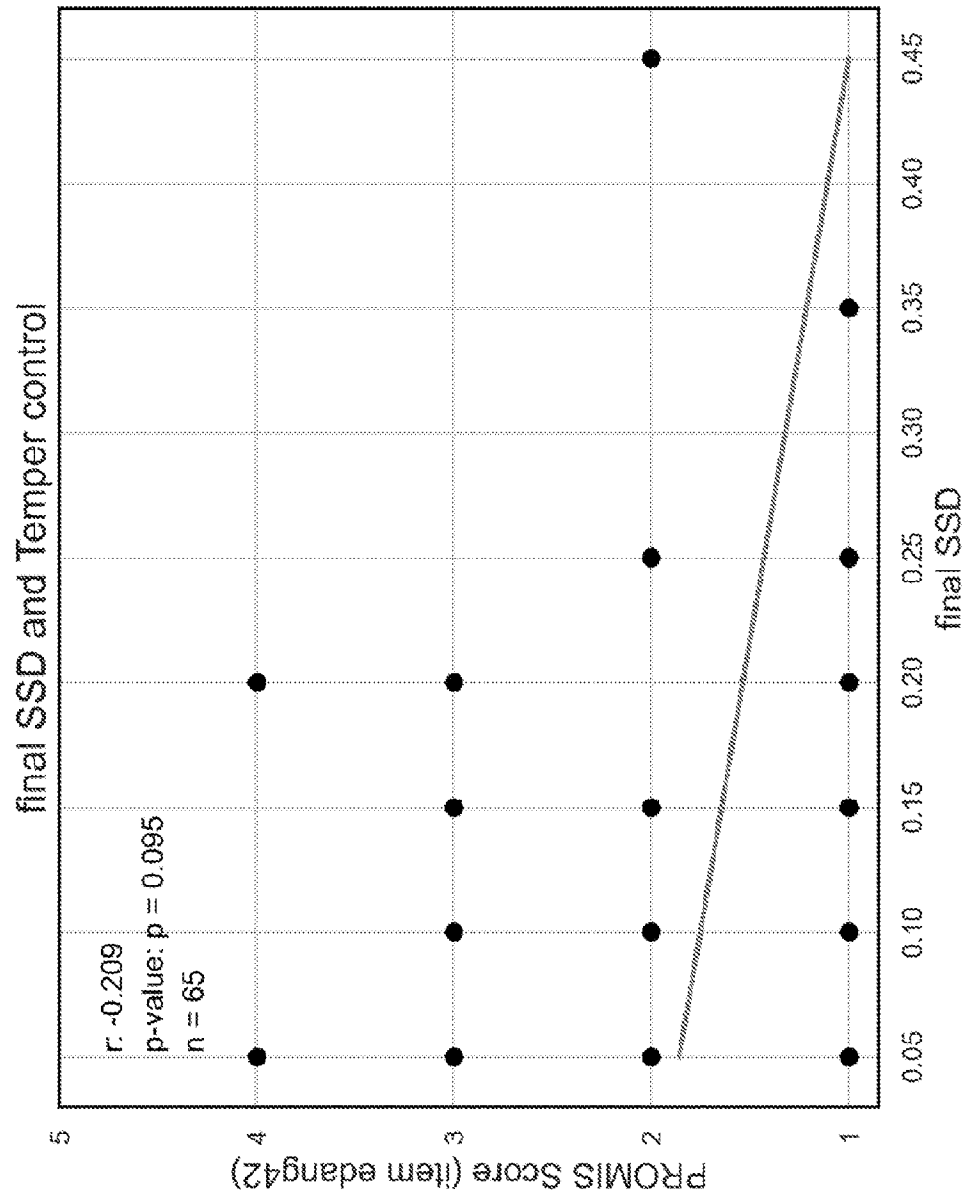


FIG. 6C

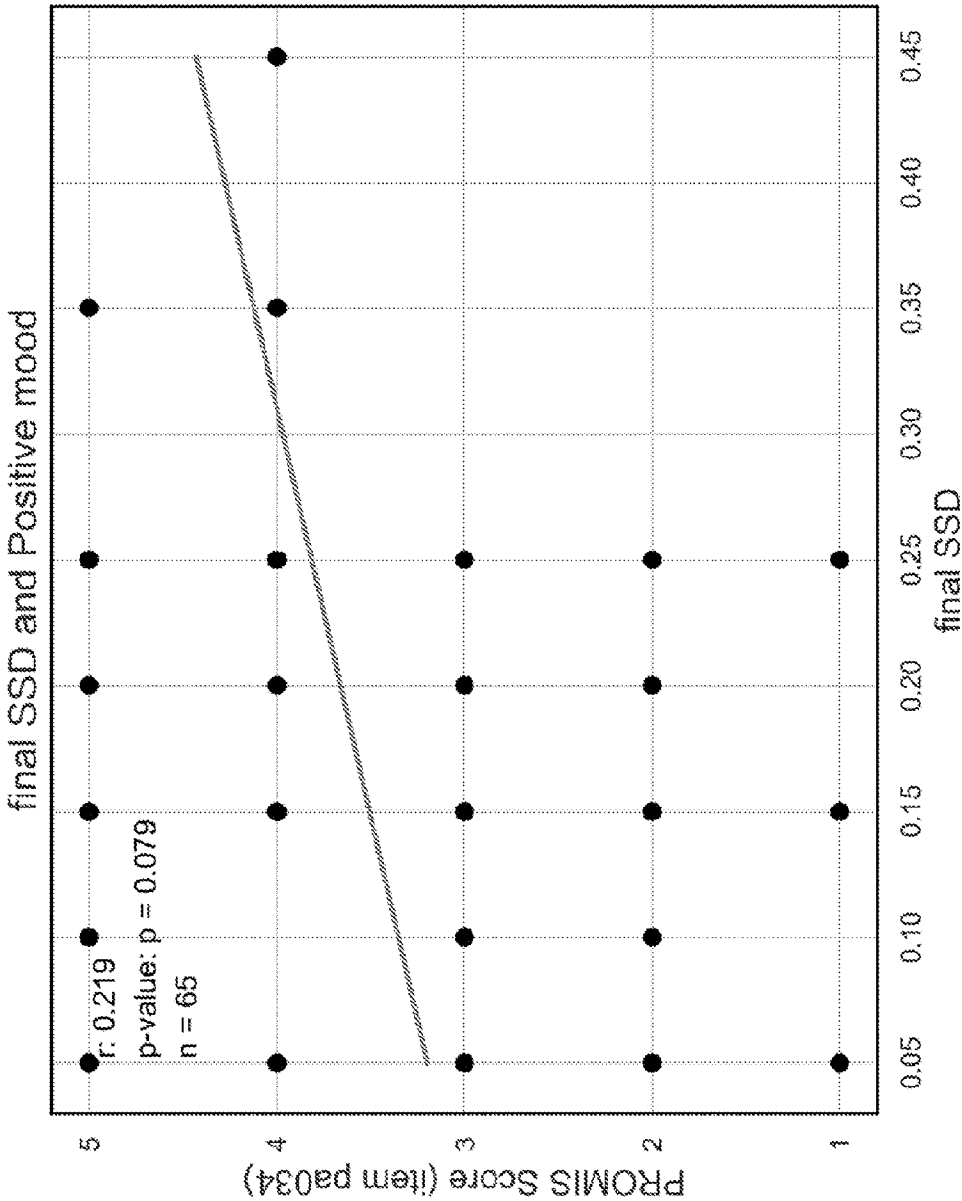


FIG. 6D

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2025/010439

A. CLASSIFICATION OF SUBJECT MATTER

INV. G16H10/20 A61B5/16 G16H20/70 G16H50/20
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G16H A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO- Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2019/216392 A1 (BOWER JEFFREY [US] ET AL) 18 July 2019 (2019-07-18) the whole document -----	1 - 54
X	US 2011/118555 A1 (DHUMNE ABHIJIT [US] ET AL) 19 May 2011 (2011-05-19) 55-60, Figures 3,4 -----	1 - 54
A	WO 2023/102125 A1 (BEHAVR INC [US]; SUMITOMO PHARMA CO LTD [JP]) 8 June 2023 (2023-06-08) the whole document -----	1 - 54
A	US 2019/378621 A1 (ELLISON TAMI ROBYN [IL]) 12 December 2019 (2019-12-12) the whole document -----	1 - 54

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Further documents are listed in the continuation of Box C.

☒

See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

3 April 2025

Date of mailing of the international search report

14/04/2025

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Authorized officer

Megalou-Nash, M

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2025/010439

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