Bilateral Alternating Tactile Stimulation (BLAST) and the Stress Response
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ABSTRACT

Anxiety disorders are among the most prevalent psychiatric illnesses and contribute to a significant chronic morbidity and decreased psychosocial functioning. Often, these disorders have their roots in past traumatic experiences, which manifest as a disordered or excessive stress (“flight or fight”) response. Treatment of these disorders is primarily pharmacologic, and although somewhat effective, many common anxiolytic drugs have side effects and are habit-forming. Therefore, there has been considerable interest in developing alternative non-pharmacologic treatment modalities. In particular, recent studies have shown that bilateral alternating tactile stimulation (BLAST) can attenuate the stress response, an effect correlated with quantifiable changes in EEG patterns. In this paper, we review the neuroanatomical structures and associated networks that are implicated in mediating the stress response and how they may contribute to various anxiety disorders. We also review the clinical effects of BLAST and other rhythmic stimulation techniques on the stress response in both normal healthy subjects and those with anxiety disorders, as well as the work showing how these effects might be mediated. Finally, we present recent work looking at the effects of BLAST on the stress response using non-invasive, wearable devices that deliver self-directed BLAST therapy. We show significant reductions in subjective levels of psychologic and physical stress through quantifiable modulation of activity in brain regions known to mediate the stress response. Future research should explore how the technology

Key words: network, anxiety, bilateral alternating tactile stimulation, stress
Introduction

Clinical Consequences and Public-Health Dimensions of Anxiety

Excessive stress has long been known to have serious long-term physical and psychological consequences. When stress is experienced, the body becomes guarded in preparation for anticipated injury or pain\(^1\). Physically, this state manifests as a sympathetic (“fight or flight”) response that modulates many physiologic variables, such as hemodynamics and neuroendocrine function. When this state is activated frequently and for extended durations, it can lead to long-term negative health effects, such as chronic musculoskeletal pain, cardiovascular problems, and an increased risk for sudden death. Psychologically, high anxiety is frequently correlated with many psychiatric illnesses.

The negative health effects of stress are pervasive in western society and represent a major source of morbidity and mortality in the United States. In addition, stress and anxiety have a less easily quantifiable effect on psychosocial functioning and quality of life. The Yerkes-Dodson model expresses the relationship between arousal, or stress, and psychosocial performance as an inverted U-shaped function, suggesting that some arousal and stress is necessary for optimal performance. However, excessive levels negatively affect one’s ability to perform efficiently\(^2\)\(^3\). The Yerkes-Dodson model has also been expanded upon to incorporate concepts of physiological arousal, which shows a similar relationship with performance. While mild-to-moderate levels of arousal can lead to increased alertness, interest, and positive emotions, hyperarousal can lead to emotional disturbance and excessive anxiety.

Anxiety and anxiety-associated disorders are characterized by a profound impairment in daily functioning or quality of life and represent a large continuing public health burden. Anxiety disorders are almost the most commonly diagnosed psychiatric illnesses in the United States and often present along with other co-morbid psychiatric symptoms, most frequently depression. The prevalence of these disorders has reached nearly epidemic proportion in the United States, with approximately 40 million American adults having a diagnosable anxiety disorder. Common anxiety disorders include, among others, generalized anxiety disorder (GAD), panic disorder, obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD). In addition to these primary anxiety disorders, anxiety is a common comorbidity in a wide range of physical and psychiatric illnesses, such as attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), insomnia and other sleep disorders. Anxiety also plays a role in alcoholism and substance abuse, often in complex and treatment refractory cases.
Although the specifics of the stress response vary with each person, many of the general psychological and physiological effects are similarly experienced across the population. This suggests that the stress response is somewhat “hard-wired,” which may help to explain why so many people experience the same or similar symptoms to excessively stressful stimuli, such as anxiety and other negative emotions, physical pain (e.g., migraines), and worsened physiological functioning with the specific form this response takes varying by individual. Studies of animal models and medical imaging data of human subjects have implicated specific neuroanatomical structures and associated functional networks that mediate this response. In this review, we present work by our group and others looking at what brain regions and associated networks mediate the stress response and how it can be modulated through different forms of rhythmic stimulation, in particular wearable devices for self-directed bilateral alternating tactile stimulation therapy (BLAST).
There are several key neuroanatomical structures involved in processing the diverse range of stressful stimuli. Together, they form a set of overlapping functional networks and include: (1) the amygdala (within the limbic system), (2) cortical regions, including the insular cortex (IC), prefrontal cortex (PFC), ventromedial PFC (vmPFC), and anterior cingulate cortex (ACC; a component of the salience network [SN]); (3) the nucleus accumbens (including the bed nucleus of stria terminalis [BNST]); and (4) diencephalic structures (e.g. thalamus, hypothalamus). In this section, we present studies which detail the role of these structures and their associated networks in mediating the stress response and, if abnormal, how they might contribute to the symptoms of certain anxiety disorders. Many of the findings that we present in this section are derived from studies based on functional imaging techniques, such as functional magnetic resonance imaging (fMRI), single-photon emission computerized tomography (SPECT), quantitative electroencephalography (qEEG), and methods that measure regional cerebral blood flow (rCBF) (i.e., laser Doppler flowmetry).

**Amygdala**

An almond-shaped set of nuclei located deep within the medial temporal lobes, the amygdala nuclei are a major limbic-system structure that play a pivotal role in the perception of fear and associated memories. **Bilateral amygdala (BLA)** cells integrate converging sensory inputs, and BLA microcircuits help to “gate” (i.e., modulate or regulate) acquisition and expression of conditioned fear responses. In patients with GAD, activation of the amygdala is associated with low tolerance for uncertainty during decision-making tasks. In many patients with PTSD, the amygdala is hyper-responsive, exaggerating fear responses that are often linked to the persistence of traumatic memories. Conversely, patients with damage to the **lateral amygdala (LA)** experience impaired memories of emotional stimuli. Animal models support the conclusion that the lateral amygdala is a locus of stimulus convergence and sensory integration during fear conditioning and is also a critical site for the expression of learned changes in behavior. Lesions to the LA can also disrupt fear conditioning, and the dorsolateral amygdala responds to both somatosensory and auditory stimuli. In fact, the amygdala is largely responsible for regulating acquisition and storage of fear memory traces. Local inhibitory neural circuitry within this structure is instrumental in modulating the body's stress response. The amygdala's intrinsic connectivity and extrinsic interaction with other key brain structures (e.g., cortex, hippocampus) are consistent with its role in integrating sensory inputs, as well as generating and extinguishing fear response outputs. In animal models (i.e., using conditioned stimuli), extinction of fear is considered to be more of an active process, involving neural plasticity and active learning, rather than merely passive forgetting. Therefore, interventions that alter amygdala activity are likely to be well-suited to influencing patients' stress responses in real time.
Insula (Insular Cortex [IC]) and Anterior Cingulate Cortex (ACC)

In general, anxiety and other adverse emotional responses result from deficits in “top-down” cortical inhibitory modulation of the limbic system (i.e., the amygdala) by the medial PFC (mPFC) and ACC.[11] Together with the amygdala, ACC, and VTA, the insula forms part of the SN. It also plays a key role in representing (and suppressing) bodily urges (e.g., in the setting of addiction[12]) and moderating subjective awareness of one’s feelings (e.g., anger, disgust), as well as empathy for others.[13] The insular cortex is involved in processing self-referential emotions, including disgust to noxious smells and tastes, anticipatory anxiety, as well as feelings of guilt, anger, and moral violation. As a component of the SN, the IC helps to switch between neural networks in the face of threatening stimuli, representing a potential modifiable neuroanatomical target.[14–16] The IC is associated with altered interoception in patients with anxiety[17] who often experience changes in predictive signaling concerning the difference between expected and observed body states in the face of enhanced signaling of salience by the amygdala. Modulation of affective processing and cognitive and emotional processes during learning (e.g., responses to conditioned stimuli) may also occur in association with IC activation. Symptom provocation is associated with increased cerebral blood flow in the bilateral IC of patients with PTSD and other anxiety disorders. The degree of activity in the right IC during risky decision-making tasks has also been correlated with harm avoidance and neuroticism.[14] Anxiety-prone patients have increased IC activation bilaterally during emotional processing, and successful treatment with the benzodiazepine, lorazepam, reduces bilateral IC activation in a dose-dependent manner.[14]

Canonical Networks Underlying the Stress Response

As illustrated in Figure 1, the IC participates in one of three canonical networks of resting-state functional connectivity: (1) the central executive network (CEN), which has key nodes in the dorsolateral PFC (dLPFC) and posterior parietal cortex (PPC); (2) the default-mode network (DMN), which includes the vmPFC and the posterior cingulate cortex (PCC); and (3) the SN, which includes the ventrolateral PFC (vLPFC) and anterior insula (fronto-insular cortex [FIC]).[15] In patients with PTSD, the rostral ACC and vmPFC fail to inhibit neural activity in the amygdala, attenuating the processes of contextual processing, emotional regulation, attention, and extinction.[5] As shown in Figure 2, event-related fMRI signals in the right FIC (rFIC) and ACC peak earlier compared to signals in the nodes of the CEN and DMN, indicating that neural responses in the rFIC and ACC precede those in the CEN and DMN.[15] Activation of the CEN and SN appears to be accompanied by deactivation of the DMN. [15] Switching among these distinct brain networks, which are implicated in different task paradigms and stimulus modalities, appears to be mediated by the rFIC, alone and in combination with the ACC.[15] Many patients with anxiety disorders have disruptions in signaling in the rFIC, which would otherwise engage the brain’s attention, working memory and higher-order processes (CEN), while disengaging non-task-relevant systems (DMN), to affect cognitive control.[15] Unlike other anxiety disorders,
PTSD is associated with decreased responsiveness in the rostral ACC and adjacent vmPFC. Work by Holmes, 2015 suggests that the PFC is a key node in the circuitry sub-serving contextual fear. Activity in the PFC is integral to higher-order cognitive processes, and the PFC is thought to be involved in a range of stress-sensitive behaviors, including cognitive set shifting, reversal learning, and extinction. This supports self-reference and awareness by linking subjective experiences across time (i.e., extended self-reference) and in the present (momentary self-reference).

The classic sympathetic nervous system response of “fight or flight,” with increased activity of noradrenergic neurons in the locus coeruleus, is counterbalanced by parasympathetic nervous system activity. Work by Hermans et al., 2011 suggests that noradrenergic activation during acute stress results in prolonged activation in areas to include the ACC and insular cortex, and subcortical regions, including the amygdala, thalamus, hypothalamus and midbrain. Information is integrated across multiple structures involved in autonomic-neuroendocrine control and vigilant attention re-orienting. These noradrenergic signals effect memory and also activate functional networks that cause disengagement from current task sets and promote rapid adaptation to the processing of novel stimuli by rearranging network activity. This may be a link between stress-induced noradrenergic activity and activation of the salience network. As shown in Figure 3, the negative effects of traumatic stress on health and behavior can be explained via a bi-hemispheric model of laterality and by auto-calibration in autonomic activity. Normal brain function is characterized by a prevailing symmetry in the activity of bilaterally homologous brain regions. In contrast, traumatic stress can elicit either a right dominant asymmetry in activation, which is associated with sympathetically mediated state of high arousal, or a leftward dominant asymmetry in activation of the same regions, which is indicative of a parasympathetic “freeze” mode. Subsequent recovery from trauma may be associated with adverse compensatory behaviors (e.g., conduct disorders, substance abuse, medication dependence) as the autonomic nervous system works to restore normal balance. Modulation of this lateralized abnormal activity in these specific brain regions provides a possible therapeutic target for future study. In the next section, we examine approaches to modulate these networks based on different types of sensory stimulation.

**Rhythmic Stimulation and the Stress Response**

Different forms of rhythmic perceptual stimulation such as auditory (e.g., music), visual, and tactile (e.g., massage, sensory processing interventions, exercise training) inputs are well-known approaches to relieve anxiety. Other non-pharmacologic strategies for anxiety reduction include mindfulness meditation, neurofeedback, relaxation training, cognitive-behavioral therapy, and different forms of play, although not all are evidence-based. These various methods are hypothesized to mediate their effects by modulating the sympathetic nervous system (SNS), resulting not only in reported relief from anxiety, pain, and other adverse psychological states, but also in lower blood pressure, lower heart rate, reduced heart rate...
variability, and lower respiration rates. Studies have shown that certain characteristics of the applied rhythmic stimuli are critical in order to see optimal therapeutic effect. Work by Servan-Schreiber et al., 2006 demonstrated that patients undergoing treatment for PTSD derived a statistically significant incremental benefit from alternating rhythmic sensory stimulation compared to simultaneous rhythmic—or continuous—stimulation. In this study, a total of 21 patients undergoing treatment for single-episode PTSD received three consecutive eye movement desensitization and reprocessing (EMDR) sessions, each with the following different types of auditory and/or kinesthetic inputs: intermittent alternating right-left (EMDR-like), intermittent (rhythmic) simultaneous bilateral, and continuous bilateral stimulation. Although each approach significantly reduced subjective ratings of distress, alternating stimulation did so more effectively. Furthermore, bilateral alternating stimulation eye movements and bilateral alternating tactile stimulation (BLAST) had a greater effect than bilateral alternating stimulation alone. The fundamental importance of bilateral alternating inputs was also demonstrated in a European study looking at the effects of different type of perceptual stimulation on normal memory retrieval. The study assessed changes from baseline in memory recall among healthy volunteers receiving either bilateral saccadic eye movements, BLAST, or alternating bilateral auditory stimulation. As shown in Table 1, there were significant increases in the number of items recalled when subjects received either horizontal bilateral saccade (eye movement–induced retrieval enhancement or left-right stimulation of both the visuomotor and somatosensory systems (BLAST), but not left-right auditory stimulation. In a study by Amano & Toichi, 2016, healthy volunteers were instructed to actively recall pleasant memories (e.g., birth of a child) while BLAST was applied, and they then underwent two forms of evaluation: (1) the Profile of Mood States (POMS) inventory, with higher scores indicating more adverse emotional states and (2) assessment of regional cerebral blood flow using near-infrared spectroscopy. As shown in Figure 4, POMS scores decreased (i.e. improved) significantly after (vs. before) BLAST. These included statistically significant reductions in the following domains: tension-anxiety, anger-hostility, fatigue-inertia (each p <0.01 after vs. before BLAST), as well as depression-dejection and confusion-bewilderment (each p<0.05). These reductions were correlated with increased ratios of [oxy-Hgb]/[deoxy-Hgb] in the right superior temporal sulcus. On the other hand, a decrease in [oxy-Hgb]/[deoxy-Hgb] within the PFC was correlated with emotional regulation and associated more with feelings of comfort and relaxation.

Eye Movement Desensitization and Reprocessing (EMDR) Therapy

Exploiting the salient effects of eye movement, eye movement desensitization and reprocessing (EMDR) was developed by Francine Shapiro and was originally targeted toward reducing intrusive painful recall in patients with PTSD. EMDR is comprised of an 8-stage protocol during which the patient contemplates traumatic memories while moving his or her eyes back and forth from left to right or while receiving other forms of bilateral stimulation in auditory or tactile form (BLAST). With repetition, this procedure is hypothesized to progressively changes traumatic (sensory), into more declarative (verbal), memories, while also decreasing the emotionality and behavioral manifestations...
(arousal and avoidance) associated with them. Studies assessing electroencephalogram (EEG) data with EMDR treatment have shown that bilateral eye movements, as opposed to blinking, lead to inter-hemispheric coherence, prefrontal cortex deactivation, and modulation of activity in the orbitofrontal and anterior cingulate cortex. EMDR appears to shift brain activity from the highly emotional areas of the limbic region to higher cortical regions allowing for cognitive processing and desensitized arousal. Studies show that EMDR reduces the distressful nature and vividness of emotional memories in healthy volunteers. Certain meta-analyses have suggested that EMDR is equally effective as cognitive-behavioral therapy (CBT) for PTSD. A consensus clinical practice guideline from the United Kingdom (NICE, 2015) assert that all patients with PTSD should be offered a course of trauma-focused psychological treatment, either trauma-focused cognitive-behavioral therapy (CBT) or EMDR. Investigating the perceptual basis of EMDR effectiveness, Nieuwenhuis et al., 2011 reported that normal memory retrieval was enhanced in response to both bilateral saccadic eye movements and alternating tactile stimulation but not to bilateral nor alternating left-right auditory stimulation.
Results and Discussion

Bilateral Alternating Tactile Stimulation (BLAST)

Research indicates that BLAST can: (1) induce feelings of positive cognition and comfort; (2) enhance memory retrieval; and (3) alter electrical brain activity, enhancing patterns associated with states of calm and deep sleep \[39\][49]. Studies by Servan-Schreiber et al. 2006 and Nieuwenhuis et al. 2013 have demonstrated that BLAST can be used to inhibit the human stress response and enhance memory recognition, used either as part of a standard therapy session or as a self-directed approach\[50\]. Advantages of BLAST include its rapid action of effect, which makes it effective in dealing with the acute attenuation of the stress response. Tracing its origins to EMDR therapy, BLAST was initially also used as an adjunct to the Emotional Freedom Technique in order to potentiate the clinical benefits of psychological counseling. \[28,51\]

BLAST has demonstrated some evidence of being an inhibitor of the human stress response and an enhancer of memory recall. Studies involving quantitative EEG data have demonstrated that BLAST facilitates de-potentiation of fear memory synapses, which results in decreased subjective ratings of emotional distress and the presence of low frequency EEG patterns in brain networks that are associated with sleep and states of deep calm. One of the main theories behind the effectiveness of applying the different modalities of bilateral alternating stimulation utilized within EMDR is the alternating hemispheric activation hypothesis, which contends that either lateral saccadic eye movement or lateral tactile stimulation activates the contralateral hemisphere much more than the ipsilateral hemisphere. Rapid alternating left-right sequences of eye movements and tactile stimuli may result in a rapidly alternating pattern of activations in the two hemispheres.\[39\]

As reviewed above, cortical structures encode, process, and regulate emotions related to aversive stimuli registered in the limbic system. Under normal conditions, these neuroanatomical structures "gate" aversive stimuli, encode competing memories, and play a role in "limbic de-potentiation," switching the brain's attentional systems to attenuate or extinguish threatening memories or stimuli. BLAST is hypothesized to help enhance the normal cortical descending inhibitory input to the limbic system (e.g., by reducing amygdala hyperactivation).\[11\] In fact, studies of patients undergoing EMDR or BLAST have demonstrated shifts in maximal qEEG activity from the emotional limbic system, including the amygdala and infra-limbic cortex, to cortical structures with a more dominant cognitive role. Work by Pagani et al, 2013 suggests that BLAST enhances the movement of traumatic memories from implicit subcortical to explicit cortical regions, which act to process and attenuate the experience.\[11\] A qEEG study by Harper et al., 2009 demonstrated that BLAST significantly de-potentiated electrical activity at synapses associated with fearful memories within the amygdala of patients with PTSD.\[52\] The study employed both eye movements and BLAST. However, participants' eyes were closed for the qEEG recording time, and BLAST was utilized during more processing time. The patients' reports of reduced distress were correlated with parallel changes in low-frequency rhythms in memory-associated brain networks that are typically associated with states of relaxation or sleep.
Specifically, the application of BLAST caused slowing of the neuronal firing rate of the frontal lobes from around 7 Hz (waking state) to about 1.5 Hz. There was also a several-fold increase in amplitude, reflecting a pattern of synaptic synchronization characteristic of de-potentiation. This high-power, low-frequency pattern of brain activity is similar to that of slow-wave sleep, which is associated with memory editing.

### Devices for Self-Directed BLAST

Although research on the clinical effect of BLAST has primarily focused on patients in therapy-directed sessions, recent work by our group have demonstrated that BLAST applied in a self-directed manner can reduce stress in healthy subjects. Wearable devices worn around subject’s wrists (dimensions: 25 mm x 37 mm x 33 m; weight: 14 grams) provides vibratory stimulation (10 – 55 Hz) in a bilateral alternating pattern based on conventional BLAST (Figure 5). Work by Serin et al., 2018 reviewed the subjective effects of BLAST on the stress response in a heterogeneous group of subjects (n = 1109) with self-reported high levels of stress and anxiety. Subjects were asked to rate their levels of emotional stress and feelings of bodily distress (i.e. upset stomach) on a scale of 0-10 before and again after applying the technology for 30 seconds. Results showed that the self-directed application for 30 seconds resulted in a statistically significant reduction in the subjective ratings of both psychological stress and anxiety-associated physical feelings of bodily distress (mean difference between ratings of psychologic (1) and physiologic (2) distress before versus after 30 seconds after BLAST was: (1) 4.76 (n = 1109; SD = 3.1; t = 51.16; df = 1108; standard error = 0.0931; p <0.0001) and (2) 2.63 (n = 1109; SD = 3.23; t = 27.12; df = 1108; standard error = 0.0971; p <0.0001) [50].
Conclusion

Approximately 40 million Americans contend daily with the distressing and debilitating symptoms of anxiety disorders, yet only about 15 million receive treatment and many suffer in silence for decades before seeking care. Results from both animal models and from clinical studies of patients with anxiety disorders (specifically PTSD) implicate several neuroanatomical structures and associated networks involved in the acquisition, modulation, attenuation, and extinction of stressful memories and other internal states. The brain regions involved in these processes are an important part of the salience network, which is critical for attending to and selecting important sensory input to process. The subcortical regions, like the amygdala, which are part of the limbic system, have a major role in the acquisition and emotional processing of fear-based memories. In contrast, the cortical regions involved, including the right fronto-insular cortex, anterior cingulate cortex, and prefrontal cortex, mediate higher-order cognitive processing and have a descending inhibitory regulation on amygdaloid activity, which leads to improved contextual processing, emotional regulation, attention, and memory extinction.

BLAST represents a novel treatment approach, grounded in EMDR theory, that may modulate the activity of specific brain regions that activate the emotional stress response and bodily sensations associated with distressing recall or physical pain. Based on the alternating hemispheric activation hypothesis, BLAST is hypothesized to reduce stress and promote subjective feelings of comfort and relaxation by shifting neural activity from the amygdala to the insular cortex in a process termed limbic de-potentiation. Wearable devices using Bluetooth or infrared technology now allows for the self-administered application of BLAST. Work by our group has shown that applying the technology can reduce the subjective feelings of psychological stress and physiologic distress associated with stressful stimuli and enhance memory formation and retrieval that correlates with altered qEEG activity showing a reduction in limbic activity and increased activity in cortical regions.

Although a promising approach to reduce symptoms of stress and anxiety, further research is needed to fully characterize the clinical effects and mechanism of action of BLAST, including:

- assessing the efficacy of BLAST in a range of anxiety associated conditions, including autism-spectrum disorder, PTSD, acute and chronic pain, generalized anxiety disorder, and addiction;
- more rigorously evaluating the clinical effects of BLAST using well-validated metrics of symptom severity, functional status, and quality of life
- quantitatively evaluating the effects of BLAST on physiologic variables associated with the autonomic stress response (e.g., hemodynamic and neuroendocrine)
• determining the effects of BLAST on activity in key brain regions (e.g., amygdala and insular cortex) using not only qEEG but also other functional imaging methods, such as functional magnetic resonance imaging, measurements of regional cerebral blood flow, and positron emission tomography

Although further research is needed to better assess the long-term efficacy and clinical outcomes, BLAST technology has demonstrated a significant attenuation of the stress response, which correlates with quantifiable changes in brain activity. Further studies are necessary to examine specific therapeutic effects for this modality and the impact on biomarkers of stress, sleep, mood, pain, and mental health disorders.

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References


Table 1. Mean (SD) Number of Recalled Items as a Function of Task Condition and Valence\textsuperscript{[39]}

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<td>5.3 (0.5)</td>
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<td>3.3 (0.4)</td>
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Reproduced with permission from Nieuwenhuis S et al.\textsuperscript{[39]}

**Figure 1.** Three major brain networks identified during cognition. fMRI activations in the central executive and salience networks and deactivations in the default mode network during auditory event segmentation. **A.** Analysis using a general linear model revealed regional activations (left) in the right anterior insula (rAI) and anterior cingulate cortex (ACC) (\textcolor{blue}{blue circles}); dorsolateral prefrontal cortex (DLPFC) and posterior cingulate cortex (PCC) (\textcolor{green}{green circles}) and deactivations (right) in the ventromedial prefrontal cortex (VMPFC) and PCC. **B.** Independent component analysis provided converging evidence for spatially distinct networks. From left to right: salience network (rAI and ACC), central executive network (rDLPFC and rPPC), and default mode network (VMPFC and PCC)\textsuperscript{[15]}. Reproduced with permission from Sridharan D et al.\textsuperscript{[15]}
Figure 2. Differential response latencies at the transition during auditory event segmentation. Latency analysis at the transition revealed early activation in the FIC and ACC, and late activation in the nodes of the central executive network (CEN) and default-mode network (DMN) (rDLPFC, rPPC, PCC, and VMPFC). All slices are identical to those shown in Figure 1. Panel A highlights an early response in the ACC (sagittal slice). Reproduced with permission from Sridharan D et al. [15]
Figure 3. Bi-hemispheric autonomic model (BHAM) for traumatic stress effects on health and behavior through auto-calibration of arousal. The *top oval* denotes state of relative symmetry (balance) in activity of bilateral homologous brain regions responsible for autonomic management. The *middle oval* denotes a right dominant asymmetry in activation of the same brain regions, indicative of traumatic stress associated with a high state of arousal. The *bottom oval* denotes a left dominant asymmetry in activation, indicative of traumatic stress associated with a parasympathetic “freeze” mode. Recovery from trauma may be associated with compensatory adverse behaviors (including but not limited to conduct disorders, especially from freeze state to progress to high arousal; and varying forms of substance abuse or medication dependence, to achieve state of balance). Effective interventions that can modulate this autonomic dysregulation could potentially aid in the normalization of brain function and decrease the likelihood of compensatory adverse behavior.[22] Reproduced with permission from Lee SW et al.[22]
Figure 4. POMS scores obtained before and after BLS therapy (n = 10). The paired t-test was used to compare test scores before and after the session (p<0.05: *, p<0.01: **). Reproduced with permission from Amano T et al. [40]
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Reduction in beta activity shown in 3-d voxelated view

Reduction in theta activity shown in 3-d voxelated view

Reduction in delta activity shown in 3-d voxelated view
Figure 5. TouchPoints™, wearable devices for self-directed bilateral alternating somatosensory therapy (BLAST).