Background and Problem:

The capacity to flexibly regulate emotional and physiological arousal in response to environmental demands is fundamental to physical and psychological health.¹ Deficits in the capacity to regulate arousal have been associated with autonomic imbalance characterized by excessive sympathetic and deficient parasympathetic control of the autonomic nervous system.^{2,3} Chronic sympathetic hyperarousal taxes autonomic stress response systems, leading to accelerated wear and tear, compromised functioning of these systems, compensatory adjustments of secondary biological systems, and ultimately to pathological disease states.²⁻⁴ Emotional injuries associated with chronic arousal dysregulation are particularly common among veterans exposed to the severe and chronic stress of combat deployments, and include depression, anxiety,⁵ and posttraumatic stress disorder (PTSD).⁶ Each of these injuries is associated with high rates of physical disease states.³

While pharmacological approaches have dominated the approach to treating these physical and psychological manifestations of stress, many service members and veterans avoid such treatment because of stigma or the fear that taking medication will harm their careers.^{8,9} Military personnel are trained in self-reliance, and the idea that they can use their own minds and bodies to overcome stress and adversity often becomes central to their identities.¹⁰ If the medical community is to effectively reach veterans and service members, it will require developing interventions that will "meet veterans where they are," and allow them to use their strengths to facilitate their own healing processes.

Heart rate variability biofeedback (HRVB) trains individuals to breathe at their resonant frequency, a respiration rate that has been shown to lead to greater baroreflex flexibility and restoration of autonomic balance.^{2,11,12} HRVB has been found to be promising in modifying both physiological and emotional responses to angerinducing stimuli;¹³ decreasing anxiety and anger in individuals with anxiety disorders¹⁴ and depressive symptoms in individuals with depression¹⁵ and PTSD; lowering symptoms of posttraumatic stress in combat veterans ¹⁶ and self-reported hostility in individuals with coronary artery disease;¹⁷ and increasing stress management¹⁸ and performance¹⁹ in active duty soldiers under high stress situations. HRVB, therefore, has the potential to be a powerful tool in the treatment of a range of stress-related problems with emotional arousal that are known to impact veterans.

To date, the application of HRVB as a technique for intervening with emotion regulation problems has been limited. Biofeedback equipment is expensive and bulky, making this treatment modality less conductive to integration into standard clinical practice settings. The requirement of cumbersome biofeedback monitors makes it impractical for patients to practice HRVB in day-to-day settings, where they are likely to have the most impact. Interventions that capitalize on mobile technology can produce greater effects than traditional clinic-based treatments because they are portable, convenient, and allow users to practice newly-acquired behavioral skills more frequently and in real-world settings. Mobile health interventions also provide a way to increase motivation and engagement through "gamification" of therapeutic tasks, and research has suggested that serious digital games hold potential for improving behavioral clinical outcomes ²⁰.

Proposed Intervention and Pilot Work:

Our laboratory has worked towards developing an integrated smartphone app with wristband biosensor to deliver a gamified heart rate variability feedback application to veterans with stress-related problems of arousal regulation. We have undertaken several pilot projects to examine the acceptability and potential effectiveness of this application. Thus far we have demonstrated that veterans find the use of biofeedback and paced breathing using a mobile smartphone application appealing and effective in both laboratory and *in situ* environments; and that they will use this technology in their day-to-day lives to practice arousal regulation techniques. We have piloted smartphone games that have paired paced breathing at a rate close to resonant frequency, and veterans have described both emotional (i.e. better managing distress at work or at home) and physiological (i.e. decreasing blood pressure readings when used just prior to daily monitoring) benefit.

Current Technological Barrier:

We initially tested the use of the Empatica E4 wristband for measuring heart rate variability (HRV) and other psychophysiological signals (e.g. electrodermal activity) for use in our application. The Empatica E4 is most accurate commercially-available wristband for collecting psychophysiological data

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(<u>https://www.empatica.com/research/e4/</u>). A related Empatica product (the Embrace) has been FDA approved for use as a medical device in the prediction of seizure activity

(<u>https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K172935</u>).^{21,22} Unfortunately, however, our testing of the E4 both in comparison with the state-of-the-art Holter monitor, and with veterans in the laboratory and in the field, found that the HRV data collection was not sufficiently reliable to allow for a useful biofeedback signal, primarily due to movement-related artifacts.²³

Technology Need:

To continue our research in this area, our laboratory will need access to a wristband sensor that can measure heart rate variability with sufficient precision and reliability to allow for accurate biofeedback when worn during normal daily activities. The E4 wristband samples at a rate of 60 Hz; most recent publications have suggested that sampling rates between 500 and1000 Hz would be required for optimal accuracy.²⁴

Public Health Impact:

The positive public health impact of reducing physical morbidity associated with stress-related emotional dysregulation would be substantial. A gamified mobile HRVB intervention has significant potential as a potent, low-cost intervention that can motivate and empower veterans and military personnel to employ physiological and emotional self-regulation skills. The use of mobile health technology as a vehicle for providing HRVB is expected to significantly increase the reach of this promising intervention.

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