Training with Adaptive Systems: Utility of Baroreflex Sensitivity

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ABSTRACT

Significant resources have been invested toward the development of systems that adapt to user functional state in real-time and based on users' physiological responses, where the user may be in a wide array of stressful situations. These adaptive systems are promising as platforms to enhance training effectiveness, yet progress to date has been somewhat limited.

The physiological responses to a stressful situation have been characterized as "fight-or-flight" or "challenge vs. threat" responses. The cardiovascular changes associated with these responses are mediated by the autonomic nervous system and include both central (e.g., heart rate, stroke volume) and peripheral (e.g., blood pressure, total peripheral resistance) changes. Blood pressure (BP) is modulated acutely by the baroreflexes. Baroreceptors are stretch-sensitive mechanoreceptors located in the vasculature which provide negative feedback to the brain; changes in BP change this stretch and ultimately lead to changes in BP and heart rate (HR). Both physical exercise and mental stress can increase HR and BP. However, baroreflex sensitivity is unchanged with physical exercise and limited evidence suggests it is altered with mental stress. Changes in baroreflex sensitivity may therefore provide an objective marker for mental stress that HR- and BP-based markers cannot. Thus, real-time monitoring of baroreflex sensitivity may be the missing component for bridging the gap in developing an effective adaptive system.

Consequently, the purpose of this study was to assess the extent to which baroreceptor sensitivity changes during acute physical stress (cold pressor test), laboratory-based mental stress (Stroop test, mental arithmetic, anagrams) and using a virtual reality environment, stressful occupationally-relevant "real-life" simulations.

We will then propose a framework for the utilization of baroreflex sensitivity measures as a tool for assessing laboratory and occupational stressors in real-time.

ABOUT THE AUTHORS

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BACKGROUND

Adaptive Training

Adaptive training (AT) has gained significant interest in the last four decades. The overarching hypothesis that drove the interest in AT was that adapting instruction to the cognitive state of the specific participant would result in faster and more effective learning. Landsberg et al. (2010) conducted a thorough review to present the "state of the science" on AT and concluded that, in general, AT seems to be an effective method of training. Coyne et al. (2009) proposed merging real time physiological assessment with principles of cognitive load theory as a framework for AT. One physiological marker that was examined as a candidate to represent some aspects of user's cognitive state in real time was Heart Rate Variability (HRV). Thayer et al. (2009) summarized research efforts associated with HRV and a variety of cognitive functions. Their findings suggested an important relationship between cognitive performance and HRV, but that further research was needed to clarify which executive functions are associated with individual differences in HRV. HRV assesses the relative balance between activation of the sympathetic (fight-or-flight) and parasympathetic nervous systems; it does not completely isolate the parasympathetic system from the sympathetic system. HRV typically presents a spectral profile of the activation of these systems. This spectral density analysis requires rather large amounts of data to present the profile, so it is difficult to assess HRV status in real time. These two factors may have terminal effects on the potential for utilizing HRV as a tool for AT. Furthermore, Kassam et al. (2009) indicated that cognitive functions, such as decision making, manifest interactive multiple physiological effects such as heart rate *and* blood pressure. Thus, identifying a physiological marker(s) that will be effective for real time adaptation remains a challenge. Spontaneous baroreflex sensitivity may have utility as just such a marker.

Spontaneous Baroreflex Sensitivity

The human cardiovascular system is incredibly complex. Part of this complexity is due to the presence of a number of overlapping control systems that interact to maintain a relatively stable, adequately elevated blood pressure (BP) in an environment where perturbations in BP are common and varied. These overlapping systems reflect this diversity in responding to challenges to BP homeostasis, since the best response for one type of perturbation may be totally inadequate for another. For example, both prolonged standing, as if at military attention, and severe blood loss pose marked challenges to BP homeostasis. Prolonged standing would be readily tolerated if all the blood vessels were as noncompliant, or stiff, as arteries. However, a severe wound would rapidly lead to lethal hemorrhagic shock. If all blood vessels were as compliant or "elastic" as veins, then humans would better tolerate severe blood loss. Unfortunately, it would be virtually impossible to stand upright for any length of time without fainting. Of course, humans *can* stand for long periods, survive substantial blood loss and tolerate myriad other challenges to BP homeostasis. This responsiveness is largely because BP is the principle variable that the cardiovascular system controls and it does so via a number of different systems.

In the short-term, BP regulation occurs primarily by neural pathways (Boulpaep, 2005). Blood pressure is continuously monitored by baroreceptors embedded in major arteries (i.e., carotid sinus, aortic arch) that communicate neurally with cardiovascular control centers in the brain. Baroreceptors are actually stretch receptors; changes in the distention of the blood vessel wall due to changes in BP alter the neural input to the brain. The brain's neural signals to the heart and peripheral blood vessels are subsequently altered. These baroreflexes consist of negative feedback loops—increases in BP cause reductions in heart rate (HR) and dilation of peripheral blood vessels while decreases in BP elicit increases in HR and peripheral vasoconstriction. These alterations normalize BP and thereby normalize the amount of stretch on the baroreceptors.

A baroreflex functions around an *operating point* which is the resting, and presumably desired, BP. This operating point is analogous to the set temperature in a household thermostat; deviations from the desired temperature trigger either the furnace or air conditioner to turn on until the temperature is normalized. Just as a homeowner can change the set temperature of a thermostat, the brain may alter the operating point in some situations. This is why an increased BP is the normal and expected response to an acute bout of cardiovascular exercise (Raven, Fadel, & Ogoh, 2006); the operating point increases with the onset of exercise but, once the exercise bout ends, will decrease to the pre-exercise operating point. Baroreflexes and a thermostat also have a *sensitivity*. Baroreflex sensitivity, or the gain, is the change in HR for a given change in BP. The sensitivity of a thermostat is fixed in that it triggers either an "on" or an "off" response from the home's HVAC system. However, baroreflexes have a variable sensitivity which can be modulated by the brain. Consequently, the magnitude of the HR response for a given change in BP may be different in different situations.

When considering the implications of baroreflex sensitivity for monitoring the stress state, both the type of stress (e.g., physical, mental) and duration of the stressor (e.g., acute, chronic) affect sensitivity. An acute bout of cardiovascular exercise does not affect sensitivity (Raven et al., 2006), but chronic cardiovascular training will increase it (Monahan et al., 2000). Chronic strength training, however, does not appear to affect sensitivity (Cooke & Carter, 2005). It is reduced with chronic mental health issues such as schizophrenia (Bär et al., 2007), depression (Broadley et al., 2005a), and anxiety (Virtanten et al., 2003) but can be improved with stress management therapy (Blumenthal et al., 2005). Previous assessments of baroreflex sensitivity responses to acute mental stress have yielded conflicting results. This may be due to the varying nature of the stressors used (Persson, 1996). For example, a passive coping task, such as watching unpleasant film clips, did not affect sensitivity while an active coping task like mental arithmetic did (Ritz et al., 2000). Likewise, painful stimuli may or may not increase baroreflex sensitivity (Adler et al., 1991).

Numerous methods exist to assess the baroreflexes (Eckberg & Sleight, 1992). All necessitate assessing HR and BP on a beat-to-beat basis. The Valsalva maneuver approach involves the participant making a relatively forceful exhalation against a closed airway while the Oxford technique entails infusing vasoactive drugs, which alter either HR or BP, into participants. The neck chamber technique requires the participant to wear a very snug, airtight neck collar and a series of positive and negative air pressures are then infused into the collar. While these are excellent research methods, they have several disadvantages. All are intrusive to a level that makes the participant well aware of the procedure, only allow for intermittent assessments of baroreflex engagement, and because they manipulate either HR or BP, require that some assumptions be made regarding triggering the baroreflex (Eckberg & Sleight, 1992; Parati, Di Rienzo & Mancia, 2000). Thus, they do not lend themselves well to "real life" assessments of baroreflex activity.

A more practical approach is to measure spontaneous changes in HR and BP and analyze these changes using various mathematical methods (e.g., regression, spectral analysis) to determine a measure of baroreflex responsiveness. These methods provide valid estimates of baroreflex sensitivity (Parati et al., 2000; Laude et al., 2004). A marked advantage of these methods is that they do not require interventions *per se*. They do not manipulate the baroreflexes via artificially altering either HR or BP; rather, they assess the "natural" baroreflex responses to perturbations in blood pressure which occur naturally as a consequence of an external event. Thus, these methods have potential for use in real time state assessments as participants engage in simulated tasks. Unfortunately, the need to have participants connected to BP and HR monitors prevents "in-field" deployment of such assessments due to mobility issues. However, these methods can certainly be utilized when participants are engaged in their tasks in virtual environments. Doing so may yield the leap towards developing effective training systems that can modify, in real-time, the training content based on the psychophysiological state of the user.

In summary, there is some evidence in the literature supporting the notion that baroreflex sensitivity changes with stress. These responses have not been systematically explored. However, if this sensitivity is found to be a viable marker of stress, then it may have promise for use in adaptive training systems. The long-term goal of this research stream is to identify physiological marker(s) that will be effective for real time use in adaptive training programs. The purpose of the present study is to determine the extent to which baroreflex sensitivity changes with acute stress with the short-term goal being to assess the potential utility of spontaneous baroreflex sensitivity as just such a marker.

METHODS

To assess the utility of baroreflex responses as a marker of stress, two studies were performed. The first was designed to assess the extent to which baroreflex responses differed between a physiological stressor and a laboratory-based psychological stressor. These stressors have been commonly employed in research environments for decades but, by design, differ markedly in the nature of the stressor. The second study compared the baroreflex responses between the laboratory psychology stressor and a "real world" occupationally relevant psychological stressor. Depending on the severity and duration of a stressor, the sympathetic nervous system (a major component of the body's autonomic nervous system) and the hypothalamic-pituitary-adrenal (HPA) axis (a major component of the neuroendocrine system) are activated (Ulrich-Lai & Herman, 2009). The methods used here were designed to activate these two systems in varying amounts.

The physiological stressor was a cold pressor test—immersing a foot in ice water. While physically uncomfortable, there was little mental effort associated with this test other than that needed to keep the foot immersed for the time required. The laboratory stressor consisted of a series of cognitive challenges performed under time pressure while observed by the researchers; as such, they included elements of uncontrollability and social evaluation. Feedback was given in the form of a highly visual timer, a scorecard denoting whether the answer was right or wrong, and auditory signals indicating the passage of time (see Figure 1). Consequently, considerable mental engagement and psychological stress was evoked. The cold pressor test has been shown to profoundly activate the sympathetic nervous system but not the hypothalamic-pituitary-adrenal (HPA) axis (Schwabe, Haddad & Schachinger, 2008). The laboratory stressor was designed to strongly activate the HPA axis (Dickerson & Kemeny, 2004) as well as elicit measurable physiological responses (Karthikeyan, Murugappan & Yaacob, 2011).

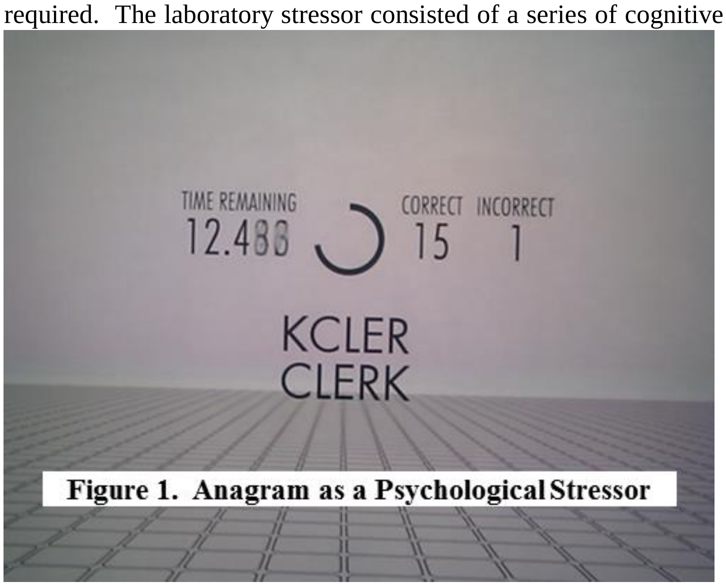

Figure 1. Anagram as a Psychological Stressor

Parenthetically, the long-term goal of this research is to assess the utility of baroreflex markers as a real-time measure of stress for ultimate use in adaptive training sessions. Consequently, these lab stressors were deployed as full-scale virtual environment models in the C6 at the Virtual Reality Applications Center (VRAC) at Iowa State University. The C6 is a six-wall projection system that can deliver three dimensional, fully immersive, interactive virtual simulations. See Figure 2 for an image of a participant fully instrumented prior to beginning the laboratory stressor.

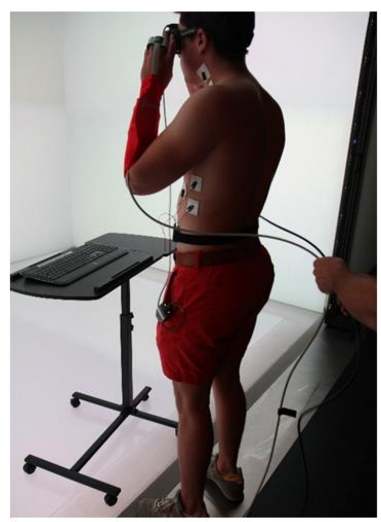

Figure 2. Participant in the C6

The second study built upon the first study and was designed to assess the extent to which baroreflex responses differed between the aforementioned laboratory psychological stressor and a "real world" psychological stressor. It was intended to bridge the knowledge gap between that which occurs in a laboratory setting and that which is seen in the field. For the latter, firefighters were exposed to two relatively common fire ground scenarios where, based on the information gleaned from the scene and from radio traffic, a decision as to how to proceed must be made. One of the two scenarios more overtly evoked time pressure, since the situation became increasingly dangerous the longer the firefighter was exposed to it. As with the laboratory-based stressor, these scenarios were not physically demanding in that the participant did not actually fight the virtual fire. However, they were like the laboratory stressor in that they were cognitively challenging (the participant had to make decisions based on the information available) and had elements of time pressure and uncontrollability (the scenarios were changing dynamically, which affected the appropriate decision choice). However, there was little social evaluation threat.

Study 1. Comparing Baroreflex Responses to Physiological vs. Psychological Laboratory Stressors

Fifteen college age subjects participated in this study (24±4 yrs, 4 females, 11 males) after providing signed informed consent. Upon arrival to the Virtual Reality Applications Center (VRAC) on Iowa State University's campus, participants were instrumented for the continuous assessment of heart rate (3-lead ECG; Biopac, Goleta, CA) and blood pressure (CNSystems, Graz, Austria). After 15 minutes quiet seated rest, each participant experienced either the physiological stressor or the psychological stressor. After 20 minutes rest, the participant underwent the other stressor; order of administration was randomized and counterbalanced. The physiological stressor consisted of the individual submerging their foot into a bucket of ice water (~4°C) for 6 minutes. The laboratory psychological stressor consisted of 1 min each of the color-word Stroop test, anagrams and mental math, repeated once for a total of 6 minutes. These stressors were displayed in 3-D on one wall of the six-sided virtual reality environment of VRAC.

Heart rate and blood pressure were recorded beat-to-beat and subsequently used to assess spontaneous baroreflex sensitivity (SBRS) using the sequence technique (Parati, Di Rienzo & Mancia, 2000). Briefly, sequences of $\geq$3 beats of either progressive increases or decreases in systolic blood pressure and R-R interval (i.e., time between consecutive heart beats, expressed in ms) that were well-correlated ($r \geq .70$) were identified. Then, the slope of the regression line between the parallel systolic blood pressure and R-R interval sequences was calculated and used as the measure of SBRS (Figure 3).

Repeated measures ANOVA were used to compare the heart rate, blood pressure and SBRS responses between the physiological stressor and the psychological stressors.

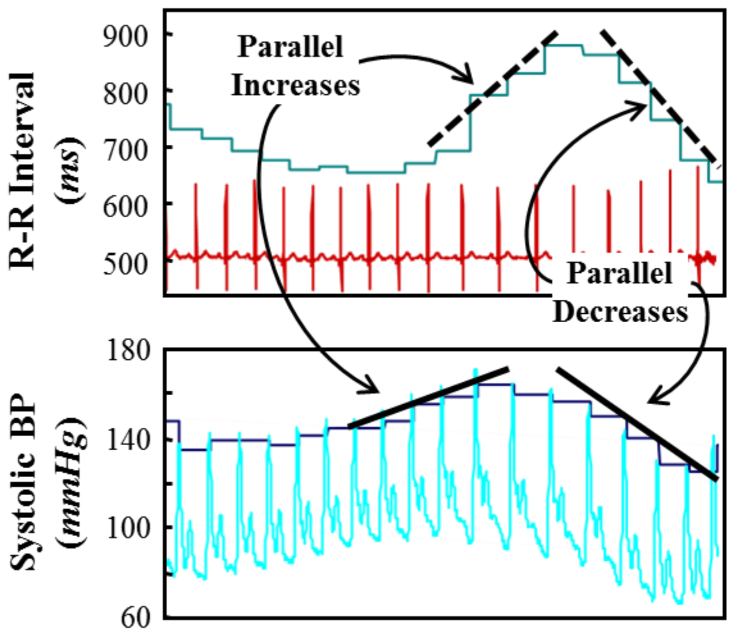

Figure 3. Parallel increases, or decreases, in R-R interval and systolic BP are used to determine SBRS.

Study 2. Comparing Baroreflex Responses to Laboratory vs Occupational Psychological Stressors

Figure 4. Participant in Virtual Reality Environment

Ten male firefighters (33±2 yrs) participated in this study after providing signed informed consent. Participants were instrumented as before and, following at least 15 minutes of quiet seated rest, experienced either the laboratory psychological stressor or an occupationally relevant psychological stressor. Again, the order of administration was randomized and counter-balanced. The laboratory stressors were as previously described except that each of the 3 stressors was 2 minutes in duration and repeated until 10 minutes had elapsed (if administered first) or the duration matched that of the occupational stressor (if administered second). The occupational stressor has been described in detail (Bayouth, Keren, Franke & Godby 2013; Keren, Franke, Bayouth, Harvey & Godby, 2013). Briefly, participants entered VRAC's C6 virtual reality environment and engaged in two stressful fire ground scenarios consisting of pre-backdraft and pre-flashover situations (Figure 4). Each scenario ended when the participant made a decision as to how to handle the situation; participants were free to "move" within each scenario and could take as much time as needed to reach the decision. At the end of each stressor, participants completed the NASA Task Load Index (NASA-TLX; Hart & Staveland, 1988) to assess workload and the Affect Grid (Russell, 1989) to assess feelings of pleasure and arousal.

Following test completion, the SBRS was determined as described for the first study and repeated measures ANOVA was used to compare the responses between the laboratory and occupationally-relevant stressors. Depending on the order of test administration, time spent in the laboratory stressor may have been more than the occupational stressor (e.g., 10 min vs. 6 min). When this occurred, only the laboratory stressor data from the same duration as the latter were analyzed (e.g., only the first 6 min of the 10 min were used).

RESULTS

In comparing the physiological stressor (the cold pressor test) to the laboratory psychological stressor, both stressors elevated HR above rest about equally. The laboratory stressor increased systolic BP considerably but the cold pressor test did not have much of an effect. Importantly, baroreflex sensitivity was reduced with the cold pressor test and even more so with the laboratory stressor. These reductions imply a graded increase in stress. When the laboratory and occupational psychological stressors were compared, both the stressors significantly increased HR over resting about the same. The laboratory stressor did not affect systolic BP but the occupational stressor tended to cause an increase in the systolic BP. Baroreflex sensitivity declined with the laboratory stressor and more so with the occupational stressor. Again, these reductions imply a graded increase in stress. This trend paralleled that seen with the first study but it was not statistically significant. The details of these results, as well as their statistical analyses, are provided in Table 1.

Table 1. Hemodynamic Responses to Stressors

	Physiological vs. Lab Psychological Stress			**Occupational vs. Laboratory Stress**		
	HR (bpm)	**BP (mmHg)**	**SBRS (ms/mmHg)**	**HR**	**BP**	**SBRS**
Rest	--	--	7.1±0.3	--	--	5.9±0.3
Physiological Stressor	+5.1±1.3*	+ 5.4±3.5	6.6±0.4*			
Laboratory Psych. Stressor	+6.7±1.0*	+16.1±4.5*	5.9±0.3*§	+6.0±1.4*	- 1.0±9.9	5.5±0.3
Occupational Psych. Stressor				+8.5±2.4*	+21.7±9.2†	5.0±0.4

"Study 1" refers to comparing responses to physiological vs psychological laboratory stressors.
"Study 2" refers to comparing responses to laboratory vs occupational psychological stressors.
*p<0.001 vs. Rest; §p<0.001 vs. Physiological Stressor; †p=0.086 vs. Rest

When comparing the responses to the two laboratory stressors in Study 1, the stressfulness of the two stressors was not formally assessed. However, feedback from the participants was consistent. They *really* disliked the cold pressor test and found the laboratory stressor to be challenging.

When comparing the responses to the two psychological stressors in Study 2, the NASA-TLX data suggested that the laboratory stressor elicited a higher perceived workload than the occupational stressor (65±6 vs. 43±17, p<0.05, unweighted range is 1-100). This difference was consistent for 5 of the 6 subscores; not surprisingly, it did not differ for the "physical demands" subscore. Data from the Affect Grid suggested that the two stressors resulted in similar levels of mild arousal (6.7±0.6, 6.3±0.6, laboratory vs. occupational stressor, range is 1-9 where 5 is "neutral arousal") but greater "pleasure" was derived from the occupational stressor than the laboratory stressor (7.5±0.3 vs. 4.8±0.7, respectively, p<0.01, where 5 is "neutral pleasure").

DISCUSSION

Extensive efforts have been devoted to identifying physiological markers that can be used effectively for real time training adaptation. Despite these efforts, limited success has been reported so far. The purpose of this research was to determine the extent to which baroreflex sensitivity, or SBRS, changes with acute stress. The need for this research stems from the potential SBRS may have as a tool to assess stress in real-time and, ultimately, be used in adaptive systems that can readily respond to the user's stress state. To the best of our knowledge, SBRS has not been assessed with this goal in mind. While relatively small in scale, the present research provides support for the notion that baroreflex sensitivity changes with changes in stress level. The comparison of the physiological and the psychological laboratory stressors indicated that exposure to the uncomfortable cold pressor test resulted in a decline in baroreflex sensitivity. Since the participants were instructed to keep their foot in the ice water as long as possible, this could be viewed as a threat related stress (Kassam et al., 2009). Since so many participants expressed a marked dislike for this test, we were somewhat surprised to find that SBRS declined even *more* with the laboratory psychological stressor. The assessment of the firefighter responses revealed a continuation of this trend in that SBRS declined with the laboratory psychological stressor but declined even more with the occupational stressor.

Research projects, such as this one, use statistical measures to compare different outcomes. Statistically significant differences are interpreted as very likely reflecting "reality." Small sample sizes, such as used in this pilot project, can hamper how readily statistically significant differences can be found when the differences likely *do* reflect "reality." We are concerned that this may have been the case with our second study involving the firefighters, where differences in baroreflex sensitivity were found but statistical significance was not. To assess the extent to which these differences may be real, an alternative procedure can be used. Cohen's *d* (Cohen, 1988) provides a measure of the effect size, or the strength of the difference between two means. These are provided in Table 2 and reflect the change in SBRS from that seen at rest. Interpreting effect sizes depends on the context of the study but in general, the larger the Cohen's *d*, the larger the "real" difference between the comparisons. Since different participants were in the 2 studies we performed, the effect sizes should not be numerically compared across studies. However, a qualitative ranking suggests that the effects of stress on the magnitude of the decline in baroreflex sensitivity follow the progression of physiological stress, then laboratory psychological stress, and then occupational psychological stress. In other words, the occupational stressor affected baroreflex sensitivity the most.

Table 2. Effect Sizes of Changes in Baroreflex Sensitivity (SBRS)

	SBRS	***Cohen's d***	**SBRS**	***Cohen's d***
Rest	7.1	--	5.9	--
Physiological Stressor	6.6	*.717*		
Laboratory Psych. Stressor	5.9	*1.33*	5.5	*.365*
Occupational Psych. Stressor			5.0	*.583*

For both the studies we performed, it is noteworthy that the SBRS response did *not* parallel the feedback from the participants regarding the relative stressfulness of the interventions. The physiological stressor was disliked considerably more by the participants than was the laboratory psychological stressor, yet the latter resulted in a larger decline in SBRS. The firefighters seemed to enjoy the challenge of the occupational stressor but, like the civilian participants, found the laboratory stressor to be frustratingly challenging. Nevertheless, SBRS declined more with the occupational stressor. It is unclear why there is an apparent disconnect between the psychological perception of various stressful stimuli and the physiological effects of these stimuli. We speculate that one mechanism underlying this disconnect may be the origins of the stress. The physiological stress of the cold pressor test likely did not activate the HPA axis of the autonomic nervous system to nearly the same magnitude as the psychological stressors. Research suggests that blocking a primary component of the HPA-mediated stress response, cortisol, also blocks declines in SBRS (Broadley et al., 2005b); this finding implies that the HPA axis is heavily involved in the stress-associated declines in SBRS. Thus, the decline in SBRS with the cold pressor test may not have been as pronounced because the HPA axis was not as engaged. Partial support for this assertion is provided by the observation that the blood pressure response, which is likely not mediated by cortisol (Broadley et al., 2005b), did not differ between the cold pressor test and the psychological stressor. *Regardless of the underlying* *physiological mechanisms, the important take-home message is that assessing baroreflex sensitivity may provide insight into the psychophysiological state of a person above and beyond what the person can express.*

Baroreflex sensitivity differed between the civilian and firefighter groups both at rest and in response to the stressors. Part of this difference is likely due to the fact that they are two different groups of people—different ages, probably different fitness levels, different reasons for participating in the studies, and the like. Another important aspect, which we did not assess, was that these two groups almost certainly differed in their life experiences related to both prior exposure to stressful events and in their coping mechanisms for that stress. By the nature of their profession, the firefighters likely had been involved in more stressful situations than the students. In addition, the firefighters may have been mildly stressed when they arrived at VRAC. They were on-duty when they participated in this project, albeit given permission by their superior to participate, while the students were receiving extra credit in a course for their participation.

Future Directions

Future research in this area will focus on two objectives. First, more research needs to be performed to better characterize the SBRS responses to different stressors as well as to identify the physiological mechanisms underlying these responses. The present research certainly suggests that SBRS is affected by different forms of stress. However, because of the small sample sizes and limited methodologies, it should be viewed as a "proof of concept" pilot study. Second and more importantly, we need to develop the methodology for the utilization of baroreflex sensitivity measures as a tool for assessing laboratory and occupational stressors in real-time. Achieving this objective will likely not be as challenging as achieving the first objective. There are currently several methods of assessing SBRS utilizing either time-domain or frequency-domain metrics (Laude et al., 2004). Virtually all of them require substantial sampling durations and/or SBRS is calculated after-the-fact. As such, they do not lend themselves to real-time assessments of changes in SBRS. This is what was done in the present study. However, a relatively new method (cross-correlation baroreflex sensitivity; Westerhof et al., 2004) may be a practical alternative. It appears to be as accurate as the more traditional methods (Westerhof et al., 2004) yet only requires a 10 second window of data and can generate values at almost one every 2 seconds. Current work in our laboratory is devoted to assessing the extent to which this method can be employed, in real-time, to create naturalistic decision making scenarios that adapts to the user's cognitive state.

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