Title: Utility of Baroreflex Sensitivity as a Marker of Stress

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Abstract

Presently, adaptive systems use various cognitive and cardiovascular measures to evaluate the functional state of the operator. One marker that has been largely ignored as an assessment tool is baroreflex sensitivity (BRS). This study examined the extent to which baroreflex sensitivity (BRS) changed in response to acute psychological and physical stressors. A total of 20 participants underwent six minute exposures to a psychological stressor and a physical stressor. Baroreceptor sensitivity, blood pressure, heart rate, heart rate variability, stroke volume, cardiac output, mean blood pressure, total peripheral resistance, left ventricular ejection time, and pre-ejection period were continuously measured at rest and throughout the testing period. Compared to rest, BRS significantly decreased during both the psychological and physical stressors. BRS was reduced more with the psychological stressor than the physical stressor. Heart rate and systolic blood pressure significantly increased above rest during the psychological stressor but not during the physical stressor. There were no significant differences from rest or between stressors for the other physiological markers. BRS was more robustly responsive than other cardiovascular measures commonly used to assess the psychophysiological response to stress suggesting BRS is a useful marker for evaluating operator functional state during psychological and physical tasks.

Keywords: Adaptive systems, baroreflex sensitivity, psychophysiological markers, psychological stress, Human-Computer.

Introduction

Human computer interaction (HCI) systems that can provide automated assistance, based on the user's immediate and changing needs, are highly desired. Effective adaptive systems can modify their support based on critical events, the environment, and the operator's performance on the current task (Feigh, Dorneich, & Hayes, 2012). One of the more promising methods for use in adaptive systems is the use of psychophysiological measures to assess changes in operator functional state (e.g., mental workload, fatigue, stress) (Scerbo et al., 2001). This information is collected through real-time sensors which attempt to detect when cognitive resources are increasingly challenged, such as when they become inadequate to fulfill the mission's demands (Dorneich, et al., 2007). Identifying states of mental overload is a high priority in adaptive systems as excessive workloads may inhibit the ability to process incoming information leading to deleterious effects on operator performance (Chen, Haas, & Barnes, 2007; Cummings, Bruni, Mercier, & Mitchell, 2007; Durantin, Gagnon, Tremblay, & Dehais, 2014; Ruff, Narayanan, Draper, 2002).

In order for an adaptive system to respond adequately, it is imperative that the psychophysiological signals reliably and accurately reflect the operator's current state. To that end, using multiple physiological measures versus a single measure provides more adequate information when assessing operator state (Parasuraman, 1990; Ryu & Myung, 2005; Wickens & Hollands, 2000). For example, when assessing operator fatigue, examining EEG bands and operator eye movement provides more evidence of a fatigued state compared to only assessing one of these measures (Schlegel, & Gaillard, 2003). Physiological data can be acquired from multiple systems including the cognitive, ocular, cardiovascular, and respiratory systems.

Signals commonly used include electroencephalography (EEG), electrooculography (EOG), electrocardiography (ECG), respiration rate, and galvanic skin response (GSR) (Scerbo, 2006). However, more recent works have also included the use of thermal imaging to assess cardiovascular and temperature responses to assess operator state (Pavlidis et al., 2007).

Mental workload has often been assessed through electrical activity of the brain via EEG or by neural and hemodynamic responses in the prefrontal cortex (i.e., fNIR) as these measures provide a reliable assessment of cognitive workload (Ayaz et al., 2012; Parasuraman, & Caggiano, 2005; Scerbo et al. 2001; Sterman, Mann, Kaiser, & Suyenobu, 1994; Takeuchi, 2000). In addition to EEG and fNIR, a novel and unobtrusive technique that is sensitive to mental workload is facial thermal imaging which measures the activity of the supraorbital area (Levine, Pavlidis, MacBride, Zhu, & Tsiamyrtzis, 2009). Cardiovascular responses, though, can also reliably detect mental workload (Grossman and Taylor, 2007; Prinzel et al., 2000; Wilson and Russel, 2003). The cardiovascular (CV) variables that respond to state changes in mental workload include heart rate and heart rate variability (HRV), blood pressure, and baroreflex sensitivity (BRS) (Althaus, Mulder, Mulder, Van Roon, & Minderaa, 1998; Van Roon, Mulder, Veldmann, & Mulder, 1995). The literature consistently shows that as the operator’s mental workload increases, heart rate and blood pressure increase while HRV decreases. While much more limited, research suggests that BRS also decreases. However, these changes are time dependent for heart rate and HRV. Short-term segments of mental tasks produce the aforementioned results. Longer lasting experiments (e.g., 45 minutes) found heart rate and HRV levels trending back towards baseline while blood pressure remained elevated and BRS remained at a distinctly lower level (Mulder et al., 1992).

In regards to adaptive systems, the most commonly studied CV measures are heart rate and HRV (Fairclough and Venables, 2006; Ting et al., 2010); blood pressure and, even more so, BRS are less commonly used in these settings (Mulder, Dijksterhuis, Stuiver, & De Waard, 2009; Stuvier et al., 2012). Measuring BRS in conjunction with heart rate and HRV, though, may provide a more comprehensive explanation of changes in these variables, especially during prolonged mental tasks. The reduction in HRV with increased mental effort is related to a reduction in the low frequency power band (0.07-0.14 Hz) (Mulder, 1979) which is associated with regulation of arterial blood pressure through the baroreflex loop (Wesseling, & Settels, 1985). Under normal conditions, the baroreflex loop tightly regulates blood pressure through regulation of sympathetic and parasympathetic outflow via modifications in effectors such as heart rate, myocardial contractility, and arterial resistance (Thomas, 2011). For example, an increase in arterial blood pressure yields an increase in parasympathetic outflow and a decrease in sympathetic nerve traffic, causing a decrease in heart rate, myocardial contractility, and arterial resistance. During emotional excitement when the “flight or fight” response is evoked, baroreflex sensitivity is inhibited by influences of the telencephalon and diencephalic systems, specifically the rostral ventrolateral medulla, which allows for inconsistent increases in both heart rate and blood pressure (Berntson, 1991). Mild stressors, such as mental arithmetic, cause similar reductions in BRS (Lipman et al., 2002; Steptoe & Sawada, 1989; Slight, Fox, Lopez, & Brooks, 1987). Thus, reductions in BRS may explain the shift in heart rate and HRV towards baseline during prolonged mental tasks.

One essential characteristic of physiological measures usable for adaptive systems is the ability of the measure to reflect changes in operator performance (Byrne & Parasuraman, 1996). Heart rate variability is associated with and predictive of operator performance (Haarmann, Boucsein, & Schaefer, 2009; Wilson and Russel, 2003; Wilson and Russel, 2007). Durantin and colleagues (2014) found HRV to be increased during extremely high task loads, where performance was the worst, compared to low level task loads which resulted in decreased HRV and high performance scores. This inverted-U response suggests that at high levels of mental overload, some cardiovascular responses may drift toward baseline levels when mental capacity is met. This response is similar to levels being reversed over long periods of task load. However, blood pressure and BRS were not examined so it is unknown if this relationship is true for these measures.

Few studies have examined BRS as a predictor of performance. Yasumasu and colleagues (2006) found BRS to be negatively correlated (*r* = -.51) with performance; continual reductions in BRS were linked with achievement of higher performance levels during a mental arithmetic task. Baroreceptor sensitivity was also the only variable which was an independent predictor of performance (Yasumasu et al., 2006). Work completed by Duschek et al. (2009) found BRS to be inversely associated with performance during a visual attention tasks. Both of these studies, however, only examined the changes in BRS during either a mental arithmetic tasks or a visual task. Most adaptive settings will require individuals to focus on many tasks at once (i.e., visual, auditory, working memory) so it would be beneficial to examine the change in BRS under multiple stressors. In addition, no study to date has systematically assessed the comparability of BRS responses to other more commonly assessed cardiovascular markers of stress state. Consequently, the present study was designed to compare the acute changes in HRV, blood pressure, and BRS during high levels of mental load and during an intense physical stressor. A second purpose of the study was to examine the relationship between BRS and performance. A third aim of the study was to examine the effector modulators that regulate blood pressure (heart rate, myocardial contractility, and arterial resistance) to further explain changes in blood pressure and BRS.

Methods

Overview of Experimental Design.

A within-subjects design was used to assess physiological changes under two conditions of stress—one consisting of a series of psychological stressors (i.e., Stroop word test, anagrams, mental arithmetic) and the other consisting of a physical stressor (i.e., cold pressor test). The psychological stressors were adapted into an interactive software application that required the participant to use a keyboard to respond to each task with the tasks displayed in 3-D on one 10 foot wall of a six-sided virtual reality system using a custom simulation engine, VirtuTrace (Figure 1). To increase distress, both visual (e.g., number of correct answers, time remaining) and auditory feedback (e.g., different tones for correct and incorrect answers) were provided. A virtual environment was chosen for this task in order to test the practicality of using BRS in this setting. The physiological stressor, foot immersion in an ice bath, was administered in the room immediately adjacent to the virtual reality environment.

Upon arrival in the laboratory, each participant was instrumented for the continuous assessment of the physiological responses. The experimental session commenced with a baseline period of 20 minutes of quiet seated rest. At the end of the rest period, participants began either the physiological or psychological stressor. The stressor lasted 6 minutes and was immediately followed by 20 minutes of quiet seated rest to allow responses to return to baseline. Participants then performed the other stressor. Order of stressor administration was determined using a randomized, counter-balanced design.

Participants

Fifteen males and five females, between the ages of 20 and 38, participated in this study. All were apparently healthy without a history of circulatory problems and denied being color blind. Participants were recruited through campus advertisement and email. Potential participants underwent an orientation session where they became familiar with the procedures of the experiment and the laboratory environment. As part of this orientation, each participant was informed of the experimental measures and signed a written consent form approved by the university institutional review board.

Physiological measures

Heart rate and Heart Rate Variability

All physiological data were recorded by an integrated hardware and software package (Biopac MP150, Acqknowledge; BIOPAC Systems, Inc., Goleta, CA). The data used for measures of heart rate and heart rate variability were collected by a 3-lead ECG configuration with disposable electrodes placed on the left rib cage, right clavicle, and the ground electrode on the right rib cage. The ECG data were collected wirelessly using a Biopac BioNomadix transmitter with data sampled at a rate of 1000Hz and amplified using a Biopac ECG100 electrocardiogram amplifier. The ECG signal was manually inspected for artifact and corrected by interpolation. The distance between the R-R intervals was calculated from the ECG signal based on a modified Pan-Tompkins QRS detector (Pan, & Tompkins, 1985) implemented by the software. These results were used to calculate heart rate. The corrected R-R intervals were then exported into Kubios HRV software (Biomedical Signal Analysis Group, Department of Applied Physics University of Kuopio, Finland) for HRV analysis. To remove trend components, data were detrended by removal of the first order linear trend using the smoothness priors method (Tarvainen, Ranta-aho, & Karjalainen, 2002). A low level of artifact correction was applied to the entire data set. Detected artifacts beats were replaced using cubic spline interpolation using a sample rate of 4Hz. A Fast Fourier transform algorithm was performed using Welch's periodogram method with a window width of 256s and window overlap of 50%. The frequency bands used were low frequency (LF): 0.04-0.15 Hz and high frequency (HF): 0.15-0.4 Hz. HF is primarily mediated by parasympathetic activity and includes the effects of respiratory activity on the cardiac internal signal (Mulder, 1979) while LF reflects sympathetic and parasympathetic activity and is associated with the regulation of short-term blood pressures (Task Force, 1996). The LF/HF ratio was calculated and changes in the LF/HF ratio were used as an indication of fluctuations in sympathetic activity. To account for temporal changes in total power, the frequency power values are expressed in normalized units.

Cardiovascular Impedance

Cardiovascular impedance was measured in order to assess the myocardial effector modulators that regulate blood pressure. Cardiovascular impedance was recorded using a spot electrode configuration with four voltage and four current electrodes. One pair of voltage electrodes was placed at the base of the neck while the lower pair was positioned in the mid-axillary line, at the level of the xiphisternal junction. The current electrodes were placed parallel to the voltage electrodes with the upper pair placed 5 cm above the neck voltage electrodes and the lower pair placed 5 cm below the thoracic electrodes (Sherwood et el., 1990). The impedance data were collected wirelessly (Biopac BioNomadix) at a sample rate of 1000 Hz and the signal was amplified using a Biopac NICO100C module. Stroke volume (SV), cardiac output (CO), left ventricular ejection time (LVET), pre-ejection period (PEP), and total peripheral resistance (TPR) were calculated from the data collection. Myocardial contractility was assessed through changes in stroke volume, cardiac output, left ventricular ejection time, and pre-ejection period. Cardiac output, in conjunction with mean arterial pressure, was also used to assess changes in total peripheral resistance.

Blood Pressure and Baroreceptor Sensitivity

Blood pressure was recorded by a noninvasive blood pressure system (Biopac NIBP100D). This method employed a double finger cuff on the left hand and a vascular unloading technique to assess arterial pressure continuously (CNSystems Medizintechnik AG, Austria). This signal was referenced to blood pressures assessed at rest with a standard arm cuff and integrated into the software package used to collect and analyze the other cardiovascular variables. Beat-to-beat systolic blood pressure (SBP) and mean arterial blood pressure (MAP) were analyzed.

Baroreflex sensitivity (BRS) was determined using the sequence technique (Parati, Di Rienzo, & Mancia, 2000). Here, sequences of greater than 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 ($r > .70$) were identified. The mean slope of the regression line between these parallel sequences was then calculated and depicted as the sensitivity of the cardiac BRS (ms/mmHg).

Psychological Stressor

Psychological stress was induced by three tests: 1) Stroop word test, 2) anagrams, and 3) mental arithmetic. These tests provoke stress in different ways (i.e., conflict vs implicit memory) and are primarily cognitive challenges. However, they have been well documented at provoking stress responses, specifically, acute cardiovascular stress responses (Fauvel et al., 1996; Boyes & French, 2010; Allen, Boquet, & Shelley, 1991). These tests also activate both the sympatho-adrenal-medullary (SAM) and the hypothalamic-pituitary-adrenal (HPA) axes (Jönsson, Wallergård, Österberg, Johansson, & Karlson, 2009).

The Stroop word test consisted of identifying the ink color of a printed word by using the designated keys of the keyboard [R (red), Y (yellow), B (blue) and G (green) for the respective colors]. Participants had 1.1 seconds to respond to each color-word. For the anagram task, a five letter scrambled word appeared on the screen and participants were to unscramble the word using the keyboard. Words were selected from a standardized list with time allotment dependent on the anagram and varying from 10 to 160 seconds (Tresselt & Mayzner, 1966). Lastly, the arithmetic task consisted of subtracting a two-digit number from a four-digit number in less than 7 seconds (Acevedo et al., 2006). Participants performed each task for 1 minute and then the series of tasks was repeated once for a total of 6 minutes.

Physical Stressor

Physical stress was provoked by a cold pressor test (Hines & Brown, 1936). The cold pressor test elicits a robust vascular sympathetic response (Mourot, Bouhaddi, & Regnard, 2009). It strongly activates the SAM axis but is less capable of activating the HPA axis (Schwabe, Haddad, & Schachinger, 2008). Participants submerged their right foot in a bucket of ice water (~4°C) for 6 minutes. This procedure was performed while participants were seated and positioned similarly to that of the psychological stressor. Participants were asked to refrain from excess movement or clenching of body parts during this time. There was no verbal communication or encouragement by the researchers during either of these 6 minute stressors.

Statistical Analyses

Mean values for HR (bpm), SV (mL), CO (L/min), LVET (ms), PEP (ms), MAP (mmHg), TPR (mmHg/L/min), HRV (LF/HF; HF; LF), and BRS (ms/mmHg) were calculated for the last 5 minutes of the rest period and for the 6 minutes of each task. A one-way within subjects repeated ANOVA for each physiological measure was carried out to determine mean differences between rest, psychological stress, and physical stress. Significant differences were located using the Holm- Šídák multiple comparisons procedure. Effect sizes for differences between stressors and resting baseline were calculated using Cohen's *d* (Cohen, 1988). The relationship between BRS and performance (percent correct) on the psychological stressors was assessed with simple linear regression analysis. The *r* coefficient is reported. The threshold of significance was set at $p < 0.05$. Values are presented as means ± standard error of the means (SEM).

Results

Participants

The final data set consisted of 15 men and 5 women between the ages of 20 and 38 years ($M = 23$, $SD = 5$) who were senior undergraduate students within the university. Due to technical problems and one male participant being unable to complete the physical stressor for the allotted time, some data points (2%) are missing from some subjects in all scenarios.

Heart Rate and HRV

A one-way ANOVA showed heart rate to be significantly changed (F (2, 19) = 10.51, $p < .001$) with the stressors. The psychological stressor had a greater effect on heart rate compared to rest ($t = 4.550$, $p < .001$, $d = 1.367$) and the physical stressor ($t = 2.73$, $p = .010$). Heart rate variability in the high and low frequency bands were changed from baseline, but these differences were of borderline significance ($p = .08$; $p = .09$, respectively). The LF/HF ratio did not differ significantly between resting and the two stressors ($p > .6$).

Impedance Measures

The statistical analysis revealed no significant results for the impedance measures ($p > .05$; Table 1). However, a medium effect size was found for LVET for the psychological stressor ($d = .50$) and the physical stressor ($d = .56$).

Blood pressure and Baroreceptor Sensitivity

Systolic blood pressure was significantly changed from rest (F (2, 15) = 9.58, $p < .001$) as pressure increased with the psychological stressor ($t = 4.2$, $p < .001$, $d = 0.9$) compared to rest and compared to the physical stressor ($t = 2.7$, $p = .012$). No significant difference between rest and physical stress was found.

A significant difference was found for BRS between rest and both stressors (F (2, 15) = 14.13, $p < .001$). BRS decreased during the psychological stressor ($t = 5.17$, $p < .001$, $d = 1.4$) and the physical stressor ($t = 2.58$, $p = .016$, $d = 0.7$) compared to rest. BRS was significantly lower during the psychological stressor compared to the physical stressor ($t = 2.41$ $p = .002$). Figure 2 shows the changes in BRS, HR, and SBP.

Table 1 presents the physiological measures obtained at rest and during the psychological and physical stressors.

Relationship between Cardiovascular Measures and Psychological Performance

Performance scores (percent correct) were higher during the Stroop word test (69%) and mental arithmetic (67%) compared to the anagram tasks (54%) (F (2, 19) = 5.61, p = 0.007). The performance scores for the anagram task were lower than either the Stroop word test (t = 3.05, p = .004) or the mental arithmetic task (t = 2.73, p = .010). There were no significant differences between the Stroop word and mental arithmetic tasks. Baroreceptor sensitivity was negatively correlated with performance during the anagram (r = -.41) and the Stroop word test (r = -.31), but these associations were not significant (p > .05).

Discussion

Computer-based adaptive systems currently use a handful of psychophysiological markers (e.g., GSR, EEG) to assess the operator's functional state. The importance of a reliable marker lies in its potential usability to adequately and non-invasively measure the operator's current state, thereby allowing the system to adjust appropriately. Cardiovascular (CV) measures reliably change with mental load and can be collected relatively non-invasively. One CV marker that has not been studied extensively for adaptive systems is baroreflex sensitivity (BRS). Prior research found BRS to be markedly changed during mental tasks (e.g., mental arithmetic). However, these changes have not been compared to a comprehensive panel of cardiovascular measures nor has the relationship between BRS and performance been extensively studied. The aim of the present study, therefore, was to assess BRS to determine its sensitivity and responsiveness during acute psychological and physical stress, compare BRS to other cardiovascular markers of stress and, finally, to examine the association between BRS and operator performance.

The principal finding of this study was that BRS was more sensitive to the stressors than the other cardiovascular measures (SV, CO, LVET, PEP, TPR, MAP, and HRV). BRS declined significantly in response to the two different kinds of stressors (psychological and physical) while the other markers did not consistently respond to both stressors. For example, heart rate increased during the psychological stressor but not during the physical stressor. This finding is consistent with previous research (Leblanc, Cote, Jobin, & Larie, 1979; Mourot, Bouhaddi, & Regnard, 2009). In addition, the psychological stressors produced a greater statically significant reduction in BRS compared to the physical stressor. These reductions in BRS were paralleled by the significant increases in heart rate and blood pressure during the psychological stressor. The reductions in BRS were most likely initiated in the central command centers of the brain by altering the BRS and then reducing the efferent response to the sensed increase in blood pressure. The magnitude of this statistically significant change in BRS from baseline due to the psychological stress was quite robust (*d* = 1.4).

The anagram task was more difficult for the subjects than either the Stroop word test or mental arithmetic task. The change in BRS was most strongly correlated with performance on the anagram task (*r* = -41). These results are similar to Yasumasu and colleagues (2006) who found performance on a psychological stressor to be inversely correlated with BRS (*r* = -.51). This relationship may be explained by the Lacey intake/ rejection theory which hypothesizes that tasks demanding internal psychological concentration and rejection of external distractions reduce baroreflex sensitivity which allows for an increase in cardiovascular activity (i.e., heart rate and blood pressure) (Lacey, & Lacey, 1970). In the present study, the psychological stressor may have produced an environment where the participants had to internally focus while blocking external disturbances. This is noteworthy here, since the external distractions during the psychological stressors were heightened via auditory cues for each correct and incorrect response. Thus, this finding supports the notion of designing adaptive systems to take over some tasks which are distracting to the operator during high cognitive demands.

One unexpected outcome was the lack of a significant HRV response to the two stressors. Though not statistically significant, the HF component responded in the expected direction for both stressors as the changes from rest reflect the fluctuations in parasympathetic tone and heart rate. The LF component, on the other hand, tended to increase during the psychological stressor and decrease during the physical stressor compared to rest. The reduction in LF during the physical stressor may be due to the suppression of arterial pressure regulation by the baroreflex loop causing the decrease in BRS. The increase during the psychological stressor can be interpreted as sympathetic activation which is supported by the increase in blood pressure and heart rate.

One limitation of the present study was the small sample size of 20 participants. While medium to large effect sizes were present, the small sample size likely affected statistical power to the point that we did not see statistical significance in the LF and HF components as well as the other CV measures. Nevertheless, the effect sizes seen with the BRS measure were larger than the other CV measures, reinforcing its potential utility as a marker of stress. A second limitation of this study was the focus on only cardiovascular stress markers. While this narrow perspective was purposeful in the present study, future studies should compare BRS to EEG, GSR, and eye tracking techniques during cognitive tasks. In conjunction, BRS should be examined during other types of tasks that may be more relatable to those performed in adaptive system machines. A third limitation of the current study was the selection of psychological stressors. While these tests are standard laboratory tests proven to provoke a stress response, there are subtle cognitive differences between each test. A final limitation of the present study was the absence of a subjective measure of stress. While verbal feedback from the subjects reinforced the stressfulness of the intervention, a subjective measure of stress may have clarified the findings.

In conclusion, BRS was significantly reduced during psychological and physical stress and to a greater degree during psychological stress. BRS was more robustly responsive to the two stressors than other, more commonly used, cardiovascular measures of stress. Our findings parallel previous work indicating that BRS reliably changes during cognitive tasks, but extends it by suggesting it may be a viable tool for assessing an operator’s functional state. In addition, BRS was associated with performance—a key component of task allocation in adaptive systems. Nevertheless, further research comparing BRS to common psychophysiological sensors in a wider array of stressors and performed in real time is greatly needed. Finally, further research should assess the feasibility of assessing BRS in real time (Westerhof et al., 2006) for use within adaptive systems.

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