Psychological acute stress measurement using a wireless adhesive biosensor

Nandakumar Selvaraj

Abstract— **Stress management is essential in this modern civilization to maintain one's stress level low and reduce health risks, since stress is one of the primary causes leading to major chronic health disorders. The present study investigates the validity of stress index (SI) metric that objectively quantifies the psychological acute stress using a disposable adhesive biosensor worn on the chest called as HealthPatch®. Eleven healthy volunteers (n=11) were attached with one HealthPatch sensor at left pectoralis major muscle along the cardiac axis to record modified Lead-II ECG. The subjects carried out a standard Trier Social Stress Test (TSST) protocol. During the study, the subjects filled out state anxiety form-Y1 of the State Anxiety Inventory questionnaire (sSTAI); salivary samples were obtained for salivary alpha-amylase (sAA) and salivary cortisol (sC) measurements; and the HealthPatch sensor data were wirelessly acquired. The data analyses revealed that sSTAI scores were significantly increased ($P<0.001$) due to TSST compared to the baseline. But, the changes in both sAA and sC measurements were not significant ($P=0.281$ and $P=0.792$, respectively). On the other hand, SI metric of HealthPatch showed significant ($P<0.001$) increase ($\sim$50%) during TSST, and shown to be sensitive to objectively track acute changes in psychological stress. Thus, HealthPatch biosensor can be valuable for continuous monitoring of psychological health and effective management of stress leading to healthy life.**

Index Terms— **Psychological stress, Heart rate variability, Trier Social Stress Test, State-Trait Anxiety Inventory.**

I. INTRODUCTION

Human body regulates its internal environment by various physiological processes, and maintains at a certain state of equilibrium called as homeostasis. Stress is referred to the disruption of homeostasis leading to a perturbed state of the human body. Stress can be triggered by various factors known as stressors including physical (e.g. diseases/illness, allergy, fatigue and poor sleep), psychological (e.g. conflicts, trauma, financial state and work/educational demands) and environmental (e.g. noise, crowd, disasters and pollution) influences. The human body's reaction to the stressors is called as stress response, which is predomiantly regulated by hypothalamic-pituitary-adrenocortical (HPA) and sympathetic-adrenal-medullary (SAM) systems [1]. These systems interact by releasing stress hormones (glucocorticoids and catecholamines), and cause physiological changes including vasomotor tones, heart rate variability (HRV), blood pressure and sweat production at the body peripherals.

Stress is beneficial to manage the demands in work/education, drives to accomplish the goals/tasks efficiently, and generate fight-or-flight response in danger. On the other hand, stress is one of the primary causes leading to major chronic health disorders including diabetes, obesity, heart disease, gastrointestinal conditions, depression and anxiety problems [2]. Therefore, stress management is essential in this modern civilization to maintain one's stress level low, and reduce health risks.

Though there is no specific "Gold Standard" reference measurement has been established for stress, stress levels are generally assessed based on self-assessment using questionnaires e.g., State-Trait Anxiety Inventory (STAI), and perceived stress scale. Self-assessment is highly impractical for continual assessment, and it is also less reliable due to bias, random responding, and social compulsion to falsify the questionnaire responses to project a positive self-image.

Salivary-based noninvasive measurements such as salivary alpha-amylase (sAA) and salivary cortisol (sC) have been employed to objectively quantify the psychosocial stress response in individuals [1, 3]. The sensitivity and reliability of salivary measurements are limited due to number of factors including the sample volume [4], type of cotton rolls/swabs, and methodological issues such as time of sampling, assay conditions, storage and compliance to the protocol [5].

Stress can also be objectively detected using the physiological changes in blood pressure, heart rate (HR), HRV, galvanic skin response and pupil diameter [6]. Wearable smart sensors are widely used nowadays to capture the physiological and behavioral data in our day-to-day lives to correlate with stress. But, there are hardly any clinical-grade physiological monitors that can accurately quantify stress levels across individuals.

HealthPatch® is a clinically validated disposable medical device worn on the chest that remotely monitors single lead ECG, HR, HRV, breathing rate, skin temperature, step count, posture and fall detection [7, 8].

HealthPatch sensor also provides continuous assessment of changes in acute psychological stress levels as Stress Index (SI). The validity of SI metric for acute stress measurement is presently investigated compared to the standard self-assessment questionnaires and salivary-based biometrics.

II. MATERIALS AND METHODS

A. Study Group

The study recruited 11 volunteers (age: 47±17 years, body mass index: 24±4.6 and female/male: 6/5) from the local community of Palo Alto, CA, USA, through online and print media. The inclusion criteria included the age limits of $21-85$ years and medical insurance coverage. The exclusion criteria included severe skin reaction to adhesives, current

Author is with Vital Connect Inc., Campbell, CA 95008, USA, e-mail: nselvaraj@vitalconnect.com; snandaa@gmail.com

pregnancy, cardiovascular diseases, mood/psychiatric disorders, nicotine/tobacco usage and substance abuse treatment. The participants provided demographic information, medical history and written informed consent.

B. Stress Questionnaire

State-Trait Anxiety Inventory [9] is a questionnaire commonly used in clinical settings to diagnose anxiety/depression, and assess the distress level. The form-Y1 of STAI, state anxiety questionnaire (sSTAI), consists of 20 statements for assessing the acute stress including "I feel calm", "I am tense", "I am at ease", "I feel nervous", and "I am jittery". Each statement is rated on a 4-point scale where 1 refers to not at all, 2 refers to some what, 3 refers to moderately so and 4 refers to very much so. The user has to circle the appropriate 4-point scale to indicate how he/she feels at the given moment. The sSTAI score of range $0-80$ is evaluated as the accumulated sum of points from all the 20 questions.

C. HealthPatch Sensor

HealthPatch is a disposable adhesive patch biosensor [7, 8] that incorporates two surface electrodes with hydrogel at the bottom side. An electronic module that consists of an embedded processor, tri-axial accelerometer and Bluetooth Low energy (BLE) transceiver is inserted in to the adhesive patch sensor and paired with a relay device for wireless data collection. HealthPatch sensor is adhered to the chest and collects ECG and tri-axial accelerations of the upper torso. The raw waveforms captured by the HealthPatch is processed by the firmware algorithms on the electronic module and generate number of physiological measures including HR, HRV, breathing rate, activity level, energy expenditure and psychological SI. The changes in psychological stress level in individuals is detected based on the changes in HR and HRV measurements at the constraint of no activity, and mapped to SI as a stress score in the range of $0-100\%$ using machine learning algorithms.

D. Experimental Design

The study was sponsored by Vital Connect Inc (Campbell, CA, USA), and conducted at a Stanford laboratory facility by the Psychiatry and Behavioral Sciences, Stanford School of Medicine (Palo Alto, CA, USA). The experimental design of this study involving human subjects was approved by Institutional Review Board. The participants were instructed to rinse their mouth with water and refrain from eating, drinking and chewing at least 15 minutes prior as well as during the study.

One HealthPatch biosensor was prepared for use with the module insertion, and pairing of the sensor with a relay device for wireless data collection in each participant. The release liner of adhesion was removed, and the patch sensor was attached at a recommended location of left pectoralis major muscle along the cardiac axis (modified Lead-II ECG). After the sensor attachment, participants filled out the sSTAI questionnaire, and provided a saliva sample in a plastic salivette container using salimetric oral swabs as baseline measurements. Data collection was initiated, and the relay device wirelessly recorded the HealthPatch data during the study. The protocol first consisted of 5 min baseline that allowed the user to relax on upright sitting posture.

Followed by the baseline measurement, the participants were introduced to the Trier Social Stress Test [3] that consists of free-speech and mental arithmetic (MA) tasks. The participants had to take over a job applicant role, prepare a free-speech for 5 min, and convince the selection committee that he/she was the perfect applicant for the job during a personal interview. The subjects were informed that the interview process will be recorded by video and audio to assess the interview performance, and not allowed to use any written concept of their speech. Following those instructions, the subjects were given 10 min to prepare their speech task.

After 10 min preparation period, the subject was guided to the interview room. One of the managers welcomed the job applicant, and asked to deliver the talk for the next 5 min. The managers maintained neutral expressions during the speech. If the subject finished the speech before 5 min have elapsed, the managers told the subject "You still have some time left and please continue". If the subject finished second time before the end of 5 min, the managers remained quite for 20 seconds, and then asked few prepared questions. At the time +15 min, the speech task was complete.

The selection committee now asked the subject to serially subtract the number 13 from 1022 as fast and accurately as possible. On every failure, the subject was required to restart at 1022 and serially subtracting the number 13. At the time +20 min, the MA task was complete, and the subject was taken back to the sensor hook-up room. The participant filled out sSTAI questionnaire, and provided second saliva sample for post-TSST measurements. The subject was allowed to relax for 5 min with optional reading materials. At the end of recovery, third saliva sample was collected as recovery measurement, and the data collection was terminated. HealthPatch data was downloaded from the relay device to an encrypted laptop for data analyses. The saliva containers were frozen with appropriate labels, and sent to the laboratory to quantify the sAA and sC levels after the study was completed.

E. Data Analysis

As acute stress reference measurement, sSTAI scores were calculated for baseline and post-TSST conditions in 11 subjects using sSTAI questionnaire responses. Wilcoxon signed rank test was used to determine the statistical significance of sSTAI scores between baseline and post-TSST conditions.

The sAA and sC measurements were obtained using standard salivary assay analyses of the collected saliva samples in 8 participants for 3 instances: (i) baseline, (ii) post-TSST and (iii) recovery period. Salivary measurements could not be obtained in 3 subjects due to various reasons including the quantity of saliva was insufficient for assay analyses.

The continuous data collection using HealthPatch sensor allowed segmentation of the protocol in to 4 stages as (a)

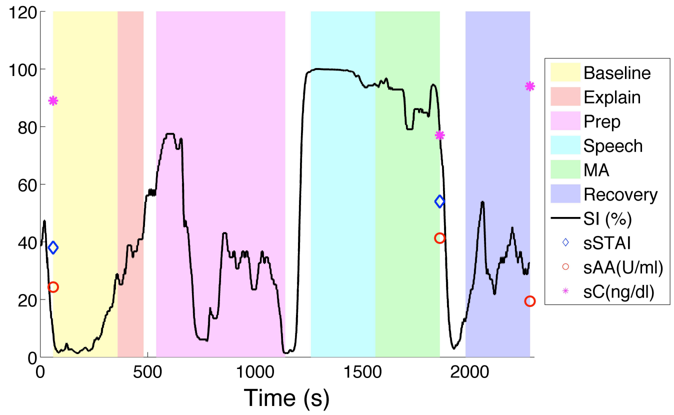

Fig. 1: A sample data collection during the acute stress protocol including state anxiety questionnaire (sSTAI) scores, salivary alpha-amylase (sAA), salivary cortisol (sC), stress index (SI) measurements.

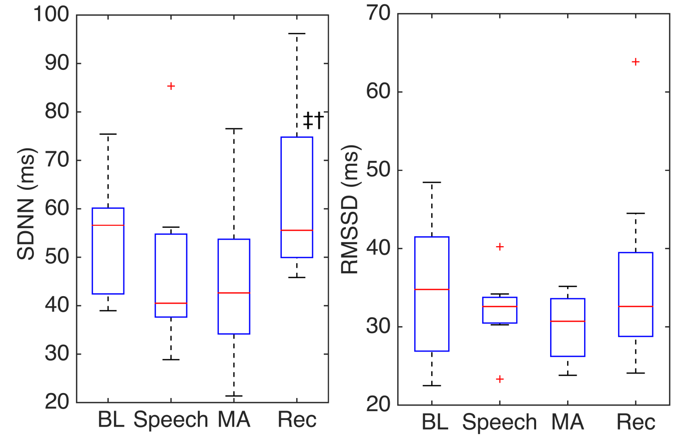

Fig. 3: SDNN and RMSSD values of HealthPatch measured (n=9) during BL, speech, MA and recovery conditions. ‡, P$<$ 0.05 compared to Speech; †, P$<$ 0.05 compared to MA.

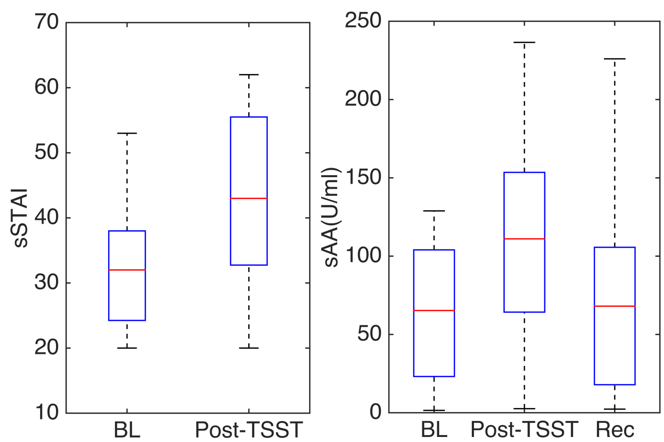

Fig. 2: The sSTAI scores (n=11) and sAA measurements (n=8) are given for acute stress test protocol conditions.

baseline (BL), (b) speech, (c) MA and (d) recovery. 3-min epochs of HealthPatch data were extracted for each stage of the protocol in 9 participants (2 subjects failed to complete the speech test, and thus excluded). The HealthPatch data streams included for data analyses were HR, standard deviation of normal-to-normal (NN) intervals (SDNN), root mean square successive differences of NN intervals (RMSSD) and SI. Statistical values of these measurements were calculated for each epoch in each individual.

Kruskal-Wallis one-way analysis of variance test with post-hoc Tukey-Kramer multiple comparison test were performed to find the statistical significance (P value set to be $<$ 0.05) in sAA, sC and HealthPatch measurements during various stages of the protocol. The values are given as mean±standard deviation (SD).

III. Results

Figure 1 illustrates a sample data including sSTAI, sAA, sC and SI measurements during the acute stress protocol. After speech and MA tasks, the discrete measurements of sSTAI and sAA were noticeably increased, but sC decreased in this subject. The time varying changes in HealthPatch's SI clearly demonstrated elevated levels of acute stress in this data during speech and MA tasks.

The reference sSTAI scores obtained in the study group (n=11) showed significant (P$<$0.001) increase in psychological acute stress due to TSST compared to the baseline (43.5±13.1 vs. 32.1±10.1) as shown in Figure 2 (left). The salivary Alpha-amylase (sAA) values obtained in 8 subjects were found to be 64.4±47.3 U/ml, 112.1±73.4 U/ml, and 76.4±72.9 U/ml for baseline, post-TSST and recovery conditions, respectively (Figure 2-right). But, the changes in sAA measurements were not significant (P=0.281). Only 3 out of 8 subjects showed noticeable increase in sAA due to TSST compared to the baseline. The salivary cortisol (sC) values measured (n=8) during baseline, post-TSST and recovery conditions were 0.14±0.06 μg/dl, 0.20±0.19 μg/dl, and 0.21±0.21μg/dl, respectively. Further, sC measurements also showed no significant changes (P=0.792) during the stress protocol.

HealthPatch measurements in 9 subjects (n=9) revealed significant differences (P=0.012) in SDNN of HRV, where the recovery phase (73.0±17.4 ms) showed significant increase compared to speech (48.5±17.9 ms) and MA (45.2±18.6 ms) stages (Figure 3-left). RMSSD of HRV did not show any significant changes (P=0.652) in its magnitude, however the variance of RMSSD decreased distinctively during speech as shown in Figure 3 (right).

HR and SI showed significant changes (P=0.003 and P$<$0.001, respectively) during the protocol as shown in Figure 4 (left and right, respectively). HR significantly increased during speech (91.1±10.8 bpm) compared to the baseline (74.8±8.2 bpm), and later significantly decreased to baseline levels during recovery (76.2±10.6 bpm). SI measure showed significant increase in acute stress during speech (84.1±17.7 %) and MA (76.0±23.7 %) stages of the protocol compared to the baseline (36.4±12.3 %), and later significantly decreased to baseline stress levels during

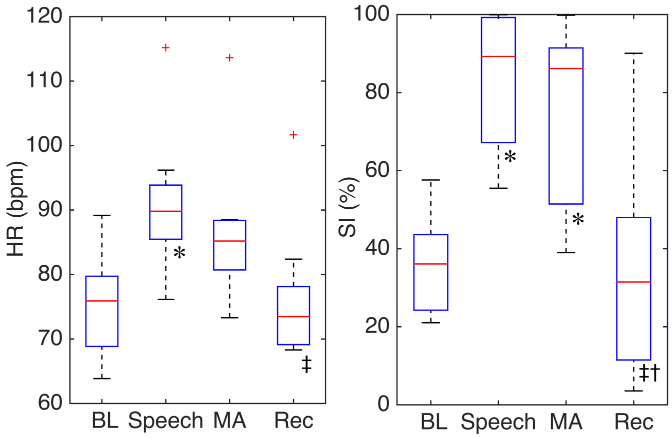

Fig. 4: HR and SI values of HealthPatch obtained (n=9) for BL, speech, MA and recovery conditions. *, P$<$ 0.05 compared to BL; ‡, P$<$ 0.05 compared to speech; †, P$<$ 0.05 compared to MA.

recovery (33.6±26.7 %). The relative changes in SI (△SI) for speech and MA stages with respect to the baseline were found to be 47.8±16.9 % and 39.6±23.7 %, respectively. The results suggest that SI metric of HealthPatch is sensitive for objective and continuous measurement of acute changes in stress level across individuals.

IV. Discussion

The present study investigated the efficacy of HealthPatch patient monitor and salivary measurements to detect the acute changes in psychological stress induced by a standard TSST protocol compared to the traditional self-assessment questionnaires. The stress responses of both hormonal (HPA) and neuronal (SAM) systems were assessed with sC and sAA/SI responses, respectively. The results indicated that both salivary-based measurements sAA and sC did not produce significant changes to reflect the increase in acute stress due to TSST. But, the HealthPatch showed significant increase in SI (∼50%) due to TSST.

The current findings that sAA stress response peaks immediately after the TSST, but showed no significant changes due to TSST are in agreement with [1]. On the other hand, sC response to acute stress is believed to peak at +10 to +20 min after TSST [1, 3] that indicates delayed onset or longer latency of stress response in sC than sAA. The sC responses measured currently at +5 min after TSST showed no significant changes due to TSST. A recent study revealed that sC hormonal responses were significantly different in different body composition groups, but the neuronal responses in sAA and HR were insignificant [10]. Thus, the salivary measurements, in particular sC, can vary widely with body composition [10], age, gender, medication/nicotine use, genetic factors and methodological issues [3, 5]. It is very challenging to interpret the cause and effect in salivary responses, which are affected by several factors. Therefore, sensitivity and reliability of salivary measurements for objective assessment of acute stress needs further investigation.

In contrast, the HR response to TSST stimulation was found to be quick and significant, and not significantly correlated with endocrine responses [3]. HR response to TSST in the current study is in agreement with [3]. Hence, SI response based on HR and HRV show high sensitivity to stress detection, and can be used to objectively track changes in psychological acute stress. The wireless HealthPatch biosensors have previously demonstrated high accuracy and wearability, and seamless data collection for long-term remote monitoring of vital signs [8]. Thus, HealthPatch's ability to capture the day-to-day patterns in HR, HRV and SI levels can be useful in many clinical applications including post-traumatic stress disorder, depression and insomnia.

In conclusion, HealthPatch's biometrics including vital signs and SI can provide feedback about the patient's stress levels, offer awareness about his/her state of mind, and has implications for prevention and detection of cardiac and stress related diseases. The study reveals that HealthPatch biosensor can be valuable for continuous monitoring of psychological health and effective management of stress leading to healthy life.

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References

[1] Y. Maruyama, A. Kawano, S. Okamoto, T. Ando, Y. Ishitobi, Y. Tanaka, A. Inoue, J. Imanaga, M. Kanehisa, H. Higuma, T. Ninomiya, J. Tsuru, H. Hanada, and J. Akiyoshi, "Differences in salivary alpha-amylase and cortisol responsiveness following exposure to electrical stimulation versus the trier social stress tests," *PLoS One*, vol. 7, no. 7, p. e39375, 2012.

[2] S. Cohen, D. Janicki-Deverts, and G. E. Miller, "Psychological stress and disease," *Jama*, vol. 298, no. 14, pp. 1685–1687, 2007.

[3] C. Kirschbaum, K.-M. Pirke, and D. H. Hellhammer, "The 'trier social stress test'–a tool for investigating psychobiological stress responses in a laboratory setting," *Neuropsychobiology*, vol. 28, no. 1-2, pp. 76–81, 1993.

[4] C. de Weerth, G. Graat, J. K. Buitelaar, and J. H. Thijssen, "Measurement of cortisol in small quantities of saliva," *Clinical chemistry*, vol. 49, no. 4, pp. 658–660, 2003.

[5] D. S. Jessop and J. M. Turner-Cobb, "Measurement and meaning of salivary cortisol: A focus on health and disease in children: Review," *Stress: The International Journal on the Biology of Stress*, vol. 11, no. 1, pp. 1–14, 2008.

[6] A. de Santos Sierra, C. S. Ávila, J. G. Casanova, and G. B. del Pozo, *Real-Time Stress Detection by Means of Physiological Signals*, J. Yang, Ed. InTech, July 2011.

[7] A. M. Chan, N. Selvaraj, N. Ferdosi, and R. Narasimhan, "Wireless patch sensor for remote monitoring of heart rate, respiration, activity, and falls," in *Engineering in Medicine and Biology Society (EMBC), 2013 35th Annual International Conference of the IEEE*. IEEE, 2013, pp. 6115–6118.

[8] N. Selvaraj, "Long-term remote monitoring of vital signs using a wireless patch sensor," in *Healthcare Innovation Conference (HIC), 2014 IEEE*, Oct 2014, pp. 83–86.

[9] C. D. Spielberger, *State-Trait Anxiety Inventory*. Wiley Online Library, 2010.

[10] S. U. Jayasinghe, S. J. Torres, C. A. Nowson, A. J. Tilbrook, and A. I. Turner, "Cortisol, alpha amylase, blood pressure and heart rate responses to food intake in men aged 50–70 years: importance of adiposity," *BMC Obesity*, vol. 1, no. 1, p. 14, 2014.