LifeQ

Acute Stress solution v0.3

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Summary

- Acute mental stress may have detrimental effects on human health.
- Currently there is no single gold standard for measuring acute mental stress, and a demand exists for practical and accessible solutions for detecting and quantifying acute mental stress events.
- In this study we demonstrate the capability of the *LifeQ Acute Stress solution V0.3* to measure acute mental stress, and to distinguish these events from other physiological events such as physical exertion/exercise. Test participants were subjected to a laboratory protocol for the induction of acute mental stress as well as an exercise protocol.
- At least 43% of induced acute stress events were detected by the solution and for each stress event that the system reported, 48.5% could be verified as real stressors induced by the TSST protocol.
- In order to distinguish acute stress events from other physiological events, we defined acute stress as an event that activates the release of the stress hormone cortisol via the Hypothalamic Pituitary Adrenal (HPA) axis. As an internal validation, the solution predicts when cortisol is secreted. As a qualitative physiological cross-check to confirm that HPA axis was indeed activated when the solution predicted activation, test participants were tested for the presence of salivary cortisol.

Key terms

- **Stress** = threatened homeostasis which results in the activation of various physiological and behavioural adaptive compensatory responses in order to re-establish homeostasis.
- **Acute stress** = stress with a short duration which is easily overcome by the body to re-establish homeostasis
- **Chronic stress** = prolonged stress sustained over weeks, months or years resulting in adverse physical and psychological outcomes when the body is unable to re-establish homeostasis.
- **Physical exertion** = increased oxygen consumption, heat production and heart rate to restore homeostasis during energy expenditure above resting levels.
- **Accuracy** = absolute mean difference between simulated cortisol level output from the internal LifeQ HPA model and measured salivary cortisol (gold standard data)
- **Precision** = the probability that a stress event detected by the algorithm is real.
- **Sensitivity** = the number of real stress events detected by the algorithm out of the known amount of real stress events in a data set.

Introduction

Stress is a major challenge in maintaining a healthy lifestyle in modern society. While young and healthy individuals may be able to handle bouts of acute mental stress, continuous exposure to acute and/or chronic stress may have long-term detrimental effects on health[1,2]. Stress management can benefit greatly from a means to easily, continuously and accurately monitor stress levels. While there are a number of easily measured stress identifiers such as increased heart rate and blood pressure,

these measures alone may not be accurate. The measurement of more complex parameters such as dehyroepiandrosterone (DHEA), cortisol and adrenocorticotropic hormone (ACTH) can be invasive and difficult to measure requiring methods like enzyme linked immunoassays (ELISA) to be performed on saliva or blood samples to determine hormone concentrations[3,4]. To date, there is no single gold standard metric for measuring acute mental stress.

The *LifeQ Acute Stress solution V0.3* was developed to identify when a subject is experiencing acute mental stress as well as quantify the level or intensity of stress being experienced based on data acquired from a wrist-based wearable device. Inputs to the *LifeQ Acute Stress solution V0.3* include photoplethysmography (PPG) and accelerometer data.

Acute stress events as well as chronic stress and physical exertion elicit similar physiological responses through activation of the fight or flight (sympathetic) autonomic nervous system, causing near immediate changes in heart and arterial vessel activity. Herein lies a key challenge of measuring acute mental stress. However, acute mental stress also activates the release of the stress hormones cortisol, DHEA and ACTH via the Hypothalamic Pituitary Adrenal (HPA) axis peaking at around 10-30 minutes after a bout of intense mental stress. This response is activated largely by acute mental stress and to a much lesser extent by physical exercise. Therefore, we defined an acute stress event as an event which causes the activation of the HPA-axis due to a mental stressor. Furthermore, the concentration of cortisol as a product of the HPA-axis is indicative of the degree to which the pathway was activated and cortisol concentration was measured in the saliva of study participants for validation purposes.[5] To this end, a model of the HPA-axis was constructed (LifeQ HPA model) based on peer-reviewed literature and used to compare measured (saliva) and predicted (model) time-varying changes in cortisol concentration.

Test Protocol

To verify the capability of the *LifeQ Acute Stress solution V0.3* to distinguish between acute stress events and other events that influence cardiovascular activity, such as exercise, study participants were subjected to a standard laboratory protocol for the reliable induction of mental stress (The Trier Social Stress Test (TSST)[6]) as well as an exercise protocol. The TSST protocol consists of 45-minute rest, 10-minute public speaking preparation, 5-minute public speaking and 5-minute mental arithmetic in front of a panel of judges (Figure 1 (left)) followed by a 20-minute rest/relax period. The subsequent exercise protocol involved walking and running on a treadmill (Figure 1 (right)). The *LifeQ Acute Stress solution V0.3* was evaluated by analyzing both TSST and exercise session data captured for each participant and the performance validated in the context of salivary cortisol measurements.

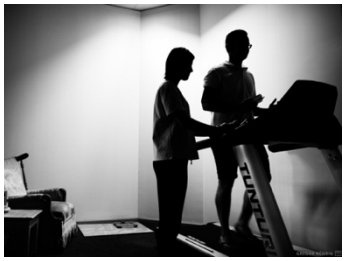


Figure 1: Left – A study participant performing public speaking in front of a panel of judges as part of the TSST protocol. Right – A study participant performing the physical exercise protocol.

Inputs and Outputs of the solution

The inputs and outputs of the *LifeQ Acute Stress solution V0.3* are summarized in Figure 2. Inputs include continuous PPG heart rate and acceleration collected from a wrist-based wearable device, as well as time zone and profile data (maximum and minimum heart rates). Outputs of the *LifeQ Acute Stress solution V0.3* available via the LifeQ API include acute stress event identification, stress intensity (%) as well as a binary confidence output (0:1).

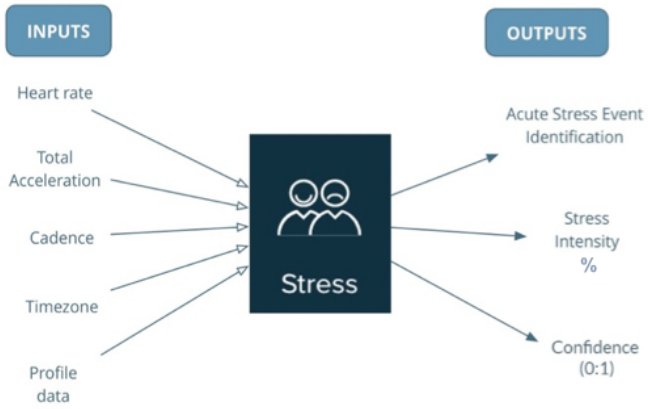
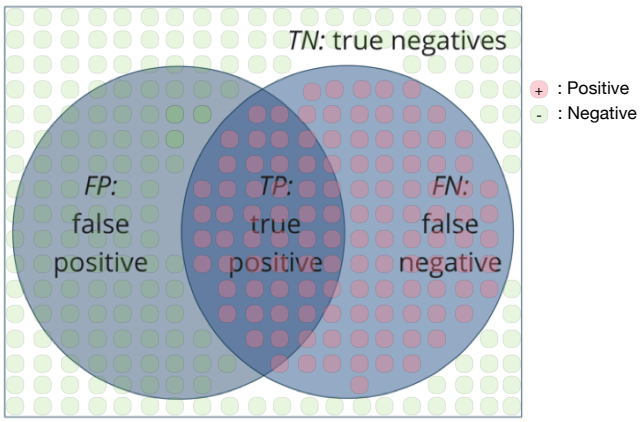


Figure 2: Inputs and outputs of the LifeQ Acute Stress solution v0.3

Validation and Accuracy

For the validation of the *LifeQ Acute Stress solution V0.3* data from seventeen (17) TSST and exercise protocols were used. Analysis was performed on a fit-all-leave-one-out basis and four statistical measures, namely precision, sensitivity, F-score and accuracy were calculated (Figure 3). The graph presented in Figure 4 shows an example of two of the three outputs of the *LifeQ Acute Stress solution v0.3* namely acute stress event identification and intensity during the TSST protocol (left) and exercise protocol data (right). The instances at which the stressors were induced, namely public speech preparation (SP), public speech delivery (SD), mental mathematics (MM) are indicated in orange and exercise, namely a treadmill walk (EW) and a treadmill run (ER) took place, are indicated with orange and green blocks respectively. The red line represents the heart rate in beats per minute (bpm) (left axis) and the dark grey sections indicate the stress intensity as output by the *LifeQ Acute Stress solution V0.3* expressed in % (right axis). Figure 4 clearly shows how acute stress events are detected during all three stressors. According to the boundaries of the TSST protocol, the precision and sensitivity were calculated by evaluating the results for true and false positives and negatives during the respective marked sections (SD, MM). The speech preparation period was not marked as a stress induced event and thus if stress was experienced during this time it was counted as a false positive. Note that three further instances of acute stress events are identified during the resting period following exercise. At first glance these may be regarded false positives. However, closer investigation of the heart rate values shows an elevated heart rate for each of these cases which may indicate that mental stress could have been experienced.



$$p = \frac{TP}{TP + FP}$$

$$s = \frac{TP}{TP + FN}$$

$$\text{F-score} = \frac{2ps}{p+s}$$

$$acc = \frac{TP + TN}{TP + TN + FP + FN}$$

Figure 3: Venn diagram and equations for calculating precision, sensitivity, F-score and accuracy.

We consider precision, sensitivity and the F-score to assess how well the *LifeQ Acute Stress solution V0.3* performs. Precision describes the percentage (%) of acute stress events detected by the solution. Sensitivity describes the percentage (%) of all positive stress events detected by the solution. The F-score is a weighted measure of precision and sensitivity; reaching it's best at 1 and worst at 0. For example, the sensitivity and precision are calculated by evaluating how often stress was detected during the initiation and withdrawal of a stressor (onset of public speaking to end of the mental arithmetic) in Figure 4. All events identified outside of this boundary are classified as false positives. Table 1 provides the precision, sensitivity and F-score of all TSST and exercise datasets combined. For future work, the incorporation of a stress intensity threshold is being explored towards eliminating false positives and negatives from the statistical calculations Table 2. Note that sensitivity decreases for each increase in precision. Validation of the *LifeQ Acute Stress solution V0.3* was performed by comparing the predicted secretion of cortisol generated using the LifeQ HPA-axis model with salivary cortisol measurements collected during the TSST protocol. An example of the model output is depicted in Figure 5. Since the immunoassay that was used to determine salivary cortisol concentrations was only 49.2% accurate, salivary cortisol concentrations could only be used as a qualitative physiological validation to confirm HPA-axis activations predicted by the model.

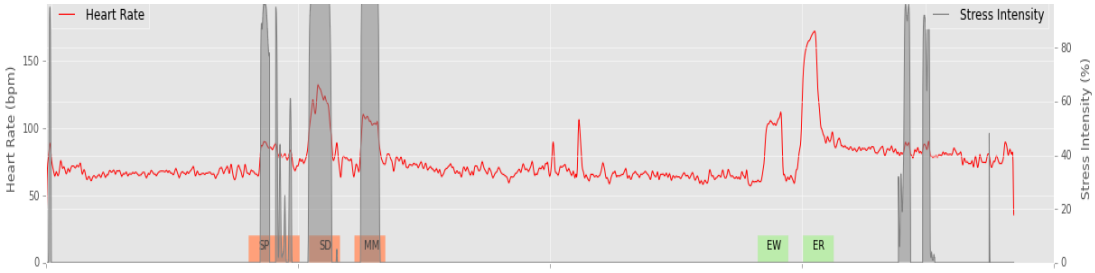


Figure 4: Stress intensity output (dark grey, stress intensity % on right axis) from the *LifeQ Acute Stress solution V0.3* for the TSST (left) and exercise (right) protocol data from a single subject. The red line represents heart rate in beats per minute (bpm) on the left axis. SP – Public speaking preparation, SD – Public speaking, MM - Mental arithmetic, EW – Treadmill exercise Walk, ER – Treadmill exercise Run.

Table 1: Precision, Sensitivity and F-score Statistics for the *LifeQ Acute Stress solution V0.3*

Evaluation of combined TSST and exercise protocol datasets	
Precision	48.49%
Sensitivity	42.99%
F-Score	0.43

Table 2: Stress intensity threshold (exploratory) and how it impacts sensitivity and precision.

	TSST and Exercise	
Stress Intensity Threshold	Sensitivity	Precision
> 0	42.99	48.49
5	41.43	51.16
10	40.21	52.21
15	39.44	53.36
20	38.85	54.34
25	38.02	55.10
30	37.28	55.97

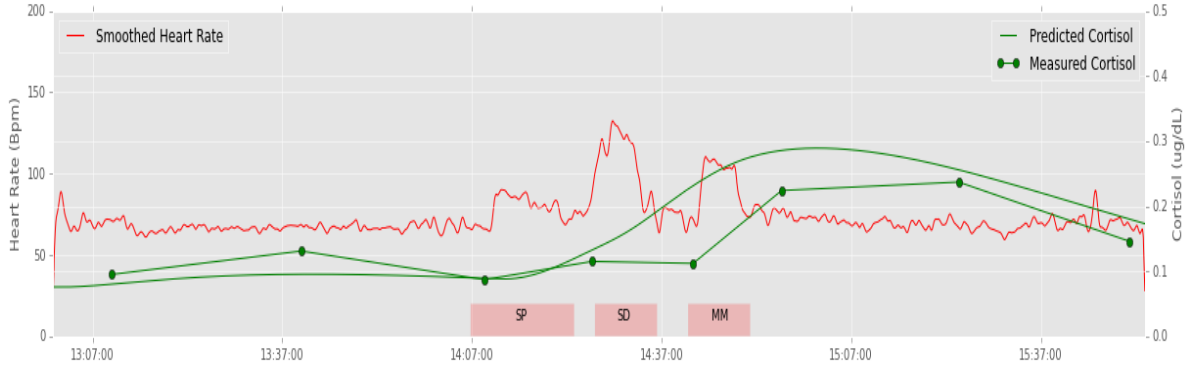


Figure 5: A comparison of cortisol (µg/dl, right-axis) measured (salivary) and predicted output from the LifeQ HPA-axis model for a TSST dataset. The red line represents the heart rate in beats per minute (bpm) on the left-axis. SP – Public speaking preparation, SD – Public speaking, MM - Mental arithmetic).

Limitations

Current model limitations

- The *LifeQ Acute Stress solution V0.3* has been assessed in the context of severe acute stress events.

- The *LifeQ Acute Stress solution V0.3* does not control for the effects of other cortisol inducing responses such as eating or caffeine and is also not able to distinguish mental stress experienced during exercise

Population Limitations

Inter-person variability is accounted for by normalizing a subject's heart rate between the maximum heart rate (age calculated) and the resting heart rate. The resting heart rate is measured in sitting position for 3 minutes after waking up.

The *LifeQ Acute Stress solution V0.3* has been developed using data from individuals who met specific exclusion criteria as listed below. It is therefore important to note that we cannot assume accuracy levels for individuals that do not adhere to these exclusions:

- Subjects between the ages of 21 - 33 years of age
- No oral contraceptives
- No chronic illness including history of, or current psychiatric diagnosis
- No feelings of unusually high levels of stress
- No medications including: anti-depressants, pain killers, sleeping pills, ADHD medication, blood thinners, insulin, steroids and prescription drugs for allergies.
- No pregnancy
- No alcohol within 48 hours of protocol
- No recreational drug use: Cannabis within the past two months, any other recreational drug within the last year
- No regular (>7 cigarettes/day)
- No shift workers

Conclusion

Using wrist-based PPG and accelerometer data from a wearable device, the *LifeQ Acute Stress solution V0.3* constitutes a non-invasive and practical method to continuously monitor acute stress events during day-to-day activities towards promoting a healthy life-style.

References

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