

# Multilevel Assessment of Mental Stress using SVM with ECOC: An EEG Approach

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**Abstract.** Mental stress has been identified as one of the major contributing factors that leads to various diseases such as heart attack, depression and stroke. To avoid this, stress quantification is important for clinical intervention and disease prevention. This study aims to investigate the feasibility of exploiting Electroencephalography (EEG) signals to discriminate between different stress levels. We propose a new assessment protocol whereby the stress level is represented by the complexity of mental arithmetic (MA) task for example, at three levels of difficulty, and the stressors are time pressure and negative feedback. Using 18-male subjects, the experimental results showed that there were significant differences in EEG response between the control and stress conditions at different levels of MA task with  $p\text{-values} < 0.001$ . Furthermore, we found a significant reduction in alpha rhythm power from one stress level to another level,  $p\text{-values} < 0.05$ . In comparison, results from self-reporting questionnaire NASA-TLX approach showed no significant differences between stress levels. In addition, we developed a discriminant analysis method based on multiclass support vector machine (SVM) with error-correcting output code (ECOC). Different stress levels were detected with an average classification accuracy of 94.79%. The Lateral Index (LI) results further showed dominant right prefrontal cortex (PFC) to mental stress (reduced alpha rhythm). The study demonstrated the feasibility of using EEG in classifying multilevel mental stress, and reported alpha rhythm power at right prefrontal cortex as a suitable index.

**Keywords:** Stress, Neuroimaging modalities, EEG, SVM+ECOC.

## 1 Introduction

Mental stress is one of the major health problems in modern society, and can be defined as the body reaction to subjected psychosocial, physical, and biological stimuli [76]. Stress involves the activation of hypothalamus-pituitary-adrenocortical (HPA) axis and sympathetic nervous system (SNS). The activation of HPA axis stimulates adrenal cortex to release glucocorticoids (cortisol), which plays an important role in the regulation of various physiological processes such as blood pressure, glucose levels, and carbohydrate metabolism [72,63]. Chronic malfunction in SNS results in a variety of physical, immunological, and emotional health problems including anxiety, depression and post-traumatic stress disorder (PTSD), heart attack, stroke, and immunological disorders [61,15,80,13]. Stress also affects the brain structure and functions. Several studies have reported that exposing to excessive stress could cause shrinkage of hippocampus [60,3,48,28]. To prevent these, stress detection especially at its early stage is important for clinical intervention and disease prevention.

Questionnaire-based self-reporting is the most commonly used method to measure an individual's level of mental stress [59]. However, self-reporting is a subjective method [57]. An objective method would be through measuring salivary cortisol and alpha amylase level [89]. Salivary cortisol is used as a bio-marker for stress studies [38]. Several studies reported that salivary cortisol significantly increased after the onset of physiological stress [53]. However, the cortisol has a slow response and its level is affected by circadian rhythm [33], i.e. the concentration level of cortisol in the early morning is higher than that in the afternoon. Salivary  $\alpha$ -amylase has also recently used as a bio-marker of sympathetic nervous system response to stress [30,22]. Significant increase in salivary  $\alpha$ -amylase was found during stressful tasks such as, playing video games [79], before and after examination [6,7,73], Trier Social Stress Test (TSST) [64,29], speech and counting task [32], and mental arithmetic task [65]. It however may vary with one's physical activity [54], where the concentration of salivary  $\alpha$ -amylase is significantly higher during exercise than in a neutral-control period.

Stress can also be assessed directly from the cortical response. Non-invasive neuroimaging modalities such as functional magnetic resonance imaging (fMRI), Positron emission topography (PET), Magnetoencephalography (MEG), Electroencephalography (EEG) and functional near infrared spectroscopy (fNIRS) are available to study brain functions and conditions of animal and human, including mental stress [36,62,34,83]. Measurements are often taken from the prefrontal cortex (PFC) [86,66,70,20], which is the brain region responsible in regulating thoughts, actions and emotions. The PFC has been identified as the most sensitive to the detrimental effects of stress exposure [3,39], and displayed behavioral and somatic responses to stress [85,43,88,68]. In this study, we quantify mental stress by measuring electrical brainwaves (EEG) at the PFC. The EEG is selected because it offers several advantages such as non-invasive data acquisition, ease to use, low cost set-up and its high temporal resolution at millisecond scale [5]. EEG signals are categorized by frequency bands: Delta (0.5-4 Hz), Theta (4-8 Hz), Alpha (8-13 Hz) and Beta (14-30 Hz). Each frequency band may be used as an index for brain states.

Few studies have used EEG to study mental stress previously. The brain region under study depends on the type of stimuli/tasks (visual, working memory or audio). Hill and Castro found high beta rhythm activity in the sensory motor area during stressful healing task [40]. Seo and Lee found similar high beta wave in the frontal and occipital lobe when negative images were presented to induce stress [77]. Another set of studies found significant increase of beta waves in the temporal lobe to odor irritation and traffic noise [14,69,84]. Thompson and Alonso separately found an increase of beta waves associated with a decrease of alpha waves in the anterior cingulate and frontal anterior cortex [82,2]. Gärtner et al found that frontal theta decreased with stressful mental arithmetic task [27]. Harmony et.al reported high delta waves, on the other hand, while solving difficult mental arithmetic task [35]. To detect mental stress, pattern recognition approaches are often adopted [58]. Table 1 summarized some of the most commonly used expert systems in classifying EEG signals individually or in combination with other physiological signals in stress related studies. Thus far, the systems are limited to detect the presence of stress only. We believe clinical

intervention/therapy to stress disorders should be carried out at the early stage; hence we are interested to classify stress into multi-level.

In this work, we investigate the feasibility of using EEG signals to classify mental stress into three levels. We propose an experimental protocol to induce three levels of stress on participants while solving an established mental arithmetic task with three levels of difficulty. Each level of the task difficulty corresponds to a level of stress. In addition, time pressure and negative feedback of peer performance are used as stressors in this study. We propose wavelet transform to extract features that are highly correlated with mental stress, and multiclass support vector machine with error correction code (ECOC) to classify the stress into three levels. The quantification of stress at multiple levels based on EEG signals is achieved for the first time.

## 2 Materials and Methods

### 2.1 Participants

Eighteen healthy male right-handed adults with an age ranges from 20-24 years old with the same level of education participated in this study. All participants were medically fit, non-smoker, and non-users of drugs that have any effect on the sympathetic nervous system. They were informed to avoid physical activity, food, caffeine, chewing gum, alcoholic consumption and soft drinks at least 2 hrs prior to the experiment [4]. Additionally, the experiment was conducted between 4.00 and 5.30 p.m to minimize the influences of circadian rhythm. Written informed consent from each participant was obtained and ethical approval in accordance with the declaration of Helsinki was granted by local ethics committee at University Teknologi PETRONAS. The participants were asked to minimize head movements and to remain calm during the entire experiment.

### 2.2 Stress induction procedure

Mental arithmetic task with three levels of difficulty was developed in this study [17]. Each level of the arithmetic task corresponds to one level of stress. The task at level one involves 3-one digit integer (ranging from 0 to 9) and uses the operands of + and/or - (example  $2-3+9$ ). At level two, the task involves 3 integers (ranging from 0 to 99) with at least 2 two-digit integers and uses the operands of +, -, and  $\times$  (example  $58-17\times 3$ ). At level three, the task involves 4 integer numbers (ranging from 0 to 99) and the operands include +, -,  $\times$  and  $\div$  (example  $99/3-76+51$ ). The answer for each question is displayed on a computer monitor among the sequence of '0' to '9' as demonstrated by Fig. 1(A). Participant selects the right answer by single left-click of the mouse.

Two stressors were deployed in this study, i.e. time pressure and negative feedback about peer performance. For time pressure, participants were trained at each level of task difficulty and the average time taken for each individual in answering the questions was recorded. This recorded time was then reduced by 10% and used as time pressure on the participants. In actual fact, the participants were expected to score less than 50% when the time given to answer each question was reduced by 10%. On the other hand, negative feedback of answering the questions ("correct", "incorrect" or "timeout") and performance indicators (one for the participant's performance and another one for the averaged peer performance fixed at 90% accuracy) were displayed on the computer monitor to further induce stress in experiment participants.

The experiment protocol was performed in four steps. First, brief introduction was given to all participants to be familiar with the proposed tasks. Second, participants were trained for five minutes at

each level of difficulty in the mental arithmetic (MA) task and time taken to answer each question was recorded.

**Table 1.** Previous studies related to EEG arousal and physiological signals classification.

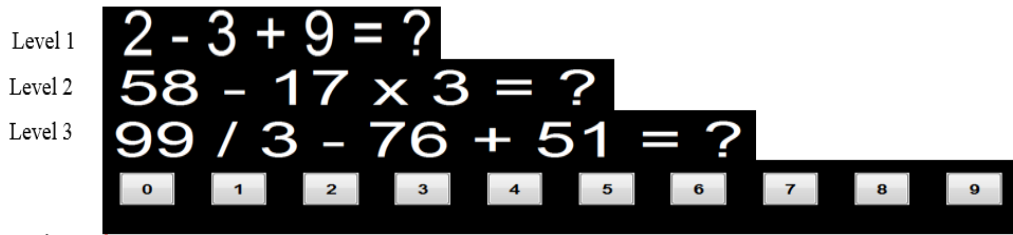
Author /Year	Physiological signals Used	Stressor	Number of Subjects	Expert system employed	Classification Accuracy
Ishino (2003) [47]	EEG	Video and puzzle games	1	NN	54.5%, 67.7%, 59% and 62.9% for happy, calm, sad and relax.
Ryu (2005) [74]	EEG and ECG	Arithmetic task	10	Multiple regression analysis	N/A only to study brain response.
Chanel (2006) [12]	EEG, ST, BP and respiration	Video and image	4	Bayes and FDA	55% for low and high arousal.
Chanel (2007) [10]	ST, BP, respiration and EEG	Recall event	1	LDA, SVM	76% and 73% using EEG and peripheral signals.
Lin (2008) [56]	EEG	Driving Simulator	6	K-NN and NBC	71% to 77% between stress and rest.
Chanel (2009) [11]	EEG, ST, BP, HRV and respiration	Recall memory	11	LDA, SVM, and RVM	63% using EEG and 70% using fusion of features
Hosseini (2010) [44]	ST,HRV and EEG	Pictures induction calm-neutral and negative-excited	15	SVM and Elman network	84.1% for two categories, calm and stress using psychological signals and 82.7% using EEG signals.
Saidatul (2011) [75]	EEG	Mental arithmetic task	5	NN	91.17% using Burg Method, 88.36% using Welch Method and 85.55% using Yule Walker for stress and relax.
Rahnuma (2011) [71]	EEG	Negative videos and images	4	MLP	71.69 %, 60.74%, 71.84% and 65.94% for happy, calm, sad and relax.
Khosrowabadi (2011) [51]	EEG	Before and after examination	26	K-NN, SVM	90% for stress and relax.
Sharma (2013) [78]	EEG, ECG,ST,BP, eye gaze and pupil diameter signals	Video: stress and non-stressed film	25	GA+SVM, GA+ANN	95% using all physiological signals and 91% using EEG signals alone.
Jun (2016) [49]	EEG	Arithmetic task and stroop	10	SVM	96% arithmetic from rest, 88% stroop from rest and 75% combination of arithmetic and stroop task.

*EEG Electroencephalography, ECG electrocardiogram, ST skin temperature, BP blood pressure, HRV hear rate variability, NN neural network, LDA linear discriminate analysis, RVM relevance vector machine, K-NN k-Nearest Neighbor, MLP multilayer perceptron, NBC naive bayes classification, GA genetic algorithm. FDA fischer's linear discriminant analysis.*

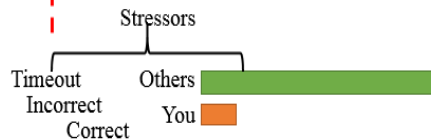
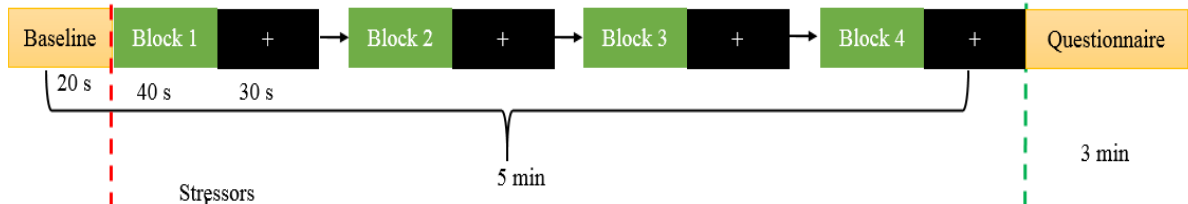
Third (i.e. control phase), the participants had their EEG signals recorded for total duration of 15 minutes while solving arithmetic problems at three levels of difficulty *without any time limit per question*. After each of the EEG recording, a questionnaire was filled by the participants self-reporting about task loading according to NASA-TLX rating scale [37]. Fourth (i.e. stress phase), similar as in the control phase, the EEG was recorded for 15 minutes under stress conditions (time limit and negative feedback) and again participants completed another questionnaire about task loading. In order to avoid any habituation or expectation effects, the order of the task conditions was balanced in which half of the participants began with the control task while the other half of the participants began with the stress task.

The entire experiment duration for each participant was about an hour, consisting of four blocks. Fig.1 gives an overview of the experimental protocol and the block design. Each block consists of 40 s of mental arithmetic task and 30 s of rest. The rest duration of 30 s was chosen to avoid the occurrence of habituation and to give sufficient time to determine brain areas activated during the MA task. During the 40 s task, several arithmetic questions are posted depends on how fast the response of the participant in answering. During the 30 s rest the computer screen displays with a white cross with black background and participants are instructed to look at the fixation cross as a visual cue for trial onset. In this experiment, we controlled the EEG recording by sending a marker via channels 23-24 of EEG BrainMaster as ‘1’ to mark the start of the MA task and ‘0’ to mark the end of the task for each block. During the experiment, all participants were instructed to answer the questions as fast and accurate as they could and not to guess the answer. The average accuracies of answering the questions at each level of the task were reported and used for subsequent performance evaluation.

A) Mental Arithmetic



B) Control



C) Stress

**Fig 1.** Experimental protocol of mental stress study. A) Levels of mental arithmetic task difficulty. Six measurements were performed in this experiment; three for control condition and three for the stress condition. B) Block design at control condition. C) Block design at stress condition. In each record (control and stress), there were four blocks. In each block, mental arithmetic was allocated for 40 s followed by 30 s rest. The vertical red dash-line marks the start of the task and vertical green dash-line marks the end of the task in each level. The sequence of the three levels was randomized to avoid any bias in results.

### 2.3 EEG measurement

We measured EEG signals from the prefrontal cortex (PFC) using Discovery 24E system (BrainMaster Technologies Inc, Bedford, OH). The system was equipped with seven active electrodes namely as FP1, FP2, F7, F3, Fz, F4, and F8 and one reference electrode (A1) attached to the earlobes as shown in Fig.2. All electrodes were placed on the PFC surface scalp based on the international 10-20 system of electrode placement. The sampling frequency for EEG was set to 256 Hz and the impedance was minimized (kept below 5k $\Omega$  in this study to avoid the noise effects due to sudden change in temperature and humidity occurred during data recording [25,50]) using small amount of gel directly to the scalp.



**Fig 2.** EEG Electrode placement and experiment setup.

### 2.4 EEG analysis

EEG data were preprocessed offline using the plug in EEGLAB 2013a toolbox [18]. Imported EEG data were bandpass filtered between 0.5 Hz and 30 Hz using 3<sup>rd</sup> order Butterworth filter. Independent component analysis (ICA) was applied to remove eye blink artefacts. The channels were decomposed into a number of independent components (by default the number of components is equal to the number of recorded channels). The component corresponding to eye blink artifacts was removed. The signals were further analyzed using wavelet transform (WT) [52]. WT is a suitable method for multi-resolution time-frequency analysis. WT decomposed EEG signals into set of functions to obtain their approximation and the corresponding coefficients at different levels. Features can then be extracted from them. The wavelet transform is formed by shifting and scaling function, as follows:

$$\psi_{a,b}(t) = \frac{1}{\sqrt{a}} \psi\left(\frac{t-b}{a}\right) \quad (1)$$

where  $a, b \in \mathbb{R}$  and  $a > 0$ . The variables  $a$ ,  $b$  and  $\mathbb{R}$  are scaling factor, shifting factor and wavelet space, respectively. The wavelet family of Dubechies-8 (db8) was used in this work to decompose EEG signals into five frequency bands (delta, theta, alpha, beta and gamma). Table 2 gives a summary of the wavelet decomposition levels and their corresponding frequency bands.

**Table 2.** EEG frequency bands and wavelet decomposition levels.

Decomposition level	Frequency bandwidth	Frequency band
DL1	64 Hz -128 Hz	Noisy signal
DL2	32 Hz -64 Hz	Noisy Gamma
DL3	16 Hz -32 Hz	Beta
DL4	8 Hz -16 Hz	Alpha
DL5	4 Hz -8 Hz	Theta
AL5	0-4 Hz	Delta

From the wavelet coefficients, we extracted the mean absolute values of the wavelet coefficients in each sub-band and the average power and energy from the activation period only. The activation period was defined from the onset of the task to the end of the task in each block. Then we averaged the four active blocks into a single block of 40 s. In this work, a window of 1 s moving-time interval was used to calculate the features of EEG signals. The power spectral density values were calculated using Eq.2.

$$P = \frac{1}{N} \sum_{n=k}^{k+N-1} |x(n)|^2 \quad (3)$$

where  $x(n)$  represents the segmented EEG signal and  $N$  is the length of the EEG clean signal. The energy of EEG frequency bands was defined as

$$E = \frac{1}{N} \sum_{-\infty}^{\infty} |x(n)|^2 \quad (3)$$

Based on our previous study [1], we found that EEG alpha band signals were highly correlated with mental stress states. Therefore we limit the analysis to EEG alpha rhythm power in this study. There is a total of 840 features for each subject in each condition of the recording phase: control and stress, where we have 40 power values, 40 mean values and 40 energy values multiply by 7 EEG measuring electrodes. Each feature is normalized to the range [-1, 1] before feeding into the classifier using Eq.4.

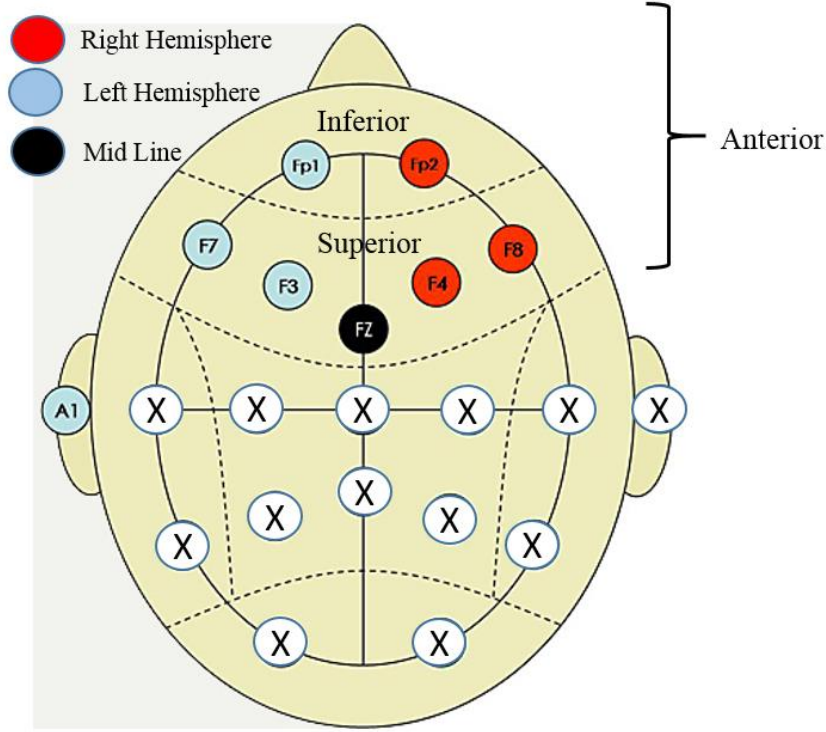
$$Feature_{norm} = \frac{x - \min(x)}{\max(x) - \min(x)} \times 2 - 1 \quad (4)$$

where  $x$  is the entire feature set,  $\min(x)$  is the minimum value in the feature set and  $\max(x)$  is the maximum value in the feature set respectively. Dominant features were then selected based on their significant response to mental stress. Independent samples t-test was used to find the significantly discriminant electrodes and features. Based on that, only the power values were considered as features in this study.

### 2.5 Lateral index at stress

In order to identify the dominant PFC region to mental stress, lateral index at stress (LIS) was calculated from alpha rhythm in all the subjects within two left and two right scalp quadrants (i.e. anterior inferior and anterior superior) as shown in Fig. 3 [46]. The anterior inferior quadrants contained medial prefrontal cortex (mPFC) and ventrolateral PFC; FP1, FP2, F7 and F8 sites. The left and right anterior inferior contained ventrolateral F7 and F8 sites respectively. Meanwhile, the anterior superior quadrants contained the dorsal F3, Fz and F4 sites, in which F3 and F4 located on the left and right anterior superior dorsolateral PFC respectively [16,81]. The LIS values were calculated according to Eq.5. The right and left variables represent the power values calculated from the contralateral electrodes, F3, F4, FP1, FP2, and F7, F8. The LIS index provides values in the range of -1 to +1. A near-zero value of LIS indicates bilateral dominance that depends on statistical analysis. Negative value indicates high level of stress on the right PFC than left PFC. One-tailed t-test was performed to determine the right or left dominance of PFC hemisphere.

$$LIS = \frac{Right - Left}{Right + Left} \quad (5)$$



**Fig 3.** EEG sensors location based on 10-20 system of electrode placement.

## 2.6 Support vector machine with ECOC

Support Vector Machine (SVM) is a supervised machine learning technique widely used for classification, regression and density estimation [87]. The technique transforms the data into a higher-dimension space using kernel function and classifies them with a hyper-plane. SVM was selected for its ability to model linear as well as more complex decision boundaries. The decision boundary hyperplane in SVM is estimated based on its training dataset by maximizing the distance between the hyperplane to the nearest data point.

The SVM is usually used in binary classification, i.e. problems with two classes. For three classes such as this (L1, L2 and L3 levels of stress), three SVM classifiers are needed. One SVM classifies L1 from the other two (L2 and L3), a second SVM classifies L2 from L1 and L3, and a third SVM classifies L3 from L1 and L2. In this work, SVM is extended to multiclass classifier by fusing SVM decisions using error-correcting output code (ECOC) [19]. Three bit codes are used, (1, -1, -1), (-1, 1, -1) and (-1, -1, 1) to represent each class/level, i.e. L1, L2 and L3 respectively. If all three SVMs classify correctly, then the multiclass-classifier-target code is met and ECOC reports no error. However, if at least one of the classifiers misclassifies, then the class with its code closest in hamming distance to the computed output code will be assigned as the answer. The SVM classifiers and ECOC algorithm were implemented using MATLAB software (Mathworks, Natick, MA).

The performance metrics of the classifier are classification accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) described in [24]. The classification accuracy



is defined as the ability of the classifier to correctly identify positive and negative results and can be evaluated using Eq.6.

$$Accuracy = \frac{TP + TN}{P + N} \times 100 \quad (6)$$

where true positive (TP) are data points correctly labeled as stress at the corresponding level and true negative (TN) are data points correctly labeled as not stress at the corresponding level. The sensitivity measures the classifier ability to correctly identify positive result and calculated using Eq.7.

$$Sensitivity = \frac{TP}{TP + FN} \times 100 \quad (7)$$

where, false negative (FN) refers to data points incorrectly labelled as stress at the corresponding level. Specificity gives a measure of the classifier ability to identify negative results defined Eq.8.

$$Specificity = \frac{TN}{TN + FP} \times 100 \quad (8)$$

where, true negative (TN) are data points correctly labels as not stress at the corresponding level, false positive (FP) refers to data points incorrectly labelled as not stress at the corresponding level. The positive and negative prediction values calculated using Eq.9 and Eq.10 respectively.

$$PPV = \frac{TP}{TP + FP} \times 100 \quad (9)$$

$$NPV = \frac{TN}{TN + FN} \times 100 \quad (10)$$

## 2.7 Statistical analysis

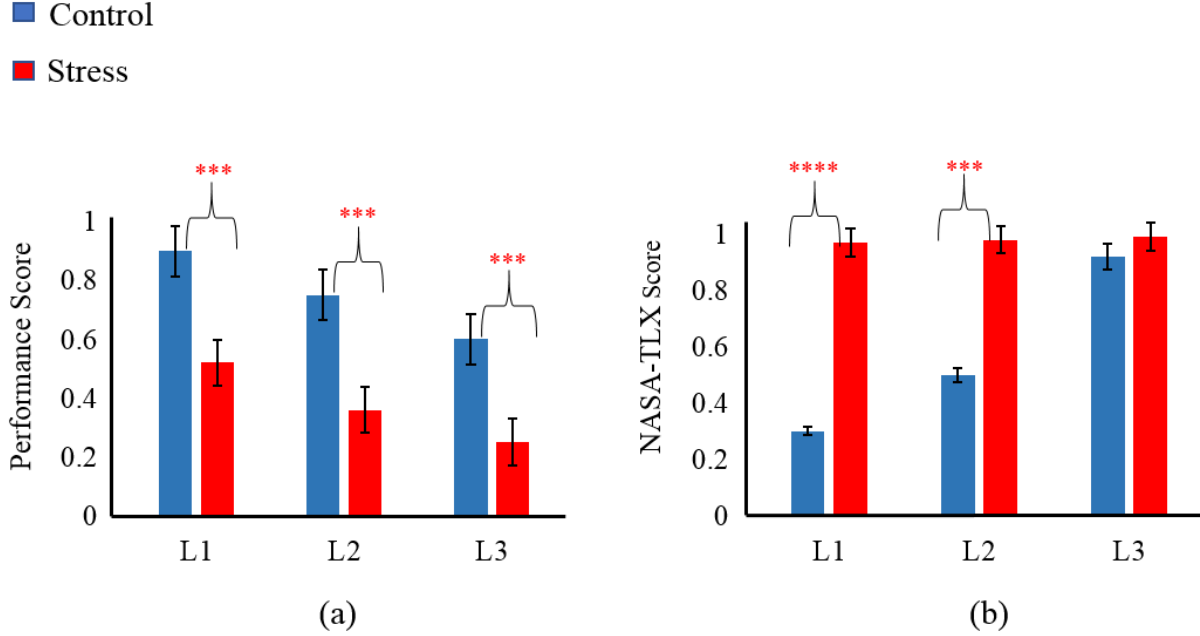
Statistical analysis on subjective scores of NASA-TLX and wavelet coefficient features for all the subjects and conditions were performed using two-sample t test. Prior to t-test, we confirmed if our data follow a Gaussian distribution. The two-sample t test was carried out with three different parameters, namely condition, the control level and the stress level. Firstly, we used two-sample t test to calculate the differences between each paired of the task difficulty (control vs stress). Secondly, we calculated the differences between different stress levels. For example, stress L1 versus others (i.e. L2 and L3), and so on. The differences were considered statistically significant if  $p < 0.05$ .

## 3 Result and Analysis

### 3.1 Performance score and NASA-TLX score

First, we look at the results of completing the MA tasks based on accuracy as we progress with level of difficulty, under control and stress condition. Fig. 4(a) shows clear reduction in performance (accuracy) with increasing the level of task difficulty/stress. We also found significant difference between control and stress condition, supporting the effectiveness of our stressors (time pressure and negative feedbacks). In this work, we adopted the standard NASA-TLX questionnaire [37] approach for comparison purpose. The NASA-TLX helps estimate mental stress by considering six established factors: mental demand, physical demand, temporal demand, performance, effort and frustration. Each factor has a score ranged from 1 to 20

with total score of 120. These scores were then normalized into the range of ‘0’ to ‘1’. Higher scores than 0.80 corresponding to high level of stress. In this case, the NASA-TLX results show significant differences between the control and stress condition in the first two levels of MA task difficulty but not the third level, as shown in Fig.4 (b). At L3, the participants responded to NASA-TLX questionnaires similarly under both control and stress conditions.



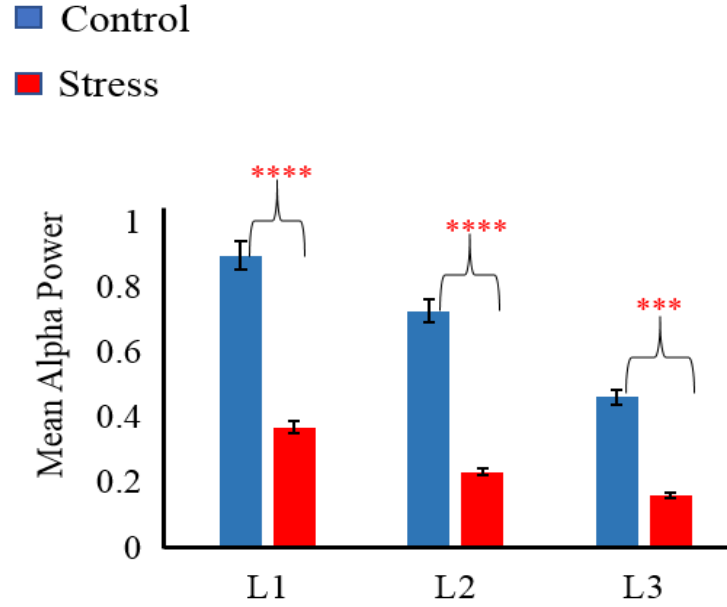
**Fig 4.** Performance accuracy in answering the questions correctly under the three level of arithmetic tasks in control and stress condition. The L1-represents level one of mental arithmetic task, L2- represents level two of mental arithmetic task and L3- represents level three of arithmetic task. The sign ‘\*’ indicates that, the significant was measured with  $p < 0.05$ , ‘\*\*\*\*’ indicates that  $p < 0.001$  and ‘\*\*\*\*\*’ indicates that  $p < 0.0001$ .

### 3.2 EEG

The mean spectral densities of EEG alpha rhythm for the three task difficulty levels under control and stress conditions are shown in Fig.5. From the figure, it is obvious that there is a significant difference between the control and stress conditions at all three task difficulty levels. The mean EEG alpha rhythm power is significantly reduced with increasing the task difficulty under both control and stress conditions. The obtained result is correlated well with the performance accuracy score reported in Section 3.1.

### 3.3 Statistical analysis

Our statistical analysis further reveals significant differences between mental arithmetic tasks under control and under stress conditions. Table 3 shows the *t-values* and the *p-values* calculated between control and stress conditions for all the three assessment methods, namely performance score (accuracy), NASA-TLX and EEG measurements. It also shows the *t-values* and the *p-values* calculated between stress levels for the three assessment methods. Performance score and EEG measurements showed significant differences between control and stress and between the control and the stress levels (from one level to another). On the other hand, NASA-TLX gives no significant differences between control L3 and stress L3, and between levels when under stress condition. We may thus conclude that stress assessment using subjective method (NASA-TLX) is not a suitable method as compared with cortical measurements using EEG in detecting different mental stress levels.



**Fig 5.** Mean Alpha rhythm power calculated from wavelet coefficients (DL4) in two mental states; control; blue colour and stress; red colour. The L1-represents level one of mental arithmetic task, L2- represents level two of mental arithmetic task and L3- represents level three of mental arithmetic task. The sign ‘\*\*\*’ indicates that, the significant was measured with  $p < 0.001$  and ‘\*\*\*\*’ indicates that  $p < 0.0001$ .

**Table 3.** Statistical analysis of subjective and objective measurements with two different parameters.

Parameter 1:		Performance Score		NASA-TLX		EEG	
Condition							
(control vs stress)	t-value	p-value	t-value	p-value	t-value	p-value	
L1	6.632	<0.001	5.841	<0.001	8.410	<0.0001	
L2	5.871	<0.001	4.210	0.001	7.712	<0.0001	
L3	5.541	<0.001	0.912	0.231	4.745	<0.0011	
Parameter 2:							
Control level							
L1 vs L2	2.731	0.014	2.821	0.010	2.714	0.014	
L2 vs L3	2.798	0.024	3.321	0.009	3.126	0.010	
L1 vs L3	3.101	0.013	4.621	0.001	3.131	0.011	
Parameter 3:							
Stress level							
L1 vs L2	2.831	0.013	Not significant		2.732	0.021	
L2 vs L3	2.914	0.021	Not significant		2.460	0.034	
L1 vs L3	3.112	0.011	Not significant		2.901	0.012	

### 3.4 Lateral Index at Stress (LIS)

The result corresponding to LIS asymmetry based on EEG alpha rhythm is summarized in Table 4. The values were calculated according to Eq 5. The LIS showed that right PFC was highly involved during mental stress in all the three levels of mental stress across all the subjects. The statistical analysis showed that LIS were significant at level one and level two of mental stress as compared to baseline, ( $p < 0.05$ ) and no significant difference was observed at level three. Note that the baseline of asymmetry was assumed to be equal, i.e. LIS = 0.

**Table 4.** Prefrontal EEG LIS for three levels of mental stress.

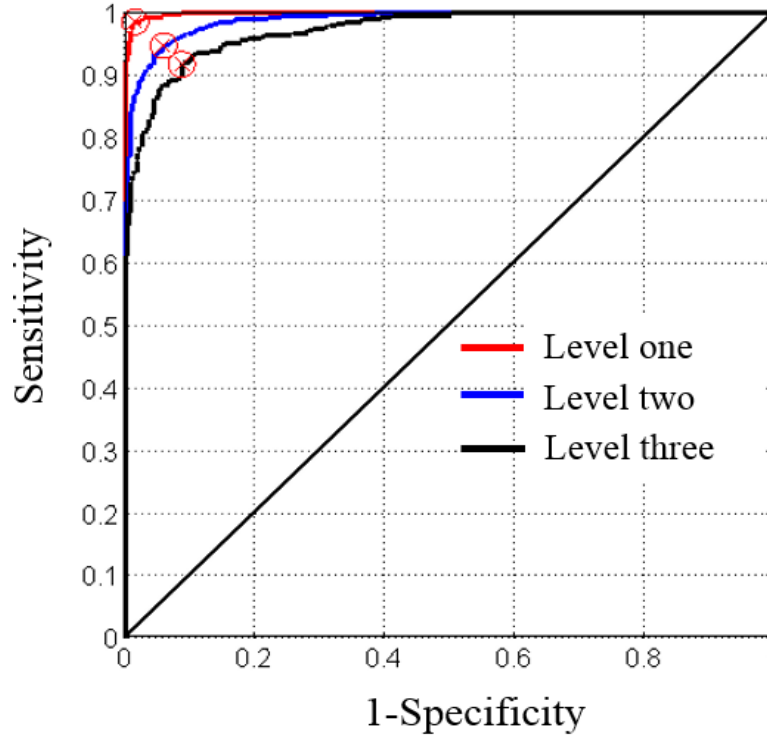
Asymmetry	Control level one	Control level two	Control level three
FP2-FP1	$-0.09 \pm 0.16$	$-0.01 \pm 0.16$	$-0.10 \pm 0.01$
F4-F3	$-0.08 \pm 0.15$	$-0.09 \pm 0.16$	$-0.12 \pm 0.04$
F8-F7	$-0.10 \pm 0.16$	$-0.10 \pm 0.15$	$-0.11 \pm 0.03$
Right-Left	$-0.09 \pm 0.16$	$-0.09 \pm 0.14$	$-0.13 \pm 0.03$
Asymmetry	Stress level one	Stress level two	Stress level three
FP2-FP1	$-0.210 \pm 0.03$	$-0.022 \pm 0.12$	$-0.001 \pm 0.07$
F4-F3	$-0.349 \pm 0.01$	$-0.130 \pm 0.03$	$-0.001 \pm 0.04$
F8-F7	$-0.228 \pm 0.02$	$-0.132 \pm 0.03$	$-0.001 \pm 0.06$
Right-Left	$-0.310 \pm 0.02$	$-0.253 \pm 0.06$	$-0.003 \pm 0.07$

### 3.5 SVM+ECOC

The average classification accuracy of mental stress levels by SVM with ECOC is summarized in Table 5. The table provides the performance metrics (accuracy, sensitivity, specificity, area under ROC curve, positive predictiv value, and negative predictive value) of the classifier under the three levels of mental stress. The results show that the accuracy drops from 97.61 to 95.37, and to 91.4 with increasing level of stress. The average classification accuracy across the three levels of stress is therefore 94.79%. ROC plot provides a view of the sensitivity and specificity of the classifier, revealing level one of mental stress with the highest accuracy as shown in Fig 6.

**Table 5.** Statistical parameters of the classifiers, SVM+ECOC.

Statistical Parametrs (%)	Level one	Multilevel SVM+ECOC	
		Level two	Level three
Accuracy	97.61	95.37	91.40
Sensitivity	97.60	96.20	92.06
Specificity	97.60	94.40	90.70
Area under ROC	99.60	98.80	97.03
PPV	97.60	94.50	90.86
NPV	97.60	96.20	91.95



**Fig 6.** ROC curves of multiclass SVM with ECOC. The red circles at the upper left corner represent the cut-off points.

#### 4 Discussion

In our previous study [1], we used EEG signals to detect mental stress from a resting (control) state. In this work, our aim is to investigate the feasibility of using EEG signals to quantify the levels of mental stress on the PFC. We proposed a new assessment protocol for the purpose, and its corresponding discriminant analysis method. Using multiclass support vector machine (SVM) with error-correcting output code (ECOC), we successfully classified the stress into three levels. Additionally, the study discussed the relationship between stress tasks, performance ability and commonly used subjective and objective assessment methods. We found that the performance score (accuracy) significantly reduced with increasing task difficulty under control and under stress conditions. The result is consistent with previous studies reporting performance decrease with high workload and job stress [42,23,21]. It is also consistent with fMRI studies which reported that performance effectiveness reduced with increasing task difficulty [31,45].

Subjective assessment using NASA-TLX demonstrated significant differences at the first two levels of task difficulty but not the third level under control condition, and was not distinguishable between all levels under stress condition. Especially at level three, participants evaluated their mental states similarly in both conditions (control and stress). Therefore, NASA-TLX is not a suitable measure for stress levels as there is little correlation between NASA-TLX scores and performance scores. In contrast, objective assessment using EEG demonstrated significant differences between the task difficulty levels under stress condition. In this work, significant decrease in alpha rhythm power was obtained at all three levels of mental stress, when compared to control condition. The study also found that alpha rhythm power was significantly reduced from one level to the next higher level. The EEG results are correlated well with the performance scores, unlike the NASA-TLX approach. The EEG results obtained in our study are consistent with previous workload studies. Previous studies showed that alpha rhythm power decreased with increasing level of workload [26,9,8,41]. Another study conducted on mothers of children with mental retardation (considered

high stress) reported significant reduce in alpha rhythm under stress [67]. Our study forms the first attempt to distinguish different stress levels using EEG technique.

The results from lateral index demonstrated the dominance of right PFC at all the three levels of mental stress with most significant at level one of mental stress. With increasing the level of stress, the value of LIS became significantly reduced. This suggests that high level of stress may impair the whole PFC activities. This result of LIS is consistent with previous studies [55,2]. The proposed multiclass support vector machine (SVM) with error-correcting output code (ECOC) also showed good performance in classifying mental stress levels. To the best of our knowledge, this is the first study using wavelet features of EEG signals with multiclass SVM and ECOC to classify mental stress levels. The classification performance metrics (accuracy, sensitivity, specificity, area under ROC curve, positive predictiv value and negative predictive value) showed promising results.

Admittedly, there are few limitations of our study needed to be addressed in future studies. Firstly, we only recruited male subjects to rule out possible effects of the hormonal cycle in our stress induction procedure. Future research will investigate whether our result (right dominant PFC to stress) can be generalized to both gender. Secondly, the number of electrodes used is of limited (7-EEG electrodes). More EEG-electrodes will be considered in future to better localize mental stress on the PFC subregion.

## *Conclusion*

In this study, we have demonstrated for the first time that EEG signals can be used to reliably discriminate between mental stress levels. The study reported significant differences between the three levels of mental stress, as measured by two-sample t-test with mean *p-values* of 0.021, 0.034, and 0.012 for level one to level two, level two to level three and level one to level three, respectively. The proposed multiclass classifier SVM with ECOC showed its potential in classifying stress levels with an average accuracy of 94.79%. Furthermore, the study revealed the dominance of the right prefrontal cortex to mental stress as supported by the results of lateral index at stress. The questionnaire approach NASA-TLX on the other hand showed no significant differences between stress levels. The proposed multilevel assessment may therefore form an important first step towards early detection of mental stress disorders.

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## *References*

1. Al-shargie F, Tang T, Badruddin N, Kiguchi M (2015) Mental Stress Quantification Using EEG Signals. In: International Conference for Innovation in Biomedical Engineering and Life Sciences. Springer Singapore, pp 15-19
2. Alonso J, Romero S, Ballester M, Antonijoan R, Mañanas M (2015) Stress assessment based on EEG univariate features and functional connectivity measures. *Physiol Meas* 36:1351
3. Arnsten AF (2009) Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Rev Neuroscie* 10:410-422
4. Bagwath Persad L (2011) Energy drinks and the neurophysiological impact of caffeine. *Front Neuroscie* 5:116

5. Berka C, Levendowski DJ, Cvetinovic MM, Petrovic MM, Davis G, Lumicao MN, Zivkovic VT, Popovic MV, Olmstead R (2004) Real-time analysis of EEG indexes of alertness, cognition, and memory acquired with a wireless EEG headset. *Int J Hum Comput Interact* 17:151-170
6. Bosch JA, Brand HS, Ligtenberg TJ, Bermond B, Hoogstraten J, Amerongen AVN (1996) Psychological stress as a determinant of protein levels and salivary-induced aggregation of *Streptococcus gordonii* in human whole saliva. *Psychosom Med* 58:374-382
7. Bosch JA, de Geus EJ, Veerman EC, Hoogstraten J, Amerongen AVN (2003) Innate secretory immunity in response to laboratory stressors that evoke distinct patterns of cardiac autonomic activity. *Psychosom Med* 65:245-258
8. Brouwer A-M, Hogervorst MA, Holewijn M, van Erp JB (2014) Evidence for effects of task difficulty but not learning on neurophysiological variables associated with effort. *Int J Psychophysiol* 93:242-252
9. Brouwer A-M, Hogervorst MA, Van Erp JB, Heffelaar T, Zimmerman PH, Oostenveld R (2012) Estimating workload using EEG spectral power and ERPs in the n-back task. *J Neural Eng* 9:045008
10. Chanel G, Ansari-Asl K, Pun T (2007) Valence-arousal evaluation using physiological signals in an emotion recall paradigm. In: *Systems, Man and Cybernetics. ISIC. IEEE*, pp 2662-2667
11. Chanel G, Kierkels JJ, Soleymani M, Pun T (2009) Short-term emotion assessment in a recall paradigm. *Int J Hum Comput Stud* 67:607-627
12. Chanel G, Kronegg J, Grandjean D, Pun T (2006) Emotion assessment: Arousal evaluation using EEG's and peripheral physiological signals. *Multimedia content representation, classification and security*, Springer pp 530-537
13. Chapin TJ, Russell-Chapin LA (2013) *Neurotherapy and Neurofeedback: Brain-based Treatment for Psychological and Behavioral Problems*. Routledge pp 95-105
14. Choi Y, Kim M, Chun C (2015) Measurement of occupants' stress based on electroencephalograms (EEG) in twelve combined environments. *Build Environ* 88:65-72
15. Cohen S, Janicki-Deverts D, Miller GE (2007) Psychological stress and disease. *JAMA Intern Med* 298:1685-1687
16. Curran T (1999) The electrophysiology of incidental and intentional retrieval: old / new effects in lexical decision and recognition memory. *Neuropsychologia* 37:771-785
17. Dedovic K, Renwick R, Mahani NK, Engert V, Lupien SJ, Pruessner JC (2005) The Montreal Imaging Stress Task: using functional imaging to investigate the effects of perceiving and processing psychosocial stress in the human brain. *J Psychiatry Neurosci* 30:319
18. Delorme A, Makeig S (2004) EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 134:9-21
19. Dietterich TG, Bakiri G (1995) Solving multiclass learning problems via error-correcting output codes. *J Artif Intell Res* 2: 263-286
20. Doi H, Nishitani S, Shinohara K (2013) NIRS as a tool for assaying emotional function in the prefrontal cortex. *Front Hum Neurosci* 7:770. doi: 10.3389/fnhum.2013.00770
21. Edwards W (2010) *Motor learning and control: from theory to practice*. Cengage Learning,
22. Engert V, Vogel S, Efanov SI, Duchesne A, Corbo V, Ali N, Pruessner JC (2011) Investigation into the cross-correlation of salivary cortisol and alpha-amylase responses to psychological stress. *Psychoneuroendocrinology* 36:1294-1302
23. Eysenck HJ (2012) A model for personality. *Springer Science & Business Media* 1: 17:20
23. Al-shargie, F., Tang, T. B., Badruddin, N., & Kiguchi, M. (2015). Simultaneous measurement of EEG-fNIRS in classifying and localizing brain activation to mental stress. In *2015 IEEE International Conference on Signal and Image Processing Applications (ICSIPA)* (pp. 282-286). IEEE.
24. Fawcett T (2006) An introduction to ROC analysis. *Pattern Recogn Lett* 27:861-874
25. Ferree TC, Luu P, Russell GS, Tucker DM (2001) Scalp electrode impedance, infection risk, and EEG data quality. *Clin Neurophysiol* 112:536-544
26. Fink A, Grabner R, Neuper C, Neubauer A (2005) EEG alpha band dissociation with increasing task demands. *Cogn Brain Res* 24:252-259

27. Gärtner M, Grimm S, Bajbouj M (2015) Frontal midline theta oscillations during mental arithmetic: effects of stress. *Front Behav Neurosci* 9. doi: 10.3389/fnbeh.2015.00096
28. Gärtner M, Rohde-Liebenau L, Grimm S, Bajbouj M (2014) Working memory-related frontal theta activity is decreased under acute stress. *Psychoneuroendocrinology* 43:105-113
29. Gordis EB, Granger DA, Susman EJ, Trickett PK (2006) Asymmetry between salivary cortisol and  $\alpha$ -amylase reactivity to stress: Relation to aggressive behavior in adolescents. *Psychoneuroendocrinology* 31:976-987
30. Granger DA, Kivlighan KT, El-SHEIKH M, Gordis EB, Stroud LR (2007) Salivary  $\alpha$ -amylase in biobehavioral research. *Ann N Y Acad Sci* 1098:122-144
31. Gray JR, Burgess GC, Schaefer A, Yarkoni T, Larsen RJ, Braver TS (2005) Affective personality differences in neural processing efficiency confirmed using fMRI. *Cog Affect Behav Neurosci* 5:182-190
32. Grillon C, Duncko R, Covington MF, Kopperman L, Kling MA (2007) Acute stress potentiates anxiety in humans. *Biol Psychiatry* 62:1183-1186
33. Hanrahan K, McCarthy AM, Kleiber C, Lutgendorf S, Tsalikian E (2006) Strategies for salivary cortisol collection and analysis in research with children. *Appl Nurs Res* 19:95-101
33. Al-Shargie, F., Tang, T. B., & Kiguchi, M. (2017). Stress assessment based on decision fusion of EEG and fNIRS signals. *IEEE Access*, 5, 19889-19896.
34. Hari R, Salmelin R (2012) Magnetoencephalography: from SQUIDs to neuroscience: *Neuroimage* 20th anniversary special edition. *Neuroimage* 61:386-396
35. Harmony T, Fernández T, Silva J, Bernal J, Díaz-Comas L, Reyes A, Marosi E, Rodríguez M, Rodríguez M (1996) EEG delta activity: an indicator of attention to internal processing during performance of mental tasks. *Int J Psychophysiol* 24:161-171
36. Harrison AH, Connolly JF (2013) Finding a way in: a review and practical evaluation of fMRI and EEG for detection and assessment in disorders of consciousness. *Neurosci Biobehav Rev* 37:1403-1419
37. Hart SG, Staveland LE (1988) Development of NASA-TLX (Task Load Index): Results of empirical and theoretical research. *Adv Psychol* 52:139-183
37. Al-shargie, F., Tang, T. B., & Kiguchi, M. (2016). Mental stress grading based on fNIRS signals. In 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (pp. 5140-5143). IEEE.
38. Hellhammer DH, Wüst S, Kudielka BM (2009) Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology* 34:163-171
39. Herman JP, Ostrander MM, Mueller NK, Figueiredo H (2005) Limbic system mechanisms of stress regulation: hypothalamo-pituitary-adrenocortical axis. *Prog Neuropsychopharmacol Biol Psychiatry* 29:1201-1213
40. Hill RW, Castro E (2009) *Healing young brains: The neurofeedback solution*. Hampton Roads Publishing
41. Hogervorst MA, Brouwer A-M, van Erp JB (2015) Combining and comparing EEG, peripheral physiology and eye-related measures for the assessment of mental workload. *Front Neurosci* 8:322
42. Hombergh P, Künzi B, Elwyn G, Doremalen J, Akkermans R, Grol R, Wensing M (2009) High workload and job stress are associated with lower practice performance in general practice: an observational study in 239 general practices in the Netherlands. *BMC Health Serv Res* 9:118. doi: 10.1186/1472-6963-9-118
43. Hoshi Y, Tamura M (1993) Detection of dynamic changes in cerebral oxygenation coupled to neuronal function during mental work in man. *Neurosci Letters* 150:5-8
44. Hosseini SA, Khalilzadeh MA (2010) Emotional stress recognition system using EEG and psychophysiological signals: Using new labelling process of EEG signals in emotional stress state. In: *Biomedical Engineering and Computer Science (ICBECS), International Conference on IEEE*, pp 1-6
45. Hwang MI (1994) Decision making under time pressure: a model for information systems research. *Info Management* 27:197-203



46. Ishikawa W, Sato M, Fukuda Y, Matsumoto T, Takemura N, Sakatani K (2014) Correlation between asymmetry of spontaneous oscillation of hemodynamic changes in the prefrontal cortex and anxiety levels: a near-infrared spectroscopy study. *BIOMEDO* 19:027005-027005. doi:10.1117/1.JBO.19.2.027005
47. Ishino K, Hagiwara M (2003) A feeling estimation system using a simple electroencephalograph. In: *Systems, Man and Cybernetics*. IEEE, pp 4204-4209
48. Joëls M, Karst H, Alfarez D, Heine VM, Qin Y, Riel Ev, Verkuyl M, Lucassen PJ, Krugers HJ (2004) Effects of chronic stress on structure and cell function in rat hippocampus and hypothalamus. *Stress: Int J Biology Stress* 7:221-231
49. Jun G, Smitha K (2016) EEG based stress level identification. In: *IEEE Proc. Systems, Man, and Cybernetics (SMC)*, pp 003270-003274
50. Kappenman ES, Luck SJ (2010) The effects of electrode impedance on data quality and statistical significance in ERP recordings. *Psychophysiology* 47:888-904
51. Khosrowabadi R, Quek C, Ang KK, Tung SW, Heijnen M A (2011) Brain-Computer Interface for classifying EEG correlates of chronic mental stress. In: *Neural Networks (IJCNN)*. IEEE, pp 757-762
52. Khushaba RN, Kodagoda S, Lal S, Dissanayake G (2011) Driver drowsiness classification using fuzzy wavelet-packet-based feature-extraction algorithm. *IEEE Trans Biomed Eng* 58:121-131
53. Kirschbaum C, Hellhammer DH (1994) Salivary cortisol in psychoneuroendocrine research: recent developments and applications. *Psychoneuroendocrinology* 19:313-333
54. Koibuchi E, Suzuki Y (2014) Exercise upregulates salivary amylase in humans (Review). *Exp Ther Med* 7:773-777
55. Lewis RS, Weekes NY, Wang TH (2007) The effect of a naturalistic stressor on frontal EEG asymmetry, stress, and health. *Biolo Psychology* 75:239-247
56. Lin C-T, Lin K-L, Ko L-W, Liang S-F, Kuo B-C, Chung I-F (2008) Nonparametric single-trial EEG feature extraction and classification of driver's cognitive responses. *EURASIP J Adv Signal Process* 2008:1-10
57. Liu T-K, Chen Y-P, Hou Z-Y, Wang C-C, Chou J-H (2014) Noninvasive evaluation of mental stress using by a refined rough set technique based on biomedical signals. *Artf Intell Med* 61:97-103
58. Lotte F, Congedo M, Lécuyer A, Lamarche F, Arnaldi B (2007) A review of classification algorithms for EEG-based brain-computer interfaces. *J Neural Eng* 4:R1
59. Masuda M, Holmes TH (1967) The social readjustment rating scale: a cross-cultural study of Japanese and Americans. *J Psychosom Res* 11:227-237
60. McEwen BS (2005) Glucocorticoids, depression, and mood disorders: structural remodeling in the brain. *Metabolism* 54:20-23
61. McEwen BS (2008) Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *Eur J Pharmacol* 583:174-185
62. Michel CM, Murray MM (2012) Towards the utilization of EEG as a brain imaging tool. *Neuroimage* 61:371-385
63. Michels N, Sioen I, Braet C, Huybrechts I, Vanaelst B, Wolters M, De Henauw S (2013) Relation between salivary cortisol as stress biomarker and dietary pattern in children. *Psychoneuroendocrinology* 38:1512-1520
64. Nater UM, La Marca R, Florin L, Moses A, Langhans W, Koller MM, Ehlert U (2006) Stress-induced changes in human salivary alpha-amylase activity—associations with adrenergic activity. *Psychoneuroendocrinology* 31:49-58
65. Noto Y, Sato T, Kudo M, Kurata K, Hirota K (2005) The relationship between salivary biomarkers and state-trait anxiety inventory score under mental arithmetic stress: a pilot study. *Anesth Analg* 101:1873-1876
66. Ossewaarde L, Qin S, Van Marle HJ, van Wingen GA, Fernández G, Hermans EJ (2011) Stress-induced reduction in reward-related prefrontal cortex function. *Neuroimage* 55:345-352
67. Peng H, Hu B, Zheng F, Fan D, Zhao W, Chen X, Yang Y, Cai Q (2013) A method of identifying chronic stress by EEG. *Pers Ubiq Comput* 17:1341-1347

68. Pruessner JC, Dedovic K, Pruessner M, Lord C, Buss C, Collins L, Dagher A, Lupien SJ (2010) Stress regulation in the central nervous system: evidence from structural and functional neuroimaging studies in human populations-2008 Curt Richter Award Winner. *Psychoneuroendocrinology* 35:179-191
69. Puterman E, O'Donovan A, Adler NE, Tomiyama AJ, Kemeny M, Wolkowitz OM, Epel E (2011) Physical activity moderates stressor-induced rumination on cortisol reactivity. *Psychosom Med* 73:604
70. Qin S, Hermans EJ, van Marle HJ, Luo J, Fernández G (2009) Acute psychological stress reduces working memory-related activity in the dorsolateral prefrontal cortex. *Biol Psychiatry* 66:25-32
71. Rahnuma KS, Wahab A, Kamaruddin N, Majid H (2011) EEG analysis for understanding stress based on affective model basis function. In: *Consumer Electronics (ISCE), IEEE 15<sup>th</sup> International Symposium on IEEE*, pp 592-597
72. Reinhardt T, Schmahl C, Wüst S, Bohus M (2012) Salivary cortisol, heart rate, electrodermal activity and subjective stress responses to the Mannheim Multicomponent Stress Test (MMST). *Psychiatry Res* 198:106-111
73. Robles TF, Shetty V, Zigler CM, Glover DA, Elashoff D, Murphy D, Yamaguchi M (2011) The feasibility of ambulatory biosensor measurement of salivary alpha amylase: relationships with self-reported and naturalistic psychological stress. *Biol Psychol* 86:50-56
74. Ryu K, Myung R (2005) Evaluation of mental workload with a combined measure based on physiological indices during a dual task of tracking and mental arithmetic. *Int J Ind Ergonom* 35:991-1009
75. Saidatul A, Paulraj MP, Yaacob S, Yusnita MA (2011) Analysis of EEG signals during relaxation and mental stress condition using AR modeling techniques. In: *Control System, Computing and Engineering (ICCSCE). IEEE*, pp 477-481
76. Selye H (1965) The Stress Syndrome. *Am J Nurs* 65:97-99
77. Seo S-H, Lee J-T (2010) Stress and EEG. INTECH Open Access Publisher
78. Sharma N, Gedeon T (2013) Modeling stress recognition in typical virtual environments. In: *Pervasive Computing Technologies for Healthcare (PervasiveHealth), 7<sup>th</sup> International Conference on IEEE*, pp 17-24
79. Skosnik PD, Chatterton RT, Swisher T, Park S (2000) Modulation of attentional inhibition by norepinephrine and cortisol after psychological stress. *Int J Psychophysiol* 36:59-68
80. Steptoe A, Kivimäki M (2012) Stress and cardiovascular disease. *Nat Rev Cardiol* 9:360-370
81. Takizawa R, Nishimura Y, Yamasue H, Kasai K (2014) Anxiety and performance: the disparate roles of prefrontal subregions under maintained psychological stress. *Cereb Cortex* 24:1858-1866
82. Thompson M, Thompson L (2007) Neurofeedback for stress management. *Principles and practice of stress management* 3:249-287
83. Tong Y (2010) Time lag dependent multimodal processing of concurrent fMRI and near-infrared spectroscopy (NIRS) data suggests a global circulatory origin for low-frequency oscillation signals in human brain. *Neuroimage* 53:553-564
84. Tran Y, Thuraishingham R, Wijesuriya N, Nguyen H, Craig A (2007) Detecting neural changes during stress and fatigue effectively: a comparison of spectral analysis and sample entropy. In: *Neural Engineering, CNE'07.3<sup>rd</sup> International IEEE/EMBS Conference*, pp 350-353
85. Uylings H, Van Eden C, De Bruin J, Feenstra M, Pennartz C (2000) The integration of stress by the hypothalamus, amygdala and prefrontal cortex: balance between the autonomic nervous system and the neuroendocrine system. *Prog Brain Res* 126:117-32
86. van der Werff SJ, van den Berg SM, Pannekoek JN, Elzinga BM, Van Der Wee NJ (2013) Neuroimaging resilience to stress: a review. *Front Behav Neurosci* 7:32 doi: 10.3389/fnbeh.2013.00039
87. Vapnik VN, Vapnik V (1998) Statistical learning theory, vol 1. Wiley New York
88. Wang J, Rao H, Wetmore GS, Furlan PM, Korczykowski M, Dinges DF, Detre JA (2005) Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. *Proc Natl Acad Sci U S A* 102:17804-17809
89. Yamaguchi M, Kanemori T, Kanemaru M, Takai N, Mizuno Y, Yoshida H (2004) Performance evaluation of salivary amylase activity monitor. *Bios Bioelectron* 20:491-497

