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## **An oculometrics-based biofeedback system to impede fatigue development during computer work**

*A proof-of-concept study*

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## RESEARCH ARTICLE

# An oculometrics-based biofeedback system to impede fatigue development during computer work: A proof-of-concept study

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## Abstract

A biofeedback system may objectively identify fatigue and provide an individualized timing plan for micro-breaks. We developed and implemented a biofeedback system based on oculometrics using continuous recordings of eye movements and pupil dilations to moderate fatigue development in its early stages. Twenty healthy young participants (10 males and 10 females) performed a cyclic computer task for 31–35 min over two sessions: 1) self-triggered micro-breaks (manual sessions), and 2) biofeedback-triggered micro-breaks (automatic sessions). The sessions were held with one-week inter-session interval and in a counterbalanced order across participants. Each session involved 180 cycles of the computer task and after each 20 cycles (a segment), the task paused for 5-s to acquire perceived fatigue using Karolinska Sleepiness Scale (KSS). Following the pause, a 25-s micro-break involving seated exercises was carried out whether it was triggered by the biofeedback system following the detection of fatigue ( $KSS \geq 5$ ) in the automatic sessions or by the participants in the manual sessions. National Aeronautics and Space Administration Task Load Index (NASA-TLX) was administered after sessions. The functioning core of the biofeedback system was based on a Decision Tree Ensemble model for fatigue classification, which was developed using an oculometrics dataset previously collected during the same computer task. The biofeedback system identified fatigue with a mean accuracy of approx. 70%. Perceived workload obtained from NASA-TLX was significantly lower in the automatic sessions compared with the manual sessions,  $p = 0.01$  Cohen's  $d_z = 0.89$ . The results give support to the effectiveness of integrating oculometrics-based biofeedback in timing plan of micro-breaks to impede fatigue development during computer work.

## Introduction

Fatigue is often reported by computer users [1,2] and associated with the development of musculoskeletal and psychological disorders [2,3] and compromised performance resulting in

agreement with the authorization from the Danish Data Protection Agency to share the data.

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accidents [4]. However, fatigue development is sometimes inevitable due to inflexible work regulations and schedules [2]. Two important issues among all should be addressed in work-related fatigue [2]. First, the regular work-rest schedules may ignore inter-individual differences in the manifestation of fatigue patterns [5,6]. Second, fatigue progression in its early stages may not necessarily lead to a significant loss of performance and thus not easily detectable from performance measures [7,8].

The development of fatigue during computer work in response to a mentally demanding task is aimed to be investigated in the proposed study, which may deal more with mental rather than physical demands of computer work. However, it has been recommended not to use adjectives (e.g. mental, cognitive) describing the locus of “fatigue” to acknowledge different underlying factors of fatigability [9]. In addition, this form of fatigue may also be referred to as acute fatigue as provoked by fast-paced or tight-scheduled work, but the manifestation of fatigue may be beyond task demands [9]. Sleep-deprived and chronic forms of fatigue should be discriminated from acute fatigue as the latter could be regulated by micro-breaks whereas the former is unlikely to be respondent to such interventions [10].

Implementing micro-breaks, i.e. short pauses without major interruption, at work is suggested to mitigate fatigue and preserve the performance in a safe level [11,12]. In addition, micro-breaks have been reported to improve mental focus [13]. It is plausible that micro-breaks can reduce discomfort especially during computer work (e.g. [14]), however, the cognitive impacts of micro-breaks require further investigations [15]. Optimal design of micro-breaks for an individual requires monitoring fatigue status and acquisition of objective information associated with fatigue [16–19]. The objective information should be provided in an unobtrusive manner to avoid any disturbance to work [16–19].

Fatigue detection has been approached by different techniques and modalities including electroencephalography [20–22], surface electromyography [23,24], mechanomyography [25,26], functional near infra-red spectroscopy [27,28], cardiac dynamics [29,30], functional magnetic resonance imaging [31,32], and eye tracking [33,34], or combinations of different modalities [35,36]. Although the findings are promising and competitive with each other in experimental situations for precise detection of fatigue, they are subject to technical limitations to apply in real-life settings. This study is focused on eye tracking, as it is technically progressing and can provide less obtrusiveness compared with the mentioned psychophysiological measurements, which is suitable for real-life settings [37].

Oculometrics are believed to be an enriched source of cognitive information and can be achieved by eye tracking [38–42]. The oculometrics may represent the underlying neural mechanism in the control and regulation of the eye movements during fatigue development [43]. Recent findings have shown that the development of fatigue may manifest earlier in the oculometrics than in physical and cognitive performance in various tasks including computer work [38,44]. Thus, oculometrics are promising biomarkers for early detection of fatigue.

An effective design of micro-breaks requires appropriate choices for the period, frequency, and the activity during the micro-breaks [45,46]. These parameters are dependent on the tasks and individuals [47]. Specifically, the frequency of micro-breaks may be determined individually based on oculometrics as sensitive metrics to fatigue development. Thus, this study aimed at the development of a biofeedback system based on oculometrics to provide personalized information on when to apply micro-breaks.

A biofeedback system is commonly comprised of an acquisition system to record physiological data from an individual, a processing unit to interpret the data, and an interface, e.g. a computer screen, to deliver information in real-time according to the processed data to the individual. The underlying idea of biofeedback is to provide cognitive interventions to enhance self-awareness to improve health and performance [48,49]. There are different

applications for biofeedback [48,49], e.g. decrease of the muscular load during computer work [16,17], adjustment of the mental load of computer games using physiological signals including pupil diameter changes [50], mental training in competitive sports [51], and counteracting stress and anxiety [52–54].

The proposed biofeedback system in this study was designed to alert participants to take micro-breaks during computer work based on oculometrics in a statistical model describing fatigue states. Of note, counteracting fatigue within this framework of cognitive intervention is favorable from the consumption of psychoactive drugs, e.g. caffeine in association with health risks [55]. We hypothesized that the oculometrics-based biofeedback system would impede fatigue development without compromising the performance of computer work.

## Methods and materials

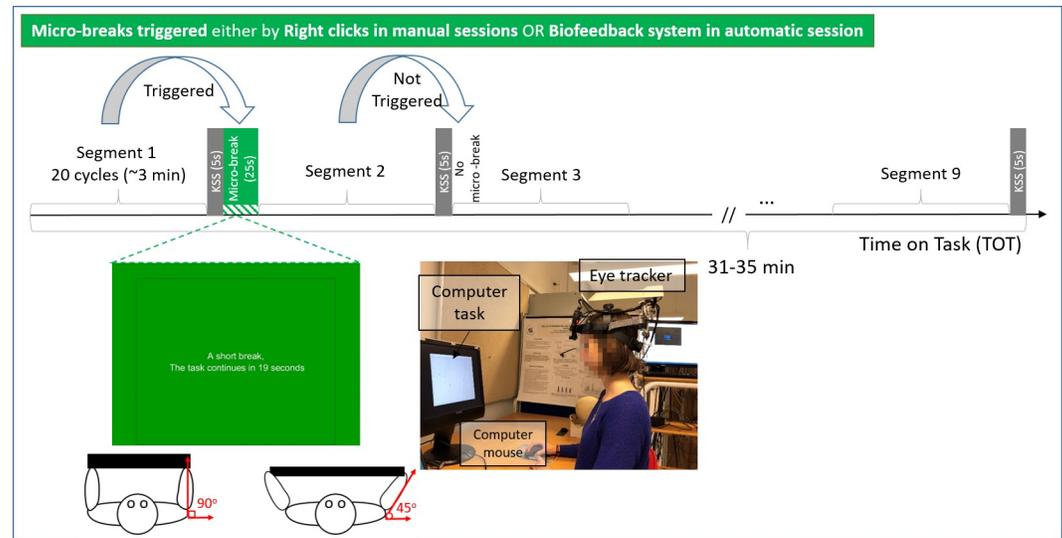
### Participants

Twenty participants, 10 females and 10 males, aged 26 (*SD* 3) years old with the height of 1.72 (*SD*.10) m, and the body mass of 69 (*SD* 15) kg were recruited. All participants had normal or corrected-to-normal vision (self-reported and examined by Snellen chart). The participants were familiar with computer work and used their right hand as their dominant side for computer mouse. Participants were asked to abstain from alcohol for 24 h, and caffeine, smoking and drugs for 12 h prior to experimental sessions. The participants reported at least 6 h (mean  $7.6 \pm 0.8$  h) of night sleep before the experimental session. The Fatigue Assessment Scale (FAS) [56] and the Visual Fatigue Scale (VFS) [57] were administered respectively to exclude participants suffering from chronic fatigue and eye strain. No participant was found with chronic fatigue and eye strain. Written informed consent was obtained from each participant. The experiment was approved by The North Denmark Region Committee on Health Research Ethics, project number N-20160023 and conducted in accordance with the Declaration of Helsinki.

### Experimental approach

A counterbalanced-measures design was employed to investigate the effectiveness of biofeedback-triggered micro-breaks in comparison with self-triggered micro-breaks. To do this, two experimental sessions were conducted in two counterbalanced sessions (days) with one-week inter-session interval.

**Computer task.** In both experimental sessions, participants were asked to perform a cyclic computer task [38] for approx. 31–35 min (Fig 1). The task [58] developed on MATLAB R2018a (The MathWorks, Natick, MA) was displayed on a 19-in screen (1280×1024 pixels, refresh rate: 120Hz) located approx. 58 cm in front of a sitting participant subtending  $27^\circ \times 22^\circ$  of visual angle. The task involved 180 cycles each taking approx. 10 s (corresponding to methods times measurement (MTM-100) [59,60]). Each cycle began by memorizing a random pattern of connected points with different shapes presented on a computer screen. The order of connecting points was determined by a textual cue displayed under the pattern, indicating the starting point. It was followed by a washout period, where no pattern was displayed, and the participants were instructed to keep their gaze on a cross in the center of the screen. The cycle continued by the presentation of the doubled-size replica of the pattern without connecting lines. To redraw the lines and replicate the presented pattern, participants were required to click on a sequence of the pattern points as targets. Once the allocated time to replicate the pattern passed, a new cycle with a different pattern was presented. In this design, the perceived level of fatigue based on Karolinska Sleepiness Scale (KSS) [61], was indicated by the



**Fig 1. The task timeline in the manual and automatic sessions (see micro-breaks).** A schematic view of the exercise and screen information during a micro-break, and the experiment set-up. [The individual in this manuscript has given written informed consent (as outlined in PLOS consent form) to publish these case details].

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participants after each 20 cycles, i.e. segment, in five seconds (KSS pause). The KSS can be rated from one (extremely alert) to 10 (extremely sleepy, can't wait to sleep).

**Micro-breaks.** Each experimental session involved either self-triggered or the biofeedback-triggered micro-breaks, respectively termed as manual and automatic sessions. In the manual sessions, the participants were instructed to press the right click button asking for a micro-break, whenever through the task they felt fatigued equivalent to  $KSS \geq 5$ . When a micro-break was triggered by a right click (or more), the task execution was interrupted after the earliest upcoming KSS pause (Fig 1). In the automatic sessions, the biofeedback system triggered the micro-break based on its prediction of KSS (explained further in the subsequent section) being  $\geq 5$  [62,63]. In this study, the micro-break consisted of a 25-s interruption of the task, while the participant took an active pause. During the micro-break, a down counter of the seconds from 25 to zero was displayed on the computer screen (Fig 1). The green color has been shown to have restorative effects on attention and cognition [64,65]. The micro-breaks involved four repetitions of seated bilateral shoulder rotations with an elastic band where the shoulders were abducted horizontally up to  $45^\circ$  while keeping the elbows fixed around  $90^\circ$ . During the micro-break, the participants were also instructed to perform mindful breathing based on [66,67] where the participants were guided to become aware of their breathing. Besides the benefits of active pauses [68] especially during computer work [69], mindful breathing is associated with oxygenation and reduced mental load and stress to counteract sustained attention [70,71]. The breathing rate was at the participants discretion, due to the diversity and individuality in breathing patterns [72].

**Familiarization and task engagement.** The participants were instructed to perform the computer task and micro-breaks in four days prior to the first session. In addition, anthropometric measures, visual acuity, and general health and fatigue questionnaires were collected. Afterwards, the participants performed the computer task for 10-min. The participants received a brief overview of the experimental procedure also in the beginning of both sessions and performed the computer task for 5-min as an additional training before commencing the

experimental protocol to reduce the learning effect. The participants were not informed about the principle of functioning of the biofeedback system. It was further explained that their choices of KSS had no effect on their performance or the biofeedback system. To evaluate the perceived workload from the tasks, the questionnaire of National Aeronautics and Space Administration Task Load Index (NASA-TLX) [73] was administered after the task termination, as it provides information on different dimensions of workload of a task [74,75]. The participants were informed that their performance was measured and compared with other participants to maintain motivation, and achieving high performance makes them candidates to win a monetary reward (100 Danish Kroner).

### The development of a statistical model for fatigue detection

To implement the biofeedback system, a statistical model of fatigue was developed based on previously collected oculometrics dataset (OLDSET) during an identical computer task [38]. The OLDSET consisted of the oculometrics extracted from gaze positions and pupil dilations, and KSS ratings from 38 participants in 40-min samples of an identical computer task without micro-breaks as described in [38]. The state of fatigue for each segment was assigned based on the KSS scores obtained after each segment. The KSS scores were dichotomized based on a threshold value of five, corresponding to being “neither alert nor sleepy”, as a transition point between alertness and fatigue. Thus, the segments with the KSS value of  $\geq 5$  were assigned to the class of fatigued and the KSS scores of  $< 5$  were assigned to the class of alert. This dichotomization criterion has been used in previous studies, e.g. [62]. It is suggested as a critical value in the association between ocular metrics and sleepiness [63]. With this dichotomization criterion, 45% of the collected segments (205 out of 456) across the entire subject pool in the OLDSET were labeled as fatigued.

Thirty-four features including oculometrics, sex, and age were used in setting up the classifier (Table 1). A series of viable classification models were examined as outlined in Table 2. A feature subset consisting of five features, i.e. Blink Frequency (BF), Percentage of the duration of closed eyes to opened eyes (PERCLOS), Saccade Frequency (SF), Saccade Peak Velocity Amplitude Relationship (SVA), and Pupil Diameter Interquartile Range (PDIR), was chosen using sequential floating forward feature selection [76]. The feature selection helps to choose a combination of features that best explain the separability of the two classes [76]. The classification criterion was the Youden's J statistic or Youden's index  $(\frac{TP}{P} + \frac{TN}{N} - 1)$  [77], where  $P$  and  $N$  are the number of instances (segments) with respectively positive (fatigued) and negative (alert) labels, and  $TP$ ,  $TN$  are respectively the number of true positive (correctly detected fatigue) and true negative (correctly detected alert) instances. Here,  $\frac{TP}{P}$  and  $\frac{TN}{N}$  are respectively True Positive Rate (TPR), and True Negative Rate (TNR). The Youden's index was computed using leave-one-person-out (LOPO) approach on a random forest model (Table 2) [78]. Different classifiers as outlined in Table 2 were examined using the selected feature subset as input and the class labels of fatigued or alert as output. In the LOPO approach, the classifier was trained using the data from all the participants except one, and it was tested using the excluded participant. This approach was performed for all the 38 participants to compute the average of classification performance across the entire participant pool. Finally, the ensemble of Decision Trees (DT Ensemble) was chosen based on its superior classification performance in terms of accuracy  $ACC = (TP + TN)/(P + N)$  ( $66 \pm 21\%$ ), TPR ( $61 \pm 29\%$ ), and TNR ( $70 \pm 22\%$ ) in comparison with the classifiers listed in Table 3, i.e. linear discriminant analysis, decision tree, k-nearest neighbors, support vector machines, Naïve Bayes, feed-forward neural networks, subtractive clustering-based Fuzzy classifier, Fuzzy c-means classifier, logistic regression classifier, and random forest.

Table 1. The feature set.

| Feature                           | Description   | Feature                              | Description  |
|-----------------------------------|---|--------------------------------------|--|
| <b>Blink-related Oculometrics</b> |   | <b>Fixation-related Oculometrics</b> |  |
| BF* [Hz]                          | Blink Frequency   | FF <sub>disp/dist</sub> [a.u.]       | The ratio of the displacement to the distance between two successive fixations                       |
| BD [s]                            | Blink Duration  | FD [s]                               | Fixation Duration  |
| BGF [Hz]                          | The Frequency of Blinks accompanied by Gaze shifts [79]             | FF [Hz]                              | Fixation Frequency   |
| IBI [s]                           | Inter-Blink Interval (excluding IBI>20 s)                           | FF <sub>disp</sub> [cm]              | Displacement between two successive fixations  |
| LBF [Hz]                          | The frequency of long blinks (>200 ms) [80]                         | FF <sub>dist</sub> [cm]              | Euclidean distance between two successive fixation centers   |
| LBR [a.u.]                        | The ratio of long blinks (>200 ms) [80] to all blinks               | OD [cm]                              | Overall Dispersion; the averaged Euclidean distance between fixation centers and center of fixations |
| DBF [Hz]                          | Double Blink Frequency (excluding IBI>700 ms) [81,82]               | LFR [%]                              | The Rate of Long Fixation (>0.9 s) [34] to all fixations   |
| BGR [a.u.]                        | The ratio of blinks accompanied by gaze shifts to all blinks [79]   | <b>Saccade-related oculometrics</b>  |  |
| TBS [s]                           | Time interval of <700 ms between a blink and its successive saccade | SVA* [s <sup>-1</sup> ]              | Saccade Peak Velocity Amplitude Relationship   |
| PERCLOS* [%]                      | Percentage of the duration of closed eyes to opened eyes            | SCD [s]                              | Saccade Duration   |
| <b>Pupil-related oculometrics</b> |   | SF* [Hz]                             | Saccade Frequency  |
| PD [mm]                           | Pupil Diameter  | SPV [°/s]                            | Saccade Peak Velocity  |
| PDIR* [mm]                        | Pupil Diameter Interquartile Range                                  | SDA [s/°]                            | Saccade Duration Amplitude Relationship  |
| PCV [a.u.]                        | Coefficient of Variation of Pupil diameter                          | SCR [°]                              | Saccade Curvature [59]   |
| PH [a.u.]                         | Instantaneous phase of the pupil dynamics [83]                      | SA [°]                               | Saccade Amplitude  |
| <b>Demographics</b>               |   | SPD [°/s <sup>2</sup> ]              | Saccade Peak Deceleration  |
| Age (continuous scale)            |   | SPA [°/s <sup>2</sup> ]              | Saccade Peak Acceleration  |
| Sex                               |   | ISI [s]                              | Short Inter-Saccade Intervals in <250 ms [84]  |
|                                   |   | KPA [a.u.]                           | Kappa Coefficient of Ambient/Focal attention [85]  |

\* The selected features for the classification model

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The classification model with the best performance (DT Ensemble) was picked to form the core of the biofeedback system. The DT Ensemble with the configuration outlined in Table 2 was trained with the whole dataset consisting of 456 samples (38 participants × 12 segments) to make a statistical model to predict the class label of each segment of the biofeedback system.

The permutation test [96] was conducted on the OLDSET to further examine the classification accuracy of the DT Ensemble against the chance level accuracy obtained from 100 randomly permuted class labels. The sensitivity to the dichotomization criterion for the KSS was also performed on the OLDSET. The classification performance of the DT ensemble was significantly higher than chance level as assessed by the permutation test for the OLDSET ( $\alpha = 0.01$ ). Changing the dichotomization criterion of KSS scores to  $\geq 6$  as fatigued for the DT Ensemble model did not lead to better classification performances than the criterion of five in the OLDSET. The receiver operating characteristics (ROC) of the training and test sets, and the confusion matrix for the DT Ensemble model are depicted in Fig 2, where the area under the ROC curves for the training (0.89) and test (0.64) sets as well as the results from the confusion matrix supported the usability of the model in the biofeedback system.

During the computer task in the current study, the feature set was obtained across 20 consecutive cycles within a segment and the core of the biofeedback system classified the segment into either the fatigued or the alert class. The section titled “Oculometrics” outlines the

Table 2. The details of the classification models.

| Model         | Description   | Configuration  | Further considerations  |
|---------------|---|--|---|
| LDA           | Linear discriminant analysis                                    | Discriminant type: pseudolinear  | Suitable to encounter singularity problems due to missing values [86]   |
| DT            | Decision Tree   | Max number of splits: 7, Maximum number of categories: 10, Min parent size: 10, Prediction selection criteria: Curvature test, Pruning criterion: error, Min leaf size: 1, Split criterion: Gini's diversity index (GDI)   | Choices for hyperparameters were based on the recommended constraints [87]  |
| KNN           | k-Nearest Neighbors   | 11-nearest neighbors classifier using the Euclidean distance metric and an exhaustive searcher   | k = 11 was chosen based on the highest classification performance in a grid search of k in [1 21], where the upper limit came from $\sqrt{n}$ , where n is the number of the training samples [88], Standardized feature set [89]   |
| SVM           | Support Vector Machines   | 2 types of SVM each using 4 different kernels.<br>1) c-SVM (c = 10).<br>2) v-SVM (v = 0.7).<br>Kernel functions:<br>Gaussian $\exp(\gamma u - v ^2)$ , Polynomial $(\gamma u'v + \sigma)^3$ , Sigmoid $\tanh(\gamma u'v + \sigma)$ , and linear $u'v$ , where: $\gamma = 0.2$ , $\sigma = 0.1$ . | The feature set was normalized using Min-Max feature scaling. Solver: Sequential Minimal Optimization (SMO) [90,91]. The SVM classifiers implemented using LIBSVM Toolbox [91]. Choices for the hyperparameters were based on grid search over c = 1, 10, and 100, v = [0.1 0.9] with the step size of 0.1. |
| NB            | Naive Bayes   | Predictor Distribution: Normal   | Different kernels (Box, Traingular, and Epanechnikov) were also tested.   |
| NN            | Feedforward Neural Network                                      | One hidden layer including five neurons in the hidden layer with scaled conjugate gradient backpropagation function.   | The number of neurons was chosen in [1 10] (with the step size of 1). 50 random initial conditions and shuffled sequences of data presentation were applied with standardized feature set [92]  |
| FIS-SC        | Fuzzy Inference System structure using subtractive clustering   | Cluster center's range of influence: 0.6, Input membership function: Gaussian, Output membership function: Linear  | Cluster center's range was chosen in grid search between [0 1] with the steps of 0.1. Different membership functions were tested  |
| FIS-FCM       | Fuzzy Inference System structure using Fuzzy C-Means clustering | FIS type: Sugeno, number of clusters: 2, input membership function: Gaussian, Output membership function: Linear   | Different membership functions were also tested, and the best was chosen (Gaussian) [93].   |
| Fusion        | Major voting scheme   | The same parameter settings for the single classifiers (LDA, DT, KNN, c-SVM with Gaussian kernel, NB, NN, FIS-SC and FIS-FCM) used.  | The class ( $C_{Fusion}$ ) was determined based on the average of the posterior probability ( $PP_i$ ) of the single classifiers, $C_{Fusion} = \lceil \frac{1}{8} (\sum_{i=1}^8 PP_i) \rceil$ , where $C_{Fusion} = 1$ indicated the class of fatigued ( $KSS \geq 5$ ) [94]                               |
| LR            | Logistic Regression Classifier                                  | Using binomial logistic regression for the two classes of fatigued and alert   | No additional option for the model.   |
| DT Ensemble   | Ensemble of Decision Tree classifiers                           | Max number of splits: 5, Ensemble method: RobustBoost, Number of learning cycles: 50, Robust Error Goal: 0.25, Robust Max Margin: 1  | Robustness against noisy samples [95] due to the subjectivity of class labels. Choices for hyperparameters were based on the recommended constraints [87]   |
| Random Forest | Ensemble of Decision Tree classifiers                           | Max number of splits: 5, Number of trees:51, The function to measure the quality of a split was GDI  | Suitable for categorical variables (e.g. sex). Choices for hyperparameters were based on the recommended constraints [87]   |

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performed analysis to obtain the oculometrics as features. If the segment was classified as fatigued, the biofeedback system triggered the micro-break command following the KSS pause after that specific segment. If the segment was classified into the alert class, no feedback was given. The architecture of the biofeedback system is depicted in Fig 3. The approaches from feature selection to model evaluation in the development of the statistical model to predict fatigue is summarized in Fig 3, and thereby the two mechanisms to trigger the micro-breaks in the automatic and manual sessions are illustrated. All aspects of the biofeedback system were implemented in MATLAB R2018a (The Mathworks, Natick, MA).

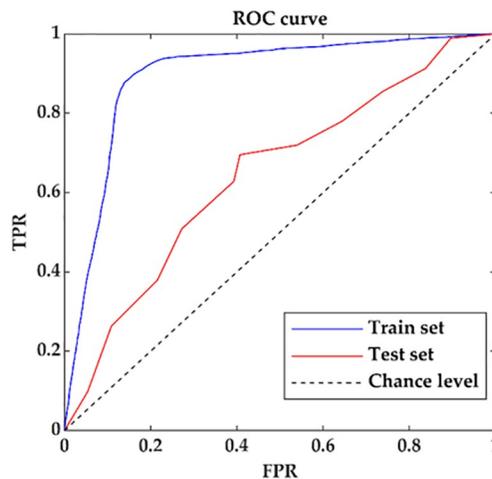
### Data acquisition and processing

A video-based monocular eye-tracker (Eye-Trac 7, Applied Science Laboratories, Bedford, MA, USA) coupled with a head tracker (Visualeyez II system set up with two VZ4000 trackers,

Table 3. The performance of the models to classify the state of fatigued ( $KSS \geq 5$ ) (Positive class) from alert (Negative class).

| Model                     | Sensitivity (TPR%) | Specificity (TNR%) | Accuracy (ACC%) |
|---------------------------|--------------------|--------------------|-----------------|
| <b>DT Ensemble</b>        | 61                 | 70                 | 66              |
| c-SVM (Gaussian kernel)   | 62                 | 67                 | 65              |
| c-SVM (Polynomial kernel) | 54                 | 67                 | 61              |
| c-SVM (Sigmoid kernel)    | 44                 | 78                 | 63              |
| c-SVM (linear kernel)     | 58                 | 67                 | 63              |
| v-SVM (Gaussian kernel)   | 61                 | 68                 | 64              |
| v-SVM (Polynomial kernel) | 48                 | 73                 | 62              |
| v-SVM (Sigmoid kernel)    | 43                 | 66                 | 56              |
| v-SVM (linear kernel)     | 58                 | 69                 | 64              |
| <b>NB</b>                 | 61                 | 68                 | 65              |
| <b>LR</b>                 | 57                 | 70                 | 64              |
| <b>Fusion</b>             | 57                 | 69                 | 63              |
| <b>Random Forest</b>      | 54                 | 68                 | 62              |
| <b>LDA</b>                | 54                 | 67                 | 61              |
| <b>NN</b>                 | 53                 | 67                 | 61              |
| <b>FIS-FCM</b>            | 54                 | 67                 | 61              |
| <b>FIS-SC</b>             | 61                 | 56                 | 59              |
| <b>KNN</b>                | 57                 | 60                 | 59              |
| <b>DT</b>                 | 56                 | 52                 | 54              |

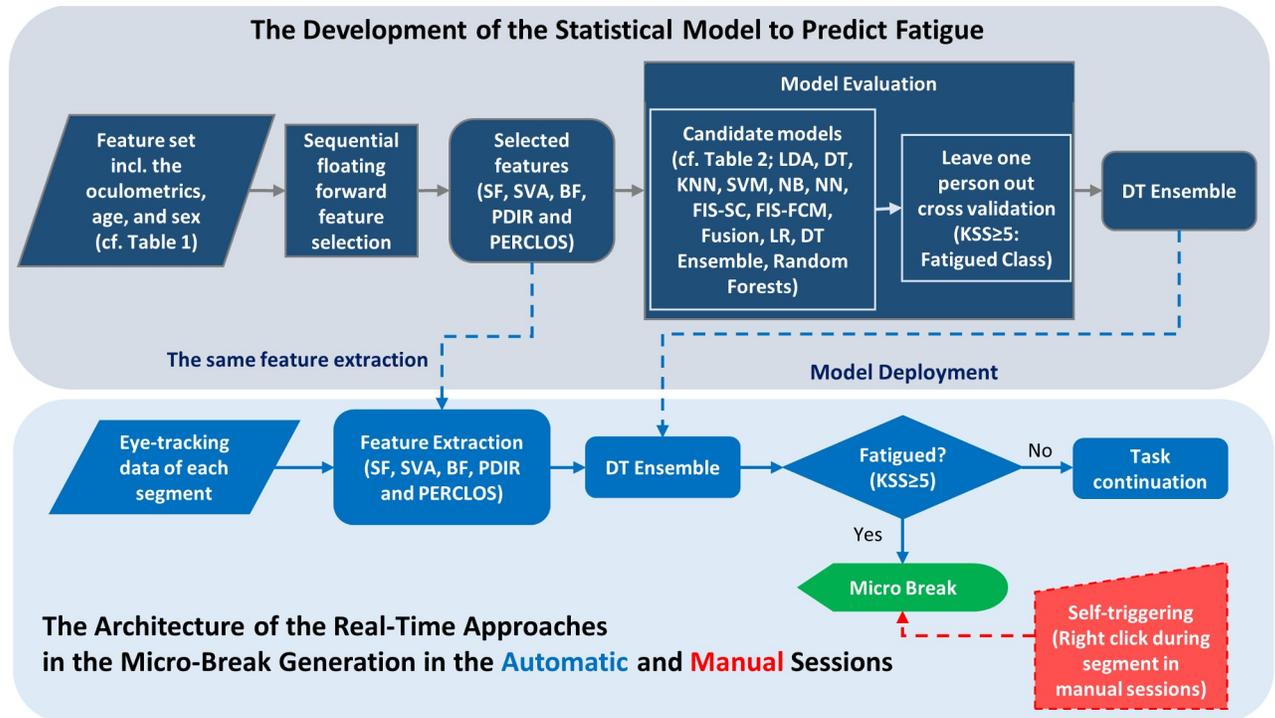
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| Confusion Matrix |                     | True Class          |                  |
|------------------|---------------------|---------------------|------------------|
|                  |                     | Positive (Fatigued) | Negative (Alert) |
| Predicted Class  | Positive (Fatigued) | 124 (60%)           | 76 (30%)         |
|                  | Negative (Alert)    | 81 (40%)            | 175 (70%)        |

Fig 2. The receiver operating characteristics (ROC) curve with the False Positive Rate (FPR) on the x-axis and the True Positive Rate (TPR) on the y-axis, depicted for the training and test sets, as well as the confusion matrix for the DT Ensemble model. The ROC curve is illustrated by computing the TPR and FPR averaged across the participants for varying values of the posterior probability threshold in [0 1] for the training and test sets. The confusion matrix was computed for the chosen KSS threshold of 5.

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**Fig 3. The architecture of the biofeedback system including the approaches to develop the statistical model to detect fatigue, and to trigger the micro-breaks.** This architecture provides the flowchart of the main steps to develop the fatigue detection model, from the feature selection to the model evaluation and the deployment of the DT-Ensemble model in the biofeedback framework wherein the data were streaming from the eye tracker in real-time and the selected features were extracted in the end of each task segment and were fed into the deployed DT-Ensemble model to trigger the micro-break if fatigue was detected in the automatic sessions (light blue path), whereas the triggering of the micro-break was only based on the decision of the participant in the manual sessions (red path).

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Phoenix Technologies Inc., Canada) was utilized to measure the eye movements, pupil diameter, and point of gaze at a sampling frequency of 360 Hz. The coupling of the eye-tracker and the head-tracker was done using built-in software to integrate eye and head positioning data and to compensate for head movements allowing free head movements during the experiment. As reported by the manufacturer, spatial precision of the eye-tracker is lower than 0.5° of visual angle. The spatial accuracy is less than 2° in the periphery of the visual field. The calibration of the eye-tracker was performed before starting the task with 9-point calibration protocol and examined before the task execution and after the task termination on the calibration points. The measured accuracy was on average 0.7 ± 0.4° across participants and did not significantly change across time ( $p > 0.6$ ). The experiments were conducted in a noise- and illumination- and temperature- controlled indoor room to rule out environmental confounding factors.

**Oculometrics.** Among all the features outlined in Table 1, the oculometrics were extracted from each segment. Saccades, blinks, and fixations were first identified for each segment using the algorithm of [97] as applied in [38]. Briefly, the algorithm initiated by the computation of visual angle between consecutive samples of point-of-gaze, followed by its derivatives to the angular velocity and acceleration using a 19-samples-length second-order Savitsky-Golay filter [97]. It applied data-driven thresholds on the angular velocity to detect saccadic samples. Zero-valued samples of pupil diameter, corresponding to closed eyes or missing pupil image provided by the built-in software of the eye-tracker, constituted blink samples, and the rest of the samples were assigned to fixations. Pupil diameter (including

linearly interpolated zero-valued samples) were filtered using a zero-phase low-pass third-order Butterworth to remove noise and artefacts [98]. Additional constraints were imposed to exclude invalid ocular events [38]. The data during the micro-breaks and KSS pauses were not included in the computation of oculometrics.

The frequency of blinks (BF), saccades (SF), and fixations (FF) were computed respectively as the number of blinks, saccades, and fixations during each segment divided by the duration of the segment. The mean duration of blinks (BD), fixations (FD), and saccades (SCD) were computed across each segment. Pupillary responses were characterized using the mean, coefficient of variation, interquartile range, instantaneous phase [83] of pupil diameter, respectively indicated by PD, PCV, PDIR, and PH. The number of closed-eyes samples (zero-valued pupil diameter) to opened-eyes samples was computed as PERCLOS. Blinks were further characterized by the frequency of blinks coincided by gaze shifts  $>2^\circ$  (BGF) [79,99] and their ratio to the number of all blinks (BGR). The mean of inter-blink interval (IBI), the frequency of blinks occurring with  $IBI < 700$  ms (DBF), the number of long blinks  $> 200$  ms [80] to the segment duration (LBF), and the ratio of long blinks to all blinks (LBR). Saccades were further quantified in terms of the mean value of their peak velocity (SPV), amplitude (SA), curvature [59] (SCR), peak amplitude of saccadic acceleration (SPA) and deceleration (SPD) profiles, inter-saccadic intervals (ISI) excluding  $ISI > 250$  ms, and the slope of the line regressing peak velocity of saccades to their amplitude (SVA) and duration (SDA). Similarly, fixations were further characterized as the ratio of long fixations ( $> 0.9$  s) [34] to all fixations (LFR).

Gaze dispersion was characterized using the mean value of gaze-point displacements and distances between two successive fixations respectively computed as Euclidean distance between the center of gaze points of two successive fixations ( $FF_{disp}$ ), the summation of Euclidean distances between successive gaze-points from the onset to offset of saccades connecting the two successive fixations ( $FF_{dist}$ ), and the ratio of the  $FF_{disp}$  to  $FF_{dist}$  for the same two successive fixations ( $FF_{disp/dist}$ ). The successive fixations exceeding over feasible saccade duration of  $> 100$  ms in this study were excluded [100]. In addition, overall dispersion (OD) was quantified as the averaged Euclidean distance between fixation centers and center of fixations. The center of fixations, gaze points and fixation centers were obtained using the mean value of their corresponding coordinates. The dynamics of visual perception were also quantified using the kappa coefficient of ambient and focal attention (KPA) as defined in [85]. The mean of time intervals ( $< 700$  ms) between a blink and its successive saccade was also extracted as a feature in association with blink perturbation effects on saccades [101].

The selected features of SF, SVA, BF, PDIR and PERCLOS were computed in the biofeedback system in the same way as they were computed from the OLDSET. To inspect the effect of the biofeedback system, the mean of the overall performance (OP) [38] across segments was computed. It represents how accurate and fast the pattern replication was done. Theoretically, the OP is a positive value with zero for the lowest performance (no click on the targets).

## Statistical analysis

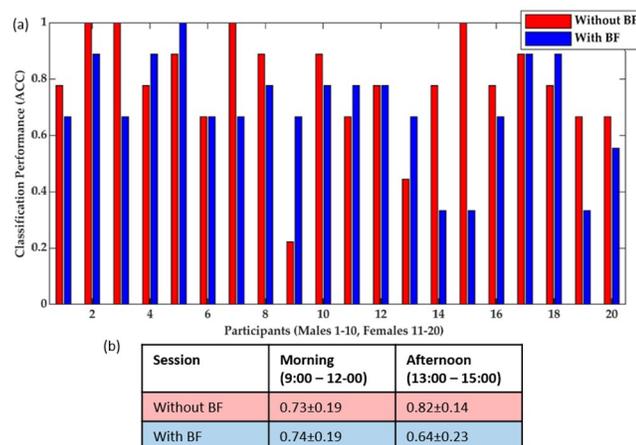
The statistical analysis was performed in SPSS 25. The classification performance of the deployed model (DT Ensemble) in the biofeedback system was reported in terms of the ACC, Sensitivity (TPR), and Specificity (TNR). The classification performance (ACC) was compared between the manual and automatic sessions using repeated measures analysis of variance (RM-ANOVA) and the interaction effect of the time of the day (morning or afternoon) on ACC was also considered. RM-ANOVA was also performed on the outcome variables (OP, KSS and oculometrics) with the time spent doing the task, Time-on-Task (TOT) (nine segments), and the automatic and the manual modes as within-subject factors (significance level

$p = 0.05$ ). Post-hoc comparisons between the segments were included in pairs indicated by Bonferroni correction. The Huynh-Feldt correction was applied if the assumption of sphericity was not met. The measure of effect size, partial eta-squared,  $\eta_p^2$ , was also reported. The perceived workload (NASA-TLX scores) and the number of micro-breaks was compared between the automatic and manual sessions using paired t-test with the effect size in terms of Cohen's  $d_z$  [102], to further evaluate the effectiveness of the biofeedback system. The normality of the variables was assessed using Shapiro–Wilk test. The KSS scores were transformed to normal distribution using square root transformation. Due to the counter-balanced order of the sessions, half of the first sessions were conducted in the manual mode (without biofeedback) and the rest half were conducted in the automatic mode (with biofeedback). The learning effect was analysed using RM-ANOVA to compare the OP across the first and second sessions. Sex-related differences in the OP, and the NASA-TLX scores, and the ACC were also reported. The Spearman's rank-order correlation was computed between every pair of the following variables in the manual and automatic sessions. The variables were the mean and standard deviation of the OP, the relative change of the KSS scores as  $(KSS_{last\ segment} - KSS_{first\ segment})/KSS_{first\ segment}$ , the number of micro-breaks, and the total and the weighted subscale scores of the NASA-TLX.

### Results

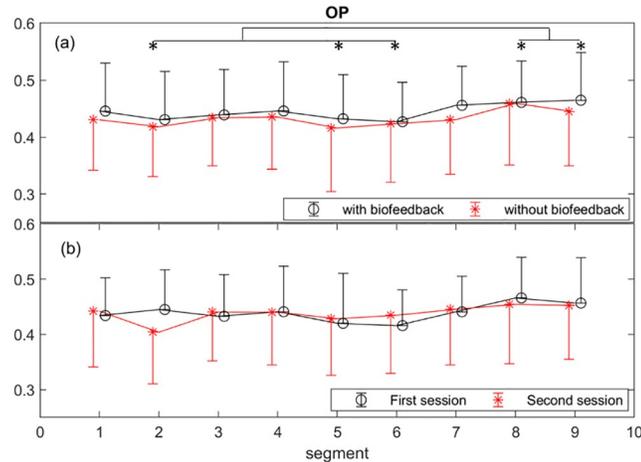
In the automatic sessions, the model (DT Ensemble) predicted fatigue with the following classification performance (Mean  $\pm$  SD): ACC (69 $\pm$ 16%), Sensitivity (59 $\pm$ 35%), and Specificity (74 $\pm$ 22%). The segments with fatigue label constituted 55 segments in total of 180 segments. Fig 4 demonstrated the classification performance (ACC) of the model in both sessions for each participant. There was neither a significant difference in the classification performance between the automatic and manual sessions, nor an interaction of the time of the day on the ACC. The ACC was approx. 10% higher on average in the male participants than in the female participants.

The OP in the presence of the biofeedback did not significantly change,  $F(1,18) = 1.3, p = .262, \eta_p^2 = .1$ , (Fig 5a). The OP increased significantly as TOT increased,  $F(8,152) = 4.7, p < .001, \eta_p^2 = .2$ . Pairwise comparisons revealed that the OP was significantly higher in segments



**Fig 4.** (a) Classification performance (ACC) of the DT Ensemble model for the male and female participants in the manual (without BF) and automatic (with BF) sessions, where BF stands for Biofeedback, (b) The ACC, Mean  $\pm$  SD, in different time of the day (Morning and Afternoon).

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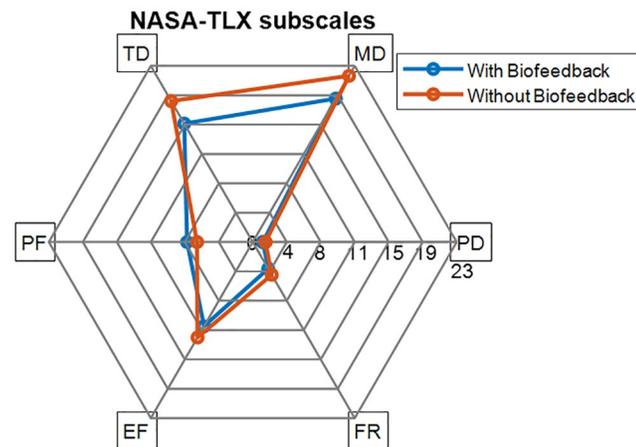
**Fig 5. Comparison of the overall performance (OP) across the automatic (with biofeedback) and manual (without biofeedback) sessions to assess the effect of micro-breaks, with the indicated segments with significant difference in the OP ( $p < 0.05$ ) (a), and across the first and second sessions to inspect whether there is a learning effect (b).** The points and error bars respectively represent the mean and standard deviation values across the participants for each segment.

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eight and nine compared with two, five, and six, Fig 5a. In addition, there was no learning effect on the OP across the first and second sessions (Fig 5b).

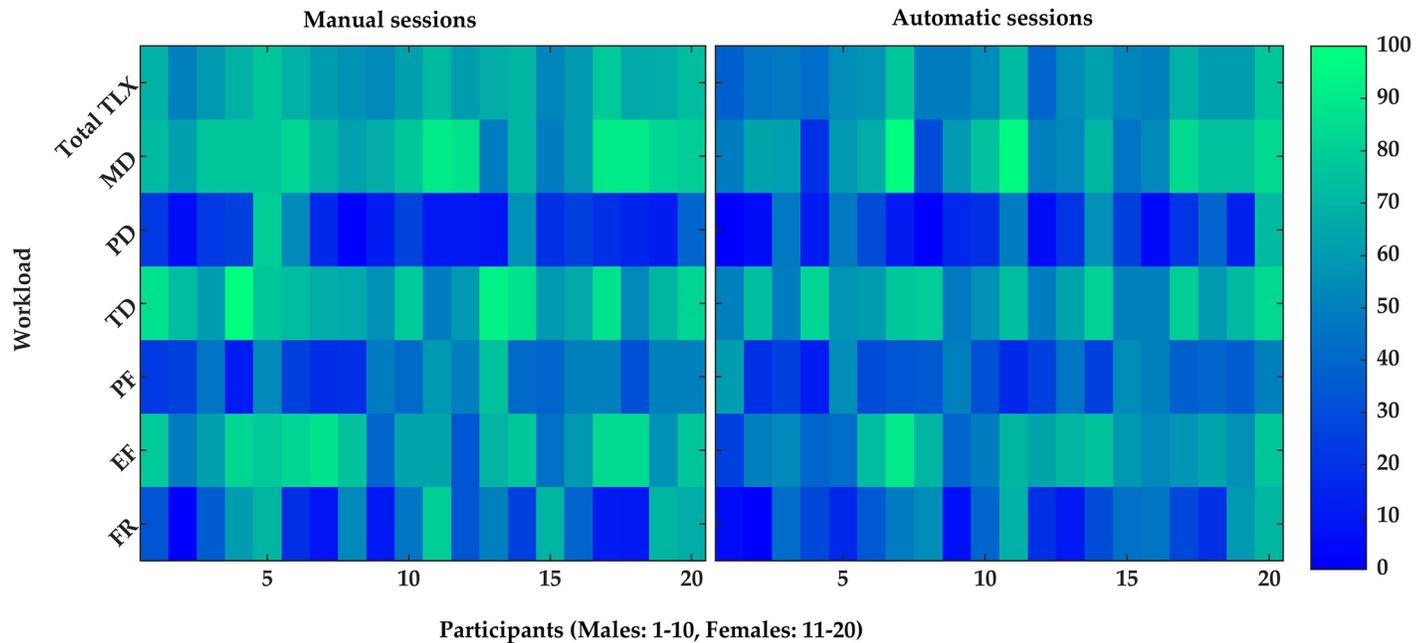
The participants reported significantly lower workload in the automatic ( $55 \pm 11$ ) than the manual sessions ( $65 \pm 8$ ) in terms of the total NASA-TLX scores,  $t(19) = 3.86$ ,  $p = 0.01$ , with the Cohen's  $d_z = 0.89$  corresponding to a large effect size according to [103]. This improvement was more pronounced in mental and temporal subscales than the other workload subscales as demonstrated in Fig 6.

To have an insight on the individual and sex-related differences in the perceived workload, the total NASA-TLX scores as well as the scores for all NASA-TLX subscales were depicted for each participant in Fig 7. In 60% of female and 70% of male participants, the total scores of



**Fig 6. The weighted scores of the NASA-TLX subscales in the automatic sessions (with biofeedback) and manual sessions (without biofeedback), where the subscales range from 0 to 33 indicating low to high levels. The subscales are Mental Demand (MD), Temporal Demand (TD), Performance (PF), Effort (EF), Frustration (FR), and Physical Demand (PD).**

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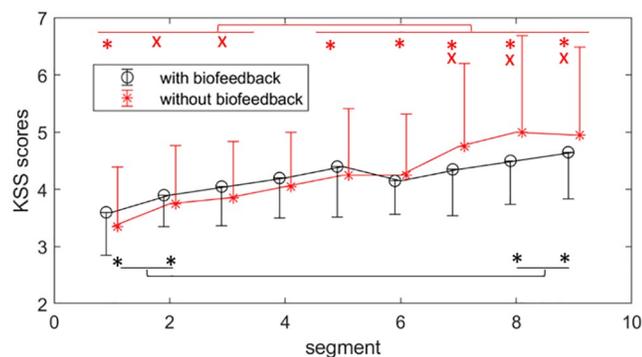


**Fig 7. The obtained ratings of total task load index (TLX) and NASA-TLX subscales, i.e. Mental Demand (MD), Physical Demand (PD), Temporal Demand (TD), Performance (PF), Effort (EF), and Frustration (FR).** The participants are separated by their sex on the x-axis to males (1–10) and females (11–20). The NASA-TLX scores are depicted separately for the automatic and manual sessions.

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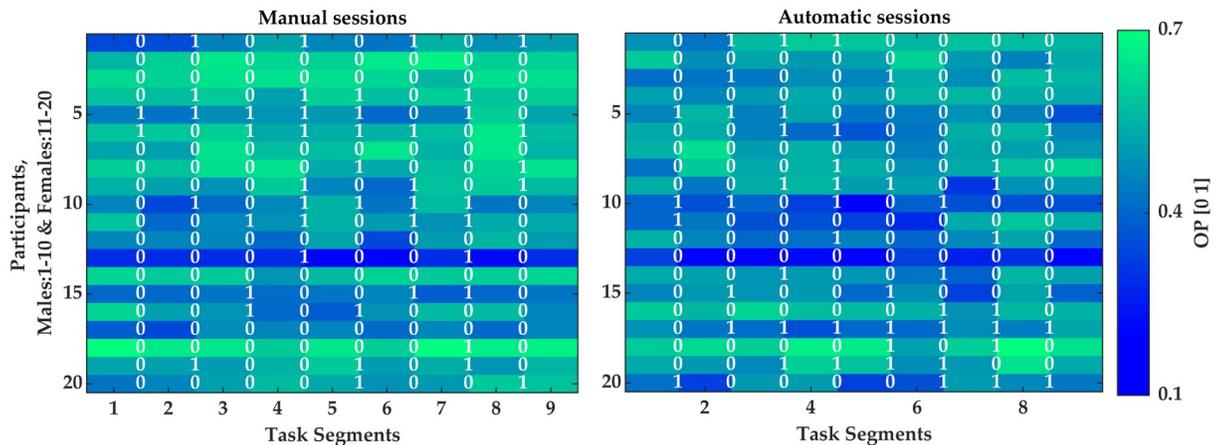
NASA-TLX were lower in the automatic sessions than in the manual sessions. The total scores were almost equal for the manual and automatic sessions for the participants number 11 and 15 (both females). In 70% of female and 60% of male participants, the mental demand was lower in the automatic sessions than in the manual sessions. 60% of female and 70% of male participants found the task less temporally demanding in the automatic sessions.

The KSS scores significantly increased in both of the manual and automatic sessions as the segments increased  $F(5.8,109.6) = 15.6, p < .001, \eta_p^2 = .4$ , Fig 8. No significant change in the KSS scores was found between the automatic and manual sessions. However, a tendency of



**Fig 8. Subjective ratings of fatigue (KSS scores) in the automatic (with biofeedback) and manual (without biofeedback) tasks.** The segments with significantly different KSS scores are indicated by the red color for the manual sessions and black color for the automatic sessions ( $p < 0.05$ ). The points and error bars respectively represent the mean and standard deviation values across the participants for each segment.

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**Fig 9. A representation of the overall performance (OP) of each participant (Y-axis) in the manual and automatic sessions.** The presence and absence of micro-breaks are indicated respectively by “1” and “0” at the end of each segment (X-axis). The OP is color coded with the color bar indicated on the right side of the graph with blue for lower and green for higher task performance.

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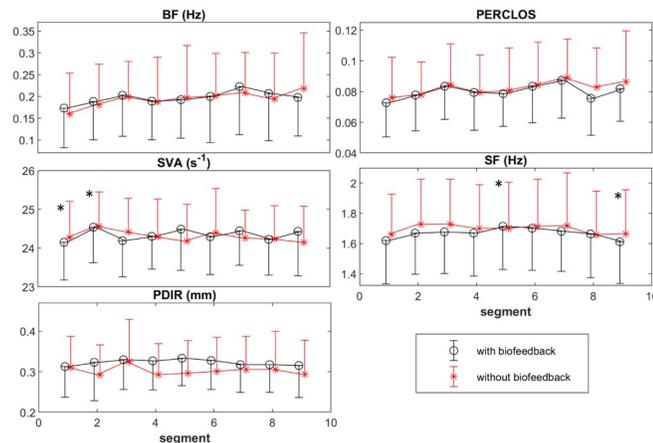
biofeedback×TOT interaction was found,  $F(5.9,113.6) = 1.7, p = .129, \eta_p^2 = .1$ . Pairwise comparisons showed that in the manual sessions, the KSS was lower in the first segment than in the segments 5–9, similarly between the segments 2–3 and 7–9, but in the automatic sessions, the significant difference was between the segments 1 and 2 being lower than both segments of 8 and 9.

The OP in automatic and manual sessions for each participant is illustrated in Fig 9. The participants are separated by their sex in Fig 9 to represent sex-related differences on the individual level. The occurrences of micro-breaks at the end of each segment is also indicated by “1” (and “0” for no micro-break) in Fig 9. More variations within the female participants can be observed in the OP than the male participants in both sessions. The standard deviation of the OP across segments averaged across the females were 0.061 whereas it was 0.056 for the males. In addition, the OP was higher in the 58% and 48% of the first segment following the micro-breaks compared with the segment prior to the micro-breaks, respectively for the male and female participants. There was no significant difference between the number of micro-breaks in the automatic sessions ( $2.9 \pm 1.9$ ) from the number of micro-breaks in the manual sessions ( $2.5 \pm 2.3$ ),  $p = .55$ .

The correlation analysis revealed that there are statistically significant relationships between a number of outcome variables in the manual sessions. The relative change of the KSS scores were positively correlated with the number of micro-breaks,  $r_s = .47, p = .039$ . The mean and the standard deviation of the OP tended to be negatively correlated,  $r_s = -.43, p = .060$ .

In the automatic sessions, there was a marginal correlation between the standard deviation of the OP and the number of micro-breaks,  $r_s = .42, p = .068$ . The number of the micro-breaks tended to positively correlate with the relative change of the KSS scores,  $r_s = .058, p = .043$ . Similar to the manual sessions, the mean and the standard deviation of the OP were negatively correlated,  $r_s = -.47, p = .037$ . No significant correlation was found between the total and weighted subscale scores of the NASA-TLX in the manual and automatic session with any of the mean and standard deviation of the OP and the range of the KSS scores.

Fig 10 is illustrated to show the changes in the recruited oculometrics in the model to predict fatigue. The BF tended to increase with TOT,  $F(5.0,95.1) = 2.2, p = .058, \eta_p^2 = .1$ . The PERCLOS increased significantly as TOT increased,  $F(8,152) = 2.3, p = .022, \eta_p^2 = .1$ . The SF



**Fig 10. The changes through TOT in the oculometrics, i.e. Blink Frequency (BF), Percentage of the duration of closed eyes to opened eyes (PERCLOS), Saccade Peak Velocity Amplitude Relationship (SVA), Saccade Frequency (SF), Pupil Diameter Interquartile Range (PDIR) used in the deployed model in the automatic (with biofeedback) sessions and manual (without biofeedback) sessions.** The points and error bars respectively represent the mean and standard deviation values across the participants for each segment. The segments with significant differences according to the pairwise comparisons are marked by “\*”, ( $p < 0.05$ ).

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decreased significantly as TOT increased,  $F(4.9,94.6) = 3.4, p = .007, \eta_p^2 = .1$ . Pairwise comparisons revealed that the SF decreased significantly from segment 5 to 9. The SVA fluctuated significantly through TOT,  $F(8,152) = 2.2, p = .027, \eta_p^2 = .1$ . The change between segments 1 and 2 was significant in SVA. No significant effect of TOT on PDIR was observed. Neither any significant effect of biofeedback nor biofeedback×TOT interaction was found in any of the oculometrics.

## Discussion

This study provided a novel framework to investigate the application of a biofeedback system to reduce fatigue development in its early stages during computer work. The proposed biofeedback system deployed a statistical model of fatigue, which used quantitative features extracted from eye movements and pupillary responses, i.e. SF, PERCLOS, PDIR, BF, and SVA. The accuracy of the statistical model was promising considering the subjectivity of KSS scores. As hypothesized, the biofeedback system with the embedded micro-breaks, effectively counteracted fatigue development reflected in delayed trending towards fatigue (Fig 8) and decreased perceived workload (Figs 6 and 7).

The involved oculometrics (SF, PERCLOS, PDIR, BF, and SVA) have been previously reported to be reliable and sensitive to fatigue progression as well as mental load [33,34,38,59,104,105]. The PERCLOS and BF are reported to increase with fatigue [34,106], which is in line with the current results. The decrease in SF and increase in BF along-side with TOT were also in agreement with previous findings [107]. Saccadic main sequence and the range of pupil diameter decreases and increased, respectively with TOT [38,108], but the SVA and PDIR did not change monotonically with TOT, most likely because of the presence of micro-breaks.

To the best of our knowledge, this was the first study to deploy a statistical model of fatigue in a biofeedback system to trigger objective micro-breaks, and thereby to elaborate self-awareness of fatigue. A few studies have contributed in noninvasive fatigue detection. In [109],

mental fatigue was detected offline using 31 statistical features from saccades, fixations, blinks, and pupillary responses exhibiting 77.1% accuracy with 10-fold cross validation via an SVM classifier. Our biofeedback system reached approx. 70% of accuracy (with an estimated misclassification rate of 0.30 in 10-fold cross-validation of the model) using the five features (versus 31 in [109]), which may facilitate real-time applications. Nine 30-s data samples collected from each participant before and after two 17-min cognitive tasks, were used to detect mental fatigue in [109]. A numerical rating scale has been used as a subjective rating of fatigue in [109], however, the samples recorded before and after the cognitive tasks have been respectively labeled as non-fatigued and fatigued, regardless of individual differences in fatigue perception as opposed to the current study. A recent study using wearable electroencephalography has classified fatigue from alertness using an SVM classifier, based on KSS threshold of five, with the accuracy of about 65% in a 10-fold cross validation [110]. In [111], fatigue, subjectively labeled using a different rating scale, has been classified via a feed-forward neural network using nine features extracted from computer user interactions with mouse and keyboard achieving an accuracy of 81% in a hold-out cross validation. The classification model proposed in [111], has been validated using the same group of individuals as opposed to the present study. Moreover, the features have been extracted over the period of one hour [111], which is much longer than a segment ( $\approx 200$  s) to trigger micro-breaks questioning the practical use of such approach.

A general limitation in the study of fatigue is the inaccuracies of subjective ratings (KSS scores). Although it is still one of the most commonly used methods to acquire fatigue level [112], it could be affected by factors such as experimental design [113] and individual's emotional state [114,115]. One may suggest the OP as an alternative to the KSS. However, the OP cannot necessarily be translated into fatigue levels in early detection of fatigue, Fig 5a. Additionally, the task performance may consistently change with TOT [7]. This is the main point of the studies investigating the maintenance of homeostasis in response to perceived fatigue via psychophysiological measures, e.g. heart rate variability [116].

Another important issue to consider is the effect of circadian rhythms on the accuracy of the fatigue state estimation [117]. Circadian rhythm is a source of variability in oculometrics [118,119] and cognition [120], which makes the prediction of fatigue quite challenging. The non-significant difference between the classification accuracy of the DT Ensemble model for the half of the participants who did the tasks in the morning (9:00–12:00) and the rest of the participants who did the tasks in the afternoon (13:00–15:00) gave support to the robustness of the model against circadian variations, (cf. Fig 4b).

An efficient and effective design for micro-breaks is quite challenging especially due to the complex interferences between physical and mental demands of a task [121,122]. Interestingly, reduced perceived workload was observed in the sessions where the micro-breaks were triggered by the biofeedback system compared with the manual sessions. More specifically, mental and temporal demands contributed more than the other subscales to the perceived workload in both manual and automatic sessions. The slight improvements of the OP, Fig 5a, and delayed inclination to fatigue, Fig 8, were observed through using the biofeedback system. Even though the improvement in the performance was statistically insignificant, one may conceive that in a long run the improvement may be of importance for the prevention of musculoskeletal disorders [16,17,123].

The relationships between the OP, perceived fatigue, and the number of micro-breaks in the manual and automatic sessions revealed some aspects of the two approaches to take micro-breaks. The positive correlation of the number of the micro-breaks with the relative change of the KSS scores, and the standard deviation of the OP, may imply that the frequency of the micro-breaks was reflected in the variations in the performance and the perceived fatigue in

the automatic session. The correlation of the number of micro-breaks and the relative change of the KSS scores were stronger in the manual sessions than the tendency in the automatic sessions, which may imply that the relative change in the perception of fatigue was less dependent to the number of micro-breaks in the automatic session. The negative correlation between the mean and standard deviation of the OP implies that as performance increases its variation is restrained. The lack of correlation of the number of the micro-breaks, the mean and standard deviation of the OP, and the range of the KSS scores the NASA-TLX scores suggests that none of these variables had any significant impact on the perceived workload of the participants. This finding indicates that the perceived workload cannot be reduced by just increasing the number of micro-breaks, giving support to the necessity of an intelligent approach to implement the micro-breaks [17].

The difference between the male and female participants were assessed on individual level in terms of their perceived workload (Fig 7), the accuracy of the model (Fig 4), and the effect of occurrences of micro-breaks on the OP (Fig 9). As mentioned in the results, the females on average exhibited similar OP to males, but at the individual level, the OP fluctuated more among females. The females perceived the task more demanding than the males in line with the higher prevalence of neck-shoulder complaints reported in females [124,125]. The performance of the statistical model to predict fatigue was higher for the males than females. Different factors may contribute to the sex-related differences, e.g. hormonal variations due to the menstrual cycle of the females [126]. Of note, the stages of the menstrual cycle were not assessed in the present study. Even though menstrual cycle may contribute to differences in fatigability among females, it is noteworthy however that this has not yet well established and contradicting results can be found in the literature regarding the menstrual cycle, e.g. [126,127]. The population size and design of the current study do not allow a thorough substantiation of the matter.

Some issues have important impacts on the design and assessment of the micro-breaks. The activities during micro-breaks should not demand for the same mental resources that a task might require [128]. Considering the multiple resource model [129], targeting the same mental resources may decline performance. Accordingly, in comparison with the task demands, the micro-breaks intuitively required little physical and mental demands as well as low vigilance to attend to down-counter displayed on the screen. The measurement of respiration rate to assess the breathings [71] was avoided to approach ecological validity for computer work as a limitation of this study. The quality of the mindful breathing could be assessed based on unobtrusive measurement of the respiration rate [130] or self-assessments of mindfulness [131]. In practice, to avoid too frequent and invalid micro-breaks, interactive micro-breaks [47] and model adaptation is suggested to study through the presented framework. In comparison with [132], the simplicity and effectiveness of the proposed micro-break as well as the unconstrained technique of eye tracking potentially meet constraints of out-of-lab settings.

## Conclusion

In line with our hypothesis, this study shows for the first time that the integration of oculometrics-based biofeedback in the design of micro-breaks is effective in fatigue mitigation during computer work. The effectiveness of the oculometrics-based biofeedback was evidenced by the decreased perception of workload and further by the postponed inclination to fatigue using the biofeedback system compared with self-triggered micro-breaks. In sum, the use of oculometrics as objective indices of fatigue in a biofeedback system may be a viable approach to impede fatigue development.

## Author Contributions

**Conceptualization:** Ramtin Zargari Marandi, Pascal Madeleine, Øyvind Omland, Nicolas Vuillerme, Afshin Samani.

**Data curation:** Ramtin Zargari Marandi.

**Formal analysis:** Ramtin Zargari Marandi.

**Funding acquisition:** Pascal Madeleine, Øyvind Omland, Nicolas Vuillerme, Afshin Samani.

**Investigation:** Ramtin Zargari Marandi.

**Methodology:** Ramtin Zargari Marandi, Afshin Samani.

**Project administration:** Pascal Madeleine, Afshin Samani.

**Resources:** Ramtin Zargari Marandi, Afshin Samani.

**Software:** Ramtin Zargari Marandi.

**Supervision:** Pascal Madeleine, Nicolas Vuillerme, Afshin Samani.

**Validation:** Ramtin Zargari Marandi.

**Visualization:** Ramtin Zargari Marandi.

**Writing – original draft:** Ramtin Zargari Marandi.

**Writing – review & editing:** Ramtin Zargari Marandi, Pascal Madeleine, Øyvind Omland, Nicolas Vuillerme, Afshin Samani.

## References

1. Silvian SP, Maiya A, Resmi AT, Page T. Antecedents of work related musculoskeletal disorders in software professionals. *Int J Enterp Netw Manag*. Inderscience Publishers Ltd; 2011; 4: 247–260.
2. Dawson D, Ian Noy Y, Härmä M, Kerstedt T, Belenky G. Modelling fatigue and the use of fatigue models in work settings. *Accid Anal Prev*. 2011; 43: 549–564. <https://doi.org/10.1016/j.aap.2009.12.030> PMID: 21130216
3. Colligan TW, Higgins EM. Workplace Stress: Etiology and Consequences. *J Workplace Behav Health*. 2005; 21: 89–97.
4. Swaen GMH, van Amelsvoort LGPM, Bültmann U, Kant I. Fatigue as a risk factor for being injured in an occupational accident: results from the Maastricht Cohort Study. *Occup Environ Med*. 2003; 60: i88–i92. [https://doi.org/10.1136/oem.60.suppl\\_1.i88](https://doi.org/10.1136/oem.60.suppl_1.i88) PMID: 12782753
5. Satterfield BC, Van Dongen HPA. Occupational fatigue, underlying sleep and circadian mechanisms, and approaches to fatigue risk management. *Fatigue Biomed Heal Behav*. 2013; 1: 118–136. <https://doi.org/10.1080/21641846.2013.798923>
6. Williamson A, Friswell R. Fatigue in the workplace: causes and countermeasures. *Fatigue Biomed Heal Behav*. Taylor & Francis; 2013; 1: 81–98.
7. Ackerman PL. 100 years without resting. *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. Washington, DC, US: American Psychological Association; 2011. pp. 11–43. <http://dx.doi.org/10.1037/12343-001>
8. Marandi RZ, Madeleine P, Vuillerme N, Omland Ø, Samani A. Early detection of fatigue based on heart rate in sedentary computer work in young and old adults. In: Bagnara S., Tartaglia R., Albolino S., Alexander T. FY (eds), editor. *Proceedings of the 20th Congress of the International Ergonomics Association (IEA 2018) IEA 2018 Advances in Intelligent Systems and Computing*. Springer; 2019. pp. 104–111. 10.1007/978-3-319-96065-4\_14
9. Enoka RM, Duchateau J. Translating fatigue to human performance. *Med Sci Sports Exerc*. 2016; 48: 2228–2238. <https://doi.org/10.1249/MSS.0000000000000929> PMID: 27015386
10. Kühnel J, Zacher H, de Bloom J, Bledow R. Take a break! Benefits of sleep and short breaks for daily work engagement. *Eur J Work Organ Psychol*. 2017; 26: 481–491. <https://doi.org/10.1080/1359432X.2016.1269750>

11. Helton WS, Russell PN. Rest is still best: The role of the qualitative and quantitative load of interruptions on vigilance. *Hum Factors*. 2017; 59: 91–100. <https://doi.org/10.1177/0018720816683509>
12. McLean L, Tingley M, Scott RN, Rickards J. Computer terminal work and the benefit of microbreaks. *Appl Ergon*. 2001; 32: 225–237. [https://doi.org/10.1016/S0003-6870\(00\)00071-5](https://doi.org/10.1016/S0003-6870(00)00071-5) PMID: 11394463
13. Hallbeck MS, Lowndes BR, Bingener J, Abdelrahman AM, Yu D, Bartley A, et al. The impact of intraoperative microbreaks with exercises on surgeons: A multi-center cohort study. *Appl Ergon*. 2017; 60: 334–341. <https://doi.org/10.1016/j.apergo.2016.12.006> PMID: 28166893
14. Barredo RDV, Mahon K. The effects of exercise and rest breaks on musculoskeletal discomfort during computer tasks: An evidence-based perspective. *J Phys Ther Sci*. 2007; 19: 151–163. <https://doi.org/10.1589/jpts.19.151>
15. Samani A, Holtermann A, Sjøgaard K, Madeleine P. Active pauses induce more variable electromyographic pattern of the trapezius muscle activity during computer work. *J Electromyogr Kinesiol*. Elsevier Ltd; 2009; 19: e430–437. <https://doi.org/10.1016/j.jelekin.2008.11.011> PMID: 19135388
16. Madeleine P, Vedsted P, Blangsted AK, Sjøgaard G, Sjøgaard K. Effects of electromyographic and mechanomyographic biofeedback on upper trapezius muscle activity during standardized computer work. *Ergonomics*. 2006; 49: 921–933. <https://doi.org/10.1080/00140130600665828> PMID: 16803724
17. Samani A, Holtermann A, Sjøgaard K, Madeleine P. Active biofeedback changes the spatial distribution of upper trapezius muscle activity during computer work. *Eur J Appl Physiol*. 2010; 110: 415–423. <https://doi.org/10.1007/s00421-010-1515-6> PMID: 20512502
18. Madeleine P. On functional motor adaptations: From the quantification of motor strategies to the prevention of musculoskeletal disorders in the neck-shoulder region. *Acta Physiol*. 2010; 199: 1–46. <https://doi.org/10.1111/j.1748-1716.2010.02145.x> PMID: 20579000
19. Samani A, Holtermann A, Sjøgaard K, Madeleine P. Advanced biofeedback from surface electromyography signals using fuzzy system. *Med Biol Eng Comput*. 2010; 48: 865–873. <https://doi.org/10.1007/s11517-010-0651-9> PMID: 20582484
20. Zhou P, Zhang C, He F, Xu R, Ming D, Zhao X, et al. How physical activities affect mental fatigue based on EEG energy, connectivity, and complexity. *Front Neurol*. 2018; 9: 915. <https://doi.org/10.3389/fneur.2018.00915> PMID: 30429822
21. Kouchaki S, Boostani R, Razavipour F. Fatigue detection using the strength of dominant EEG source: A beamforming approach. *Biomed Eng Appl Basis Commun*. 2018; 30: 1–22. <https://doi.org/10.4015/s1016237218500230>
22. Wascher E, Rasch B, Sängler J, Hoffmann S, Schneider D, Rinckenauer G, et al. Frontal theta activity reflects distinct aspects of mental fatigue. *Biol Psychol*. 2014; 96: 57–65. <https://doi.org/10.1016/j.biopsycho.2013.11.010> PMID: 24309160
23. Samani A, Srinivasan D, Mathiassen SE, Madeleine P. Variability in spatio-temporal pattern of trapezius activity and coordination of hand-arm muscles during a sustained repetitive dynamic task. *Exp Brain Res*. 2017; 235: 389–400. <https://doi.org/10.1007/s00221-016-4798-y> PMID: 27743011
24. Farina D, Leclerc F, Arendt-Nielsen L, Buttelli O, Madeleine P. The change in spatial distribution of upper trapezius muscle activity is correlated to contraction duration. *J Electromyogr Kinesiol*. 2008; 18: 16–25. <https://doi.org/10.1016/j.jelekin.2006.08.005> PMID: 17049273
25. Madeleine P, Farina D. Time to task failure in shoulder elevation is associated to increase in amplitude and to spatial heterogeneity of upper trapezius mechanomyographic signals. *Eur J Appl Physiol*. 2008; 102: 325–333. <https://doi.org/10.1007/s00421-007-0589-2> PMID: 17943307
26. Kawczyński A, Nie H, Jaskólska A, Jaskólski A, Arendt-Nielsen L, Madeleine P. Mechanomyography and electromyography during and after fatiguing shoulder eccentric contractions in males and females. *Scand J Med Sci Sport*. 2007; 17: 172–179. <https://doi.org/10.1111/j.1600-0838.2006.00551.x> PMID: 17394479
27. Ahn S, Nguyen T, Jang H, Kim JG, Jun SC. Exploring neuro-physiological correlates of drivers' mental fatigue caused by sleep deprivation using simultaneous EEG, ECG, and fNIRS data. *Front Hum Neurosci*. 2016; 10: 219. <https://doi.org/10.3389/fnhum.2016.00219>
28. Chuang CH, Cao Z, King JT, Wu BS, Wang YK, Lin CT. Brain electrodynamic and hemodynamic signatures against fatigue during driving. *Front Neurosci*. 2018; 12: 181. <https://doi.org/10.3389/fnins.2018.00181> PMID: 29636658
29. Yung M, Lang AE, Stobart J, Kocielek AM, Milosavljevic S, Trask C. The combined fatigue effects of sequential exposure to seated whole body vibration and physical, mental, or concurrent work demands. *PLoS One*. Public Library of Science; 2017; 12: e0188468. <https://doi.org/10.1371/journal.pone.0188468> PMID: 29236752

30. Zhang C, Zheng CX, Yu XL. Automatic recognition of cognitive fatigue from physiological indices by using wavelet packet transform and kernel learning algorithms. *Expert Syst Appl*. 2009; 36: 4664–4671. <https://doi.org/10.1016/j.eswa.2008.06.022>
31. Esposito F, Otto T, Zijlstra FRH, Goebel R. Spatially distributed effects of mental exhaustion on resting-state fMRI networks. *PLoS One*. 2014; 9: e94222. <https://doi.org/10.1371/journal.pone.0094222> PMID: 24705397
32. Cook DB, O'Connor PJ, Lange G, Steffener J. Functional neuroimaging correlates of mental fatigue induced by cognition among chronic fatigue syndrome patients and controls. *Neuroimage*. 2007; 36: 108–122. <https://doi.org/10.1016/j.neuroimage.2007.02.033> PMID: 17408973
33. Di Stasi LL, Renner R, Catena A, Cañas JJ, Velichkovsky BM, Pannasch S. Towards a driver fatigue test based on the saccadic main sequence: A partial validation by subjective report data. *Transp Res Part C Emerg Technol*. 2012; 21: 122–133. <https://doi.org/10.1016/j.trc.2011.07.002>
34. Schleicher R, Galley N, Briest S, Galley L. Blinks and saccades as indicators of fatigue in sleepiness warnings: looking tired? *Ergonomics*. 2008; 51: 982–1010. <https://doi.org/10.1080/00140130701817062> PMID: 18568959
35. Gergelyfi M, Jacob B, Olivier E, Zénon A. Dissociation between mental fatigue and motivational state during prolonged mental activity. *Front Behav Neurosci*. 2015; 9: 176. <https://doi.org/10.3389/fnbeh.2015.00176> PMID: 26217203
36. Roy RN, Charbonnier S, Bonnet S. Eye blink characterization from frontal EEG electrodes using source separation and pattern recognition algorithms. *Biomed Signal Process Control*. 2014; 14: 256–264. <https://doi.org/10.1016/j.bspc.2014.08.007>
37. Di Stasi LL, Marchitto M, Antolí A, Cañas JJ. Saccadic peak velocity as an alternative index of operator attention: A short review. *Rev Eur Psychol Appl*. 2013; 63: 335–343. <https://doi.org/10.1016/j.erap.2013.09.001>
38. Marandi RZ, Madeleine P, Omland Ø, Vuillerme N, Samani A. Eye movement characteristics reflected fatigue development in both young and elderly individuals. *Sci Rep*. 2018; 8: 13148. <https://doi.org/10.1038/s41598-018-31577-1> PMID: 30177693
39. Marandi RZ, Sabzpoushan SH. Using eye movement analysis to study auditory effects on visual memory recall. *Basic Clin Neurosci*. 2014; 5: 55–65. PMID: 25436085
40. Marandi RZ, Sabzpoushan SH. Qualitative modeling of the decision-making process using electrooculography. *Behav Res Methods*. 2014; 47: 1404–1412. <https://doi.org/10.3758/s13428-014-0549-9> PMID: 25515839
41. Poole A, Ball LJ. Eye tracking in Human-Computer Interaction and usability research: current status and future prospects. *Encyclopedia of Human-Computer Interaction*. IGI Global; 2005. pp. 211–219. <https://doi.org/10.4018/978-1-59140-562-7>
42. Henderson JM, Shinkareva S V., Wang J, Luke SG, Olejarczyk J. Predicting cognitive state from eye movements. *PLoS One*. 2013; 8: e64937. <https://doi.org/10.1371/journal.pone.0064937> PMID: 23734228
43. Di Stasi LL, Catena A, Cañas JJ, Macknik SL, Martinez-Conde S. Saccadic velocity as an arousal index in naturalistic tasks. *Neuroscience and Biobehavioral Reviews*. 2013. pp. 968–975. <https://doi.org/10.1016/j.neubiorev.2013.03.011> PMID: 23541685
44. Di Stasi LL, McCamy MB, Macknik SL, Mankin JA, Hooft N, Catena A, et al. Saccadic eye movement metrics reflect surgical residents' fatigue. *Ann Surg*. 2014; 259: 824–829. <https://doi.org/10.1097/SLA.0000000000000260>
45. Bailey BP, Konstan JA, Carlis J V. Measuring the effects of interruptions on task performance in the user interface. *Proceedings of the IEEE International Conference on Systems, Man and Cybernetics*. 2000. pp. 757–762. 10.1109/ICSMC.2000.885940
46. Tucker P. The impact of rest breaks upon accident risk, fatigue and performance: A review. *Work Stress*. 2003; 17: 123–137. <https://doi.org/10.1080/0267837031000155949>
47. Morris D, Brush a. JB, Meyers BR. SuperBreak: using interactivity to enhance ergonomic typing breaks. *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*. ACM; 2008. pp. 1817–1826. 10.1145/1357054.1357337
48. Giggins OM, Persson UMC, Caulfield B. Biofeedback in rehabilitation. *J Neuroeng Rehabil*. 2013; 10: 60. <https://doi.org/10.1186/1743-0003-10-60> PMID: 23777436
49. McKee MG. Biofeedback: An overview in the context of heart-brain medicine. *Cleve Clin J Med*. 2008; 75: S31. PMID: 18540143
50. Szegletes L, Köles M, Forstner B. The design of a biofeedback framework for dynamic difficulty adjustment in games. *Cognitive Infocommunications (CogInfoCom)*, 2014 5th IEEE Conference on. 2014. pp. 295–299.

51. Xiong J. The functions and methods of mental training on competitive sports. *Phys Procedia*. 2012; 33: 2011–2014. <https://doi.org/10.1016/j.phpro.2012.05.316>
52. Wells R, Outhred T, Heathers JAJ, Quintana DS, Kemp AH. Matter over mind: A randomised-controlled trial of single-session biofeedback training on performance anxiety and heart rate variability in musicians. *PLoS One*. 2012; 7: e46597. <https://doi.org/10.1371/journal.pone.0046597> PMID: 23056361
53. Bouchard S, Bernier F, Boivin É, Morin B, Robillard G. Using biofeedback while immersed in a stressful videogame increases the effectiveness of stress management skills in soldiers. *PLoS One*. 2012; 7: e36169. <https://doi.org/10.1371/journal.pone.0036169> PMID: 22558370
54. Deschodt-Arsac V, Lalanne R, Spiluttini B, Bertin C, Arsac LM. Effects of heart rate variability biofeedback training in athletes exposed to stress of university examinations. *PLoS One*. 2018; 13: e0201388. <https://doi.org/10.1371/journal.pone.0201388> PMID: 30048519
55. Temple JL, Bernard C, Lipshultz SE, Czachor JD, Westphal JA, Mestre MA. The safety of ingested caffeine: A comprehensive review. *Front Psychiatry*. 2017; 8: 80. <https://doi.org/10.3389/fpsy.2017.00080> PMID: 28603504
56. Michielsen HJ, De Vries J, Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *J Psychosom Res*. 2003; 54: 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6) PMID: 12670612
57. Heuer H, Hollendiek G, Kröger H, Römer T. Die ruhelage der augen und ihr einfluss auf beobachtung-sabstand und visuelle ermuedung bei bildschirmarbeit. *Z Exp Angew Psychol*. 1989; 36: 538–566.
58. Marandi RZ. WAME1.0, a standardized computer task to induce cognitive load, and develop fatigue [Internet]. Aalborg, Denmark: Center for Open Science; 2019. <https://doi.org/10.17605/OSF.IO/2FC7S>
59. Marandi RZ, Madeleine P, Omland Ø, Vuillerme N, Samani A. Reliability of oculometrics during a mentally demanding task in young and old adults. *IEEE Access*. 2018; 6: 17500–17517. <https://doi.org/10.1109/ACCESS.2018.2819211>
60. Laring J, Forsman M, Kadefors R, Örtengren R. MTM-based ergonomic workload analysis. *Int J Ind Ergon*. 2002; 30: 135–148. [https://doi.org/10.1016/S0169-8141\(02\)00091-4](https://doi.org/10.1016/S0169-8141(02)00091-4)
61. Åkerstedt T, Gillberg M. Subjective and objective sleepiness in the active individual. *Int J Neurosci*. 1990; 52: 29–37. <https://doi.org/10.3109/00207459008994241> PMID: 2265922
62. Mahachandra M, Satalaksana IZ, Suryadi K. Sleepiness pattern of indonesian professional driver based on subjective scale and eye closure activity. *Int J Basic Appl Sci*. 2011; 11: 87–96.
63. Ftouni S, Sletten TL, Howard M, Anderson C, Lenné MG, Lockley SW, et al. Objective and subjective measures of sleepiness, and their associations with on-road driving events in shift workers. *J Sleep Res*. 2013; 22: 58–69. <https://doi.org/10.1111/j.1365-2869.2012.01038.x> PMID: 22861524
64. Michaelis J. The restorative effects of color and environment type on cognitive functioning. University of Central Florida. 2013.
65. Lee KE, Williams KJH, Sargent LD, Williams NSG, Johnson KA. 40-second green roof views sustain attention: The role of micro-breaks in attention restoration. *J Environ Psychol*. 2015; 42: 182–189. <https://doi.org/10.1016/j.jenvp.2015.04.003>
66. Feldman G, Greeson J, Senville J. Differential effects of mindful breathing, progressive muscle relaxation, and loving-kindness meditation on decentering and negative reactions to repetitive thoughts. *Behav Res Ther*. 2010; 48: 1002–1011. <https://doi.org/10.1016/j.brat.2010.06.006> PMID: 20633873
67. Arch JJ, Craske MG. Mechanisms of mindfulness: Emotion regulation following a focused breathing induction. *Behav Res Ther*. 2006; 44: 1849–1858. <https://doi.org/10.1016/j.brat.2005.12.007> PMID: 16460668
68. Abdelall ES, Lowndes BR, Abdelrahman AM, Hawthorne HJ, Hallbeck MS. Mini breaks, many benefits: Development and pilot testing of an intraoperative microbreak stretch web-application for surgeons. Proceedings of the Human Factors and Ergonomics Society Annual Meeting. Los Angeles, CA: SAGE Publications; 2018. pp. 1042–1046. 10.1177/1541931218621240
69. Kelso D. Effects of frequent, active microbreaks during computer operation. San Jose State University. 2001.
70. Vlemincx E, Taelman J, De Peuter S, Van Diest I, Van Den Bergh O. Sigh rate and respiratory variability during mental load and sustained attention. *Psychophysiology*. 2011; 48: 117–120. <https://doi.org/10.1111/j.1469-8986.2010.01043.x> PMID: 20536901
71. Prinsloo GE, Derman WE, Lambert MI, Laurie Rauch HG. The effect of a single session of short duration biofeedback-induced deep breathing on measures of heart rate variability during laboratory-induced cognitive stress: A pilot study. *Appl Psychophysiol Biofeedback*. 2013; 38: 81–90. <https://doi.org/10.1007/s10484-013-9210-0> PMID: 23435801

72. Benchetrit G. Breathing pattern in humans: Diversity and individuality. *Respir Physiol.* 2000; 122: 123–129. [https://doi.org/10.1016/S0034-5687\(00\)00154-7](https://doi.org/10.1016/S0034-5687(00)00154-7) PMID: 10967339
73. Hart, Sandra G. NASA-task load index (NASA-TLX); 20 years later. Proceedings of the human factors and ergonomics society annual meeting. Los Angeles, CA: Sage publications; 2006. pp. 904–908. 10.1037/e577632012-009
74. Cao A, Chintamani KK, Pandya AK, Ellis RD. NASA TLX: Software for assessing subjective mental workload. *Behav Res Methods.* 2009; 41: 113–117. <https://doi.org/10.3758/BRM.41.1.113> PMID: 19182130
75. Felton EA, Williams JC, Vanderheiden GC, Radwin RG. Mental workload during brain-computer interface training. *Ergonomics.* 2012; 55: 526–537. <https://doi.org/10.1080/00140139.2012.662526> PMID: 22506483
76. Pudil P, Novovicova J, Kittler J. Floating search methods in feature-selection. *Pattern Recognit Lett.* 1994; 15: 1119–1125. [https://doi.org/10.1016/0167-8655\(94\)90127-9](https://doi.org/10.1016/0167-8655(94)90127-9)
77. Powers DM. Evaluation: from precision, recall and F-measure to ROC, informedness, markedness and correlation. *J Mach Learn Technol.* 2011; 2: 37–63.
78. Ren Q, Cheng H, Han H. Research on machine learning framework based on random forest algorithm. AIP Conference Proceedings. AIP Publishing; 2017. p. 80020.
79. Yorzinski JL. Eye blinking in an avian species is associated with gaze shifts. *Sci Rep.* 2016; 6: p.32471. <https://doi.org/10.1038/srep32471> PMID: 27572457
80. Aleksandra Krolak PS. Eye-blink detection system for human-computer interaction. *Univers Access Inf Soc.* 2012; 11: 409–419. <https://doi.org/10.1007/s10209-011-0256-6>
81. Nakanishi M, Mitsukura Y, Wang YY-T, Wang YY-T, Jung T-P. Online voluntary eye blink detection using electrooculogram. International Symposium on Nonlinear Theory and Its Applications. Palma Mallorca, Spain; 2014. pp. 114–117. 10.15248/proc.1.114
82. Fogelton A, Benesova W. Eye blink detection based on motion vectors analysis. *Comput Vis Image Underst.* 2016; 148: 23–33. <https://doi.org/10.1016/j.cviu.2016.03.011>
83. Yamada Y. Age estimation using feature of eye movement. United States patent application; US 15/345,876, 2018.
84. Wakui H, Hirata Y. Detection of reduced arousal by saccadic eye movement. *Japanese Soc Med Biol Eng.* 2014; 51: 328–341.
85. Krejtz K, Duchowski A, Krejtz I, Szarkowska A, Kopacz A. Discerning ambient/focal attention with coefficient k. *ACM Trans Appl Percept.* 2016; 13: 11. <https://doi.org/10.1145/2896452>
86. Raudys S, Duin RPW. Expected classification error of the Fisher linear classifier with pseudo-inverse covariance matrix. *Pattern Recognit Lett.* 1998; 19: 385–392. [https://doi.org/10.1016/S0167-8655\(98\)00016-6](https://doi.org/10.1016/S0167-8655(98)00016-6)
87. Cutler A, Cutler DR, Stevens JR. Random forests. *Ensemble Machine Learning: Methods and Applications.* Boston, MA: Springer; 2012. pp. 157–175.
88. Duda RO, Hart PE, Stork DG. Pattern classification. *Pattern Analysis and Applications.* John Wiley & Sons; 1998. <https://doi.org/10.1007/BF01237942>
89. Al Shalabi L, Shaaban Z. Normalization as a preprocessing engine for data mining and the approach of preference matrix. International Conference on Dependability of Computer Systems. IEEE; 2006. pp. 207–214. 10.1109/DEPCOS-RELCOMEX.2006.38
90. Fan R, Chen P, Lin C. Working set selection using second order information for training support vector machines. *J Mach Learn Res.* 2005; 6: 1889–1918.
91. Chang C, Lin C. LIBSVM: a library for support vector machines. *ACM Trans Intell Syst Technol.* 2011; 2: 27:1–27:7. <https://doi.org/10.1145/1961189.1961199>
92. Kothari SC, Oh H. Neural networks for pattern recognition. In: Marshall C. Yovits, editor. *Advances in Computers.* Academic Press, Inc.; 1993. pp. 119–166. [https://doi.org/10.1016/S0065-2458\(08\)60404-0](https://doi.org/10.1016/S0065-2458(08)60404-0)
93. Evers FT, Höppner F, Klawonn F, Kruse R, Runkler T. Fuzzy cluster analysis: methods for classification, data analysis and image recognition. John Wiley & Sons; 1999.
94. James G. Majority vote classifiers: theory and applications. Stanford University. 1998.
95. Freund Y. A more robust boosting algorithm. *arXiv Prepr arXiv09052138.* 2009;
96. Combrisson E, Jerbi K. Exceeding chance level by chance: The caveat of theoretical chance levels in brain signal classification and statistical assessment of decoding accuracy. *J Neurosci Methods.* 2015; 250: 126–136. <https://doi.org/10.1016/j.jneumeth.2015.01.010> PMID: 25596422

97. Nyström M, Holmqvist K. An adaptive algorithm for fixation, saccade, and glissade detection in eye-tracking data. *Behav Res Methods*. 2010; 42: 188–204. <https://doi.org/10.3758/BRM.42.1.188> PMID: 20160299
98. Caffier PP, Erdmann U, Ullsperger P. Experimental evaluation of eye-blink parameters as a drowsiness measure. *Eur J Appl Physiol*. 2003; 89: 319–325. <https://doi.org/10.1007/s00421-003-0807-5> PMID: 12736840
99. Riggs LA, Kelly JP, Manning KA, Moore RK. Blink-related eye movements. *Investig Ophthalmol Vis Sci*. 1987; 28: 334–3452.
100. Harris CM, Wolpert DM. The main sequence of saccades optimizes speed-accuracy trade-off. *Biol Cybern*. 2006; 95: 21–29. <https://doi.org/10.1007/s00422-006-0064-x> PMID: 16555070
101. Katnani HA, van Opstal AJ, Gandhi NJ. Blink perturbation effects on saccades evoked by microstimulation of the superior colliculus. *PLoS One*. 2012; 7: e51843. <https://doi.org/10.1371/journal.pone.0051843> PMID: 23251639
102. Cohen J. *Statistical power analysis for the behavioural science*. Statistical Power Analysis for the Behavioural Science. 2nd ed. 1988.
103. Sawilowsky SS. New effect size rules of thumb. *J Mod Appl Stat Methods*. 2009; 8: 597–599. <https://doi.org/10.22237/jmasm/1257035100>
104. Wilhelm BJ, Heine C, Widmann A, Durst W, Lüdtkke H, Otto G. How sleepy are construction workers during extended shifts? An objective investigation of spontaneous pupillary oscillations in tunnel workmen. *Somnologie-schlaforsch und Schlafmedizin*. 2010; 14: 200–206. <https://doi.org/10.1007/s11818-010-0480-y>
105. Sampei K, Ogawa M, Torres C, Sato M, Miki N. Mental fatigue monitoring using a wearable transparent eye detection system. *Micromachines*. 2016; 7: 20. <https://doi.org/10.3390/mi7020020> PMID: 30407393
106. Puspasari MA, Iridiastadi H, Sutalaksana IZ, Sjafruddin A. Fatigue classification of ocular indicators using support vector machine. 2018 International Conference on Intelligent Informatics and Biomedical Sciences (ICIIBMS). IEEE; 2018. pp. 66–69. 10.1109/ICIIBMS.2018.8549999
107. Di Stasi LL, McCamy MB, Pannasch S, Renner R, Catena A, Cañas JJ, et al. Effects of driving time on microsaccadic dynamics. *Exp Brain Res*. 2014; 233: 599–605. <https://doi.org/10.1007/s00221-014-4139-y> PMID: 25417191
108. Di Stasi LL, McCamy MB, Catena AA, Macknik SL, Cañas JJJ, Martinez-Conde S. Microsaccade and drift dynamics reflect mental fatigue. *Eur J Neurosci*. Wiley Online Library; 2013; 38: 2389–2398. <https://doi.org/10.1111/ejn.12248> PMID: 23675850
109. Yamada Y, Kobayashi M. Detecting mental fatigue from eye-tracking data gathered while watching video: Evaluation in younger and older adults. *Artif Intell Med*. 2018; 91: 39–48. <https://doi.org/10.1016/j.artmed.2018.06.005> PMID: 30026049
110. Ogino M, Mitsukura Y. Portable drowsiness detection through use of a prefrontal single-channel electroencephalogram. *Sensors*. Multidisciplinary Digital Publishing Institute; 2018; 18: 4477.
111. Pimenta A, Carneiro D, Neves J, Novais P. A neural network to classify fatigue from human-computer interaction. *Neurocomputing*. 2016; 172: 413–426. <https://doi.org/10.1016/j.neucom.2015.03.105>
112. Kaida K, Takahashi M, Åkerstedt T, Nakata A, Otsuka Y, Haratani T, et al. Validation of the Karolinska sleepiness scale against performance and EEG variables. *Clin Neurophysiol*. 2006; 117: 1574–1581. <https://doi.org/10.1016/j.clinph.2006.03.011> PMID: 16679057
113. Åkerstedt T, Anund A, Axelsson J, Kecklund G. Subjective sleepiness is a sensitive indicator of insufficient sleep and impaired waking function. *J Sleep Res*. 2014; 23: 242–254. <https://doi.org/10.1111/jsr.12158> PMID: 24750198
114. Gröhn M, Ahonen L, Huotilainen M. Effects of pleasant and unpleasant auditory mood induction on the performance and in brain activity in cognitive tasks. *Proceedings of the 18th International Conference on Auditory Display*. Atlanta, GA, USA; 2012. pp. 18–21.
115. Shahid A, Shen J, Shapiro CM. Measurements of sleepiness and fatigue. *J Psychosom Res*. 2010; 69: 81–89. <https://doi.org/10.1016/j.jpsychores.2010.04.001> PMID: 20630266
116. Zhang C, Yu X. Estimating mental fatigue based on electroencephalogram and heart rate variability. *Polish J Med Phys Eng*. 2010; 16: 67–84. <https://doi.org/10.2478/v10013-010-0007-7>
117. Liu CC, Hosking SG, Lenné MG. Predicting driver drowsiness using vehicle measures: Recent insights and future challenges. *J Safety Res*. 2009; 40: 239–245. <https://doi.org/10.1016/j.jsr.2009.04.005> PMID: 19778647
118. Schälén L, Pyykkö I, Juhola M, Magnusson M, Jäntti V, Henriksson N. Intra-individual variation in oculomotor performance in man. *Acta Otolaryngol*. 1983; 96: 212–217. <https://doi.org/10.3109/00016488309123036>

119. Cazzoli D, Antoniadou CA, Kennard C, Nyffeler T, Bassetti CL, Müri RM. Eye movements discriminate fatigue due to chronotypical factors and time spent on task—A double dissociation. *PLoS One*. 2014; 9: e87146. <https://doi.org/10.1371/journal.pone.0087146>
120. Schmidt C, Collette F, Cajochen C, Peigneux P. A time to think: Circadian rhythms in human cognition. *Cogn Neuropsychol*. 2007; 24: 755–789. <https://doi.org/10.1080/02643290701754158> PMID: 18066734
121. Epling SL, Blakely MJ, Russell PN, Helton WS. Free recall and outdoor running: cognitive and physical demand interference. *Exp Brain Res*. 2016; 234: 2979–2987. <https://doi.org/10.1007/s00221-016-4700-y> PMID: 27299913
122. Yang G, Lin Y, Bhattacharya P. A driver fatigue recognition model based on information fusion and dynamic Bayesian network. *Inf Sci (Ny)*. 2010; 180: 1942–1954. <https://doi.org/10.1016/j.ins.2010.01.011>
123. Steinborn MB, Huestegge L. A walk down the lane gives wings to your brain. Restorative benefits of rest breaks on cognition and self-control. *Appl Cogn Psychol*. 2016; 30: 795–805. <https://doi.org/10.1002/acp.3255>
124. Wærsted M, Hanvold TN, Veiersted KB. Computer work and musculoskeletal disorders of the neck and upper extremity: A systematic review. *BMC Musculoskelet Disord*. 2010; 11: 79. <https://doi.org/10.1186/1471-2474-11-79> PMID: 20429925
125. Madeleine P, Vangsgaard S, Hviid Andersen J, Ge HY, Arendt-Nielsen L. Computer work and self-reported variables on anthropometrics, computer usage, work ability, productivity, pain, and physical activity. *BMC Musculoskelet Disord*. 2013; 14: 226. <https://doi.org/10.1186/1471-2474-14-226> PMID: 23915209
126. Clemes SA. The influence of the menstrual cycle on visually-induced discomfort. Loughborough University. 2004.
127. Ferguson DP, Barthel SC, Pruett ML, Buckingham TM, Waaso PR. Physiological responses of male and female race car drivers during competition. *Med Sci Sports Exerc*. 2019; In-Press.
128. Kim S, Park YA, Niu Q. Micro-break activities at work to recover from daily work demands. *J Organ Behav*. 2017; 38: 28–44. <https://doi.org/10.1002/job.2109>
129. Wickens CD. Processing resources and attention. In: Damos D, editor. *Multiple Task Performance*. Taylor & Francis; 1991. pp. 3–34. Parasuraman R., Davies R.
130. Zheng YL, Ding XR, Poon CCY, Lo BPL, Zhang H, Zhou XL, et al. Unobtrusive sensing and wearable devices for health informatics. *IEEE Trans Biomed Eng*. 2014; <https://doi.org/10.1109/TBME.2014.2309951> PMID: 24759283
131. Burg JM, Michalak J. The healthy quality of mindful breathing: Associations with rumination and depression. *Cognit Ther Res*. 2011; 35: 179–185. <https://doi.org/10.1007/s10608-010-9343-x>
132. Januario LB, Moreira R de FC, Cid MM, Samani A, Madeleine P, Oliveira AB. Effects of active pause pattern of surface electromyographic activity among subjects performing monotonous tasks: A systematic review. *J Electromyogr Kinesiol*. 2016; 30: 196–208. <https://doi.org/10.1016/j.jelekin.2016.07.009> PMID: 27494647