Continuous monitoring of cognitive load using advanced computerized analysis of brain signals during virtual simulator training for laparoscopic surgery, reflects laparoscopic dexterity. A comparative study using a novel wireless device.

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Abstract

Introduction: Simulation-based training is an effective tool for acquiring practical skills, the question remains as to which methods should be utilized to optimize this process and for a better assessment of improved manual dexterity. Specifically, it is not fully understood which brain processes during simulation-based training will translate to better skill acquisition through practice. As cognitive load decreases with better performance, we used a novel method for brain assessment that enables an extraction of a cognitive load neurological biomarker.

Methods: 38 participants were assigned into 3 experiments examining their behavioral performance undergoing a task with the Simbionix LAP MENTOR™ simulator, while their brain activity was measured using a single-electrode EEG by Aurora by Neurosteer®. Each task was repeated 3 times with difference session setups (in three consecutive days, Exp 1, on the same session, Exp 2, and with a 3 trials repetition on the consecutive day, Exp 3). Correlations between a cognitive biomarker (VC9) and behavioral performance measurements (e.g. accuracy, economy of movement and time to exceed the task).

Results: Exp 1 results exhibited an improvement in behavioral performance with no correlation or difference in VC9. As a result of prolonging session time to three trials, VC9 activity decreased with higher participants performance both in Exp.2 and in Exp. 3. In addition, behavioral performance improved and VC9 activity decreased during the three trials of Exp. 2 but not throughout the three trials of Exp. 3 which occurred on the consecutive day.

Discussion: Altogether, VC9 is found to be an effective biological measurement for the assessment of cognitive load while performing laparoscopic tasks using the surgical simulator. As surgical simulations allow to gain important skills and experience needed to perform procedures without any patient risk, it is crucial to fully evaluate and optimize the effect of these simulations on medical staff. This could potentially be expanded to evaluate the efficacy different medical simulations to help medical staff and to measure cognitive and mental load under real laparoscopic surgeries.
**Introduction**

Medical simulations are a common and widespread tool for medical education. Medical simulations can emulate common scenarios in clinical practice, and through interactive interplay and hands-on teaching, improve the efficacy and quality of teaching for healthcare professionals [1]. These simulations can be particularly beneficial for surgical staff, as they allow residents to practice and perfect complex procedures, ensuring they have enough experience and practice before real patient contact [2]. As laparoscopic surgeries demand unique eye-hands coordination and are performed while the surgeon indirectly observes the intra-abdominal contents without tactile sensation ability and through a camera view, they are ideal candidates for virtual reality simulators. Indeed, these simulators have been shown to greatly improve the surgeon’s operating skills and reduce operating time [3-8].

Seeing as simulation-based training is an effective tool for acquiring practical skills, the question remains as to which methods should be utilized to optimize this process and for a better assessment of improved manual dexterity. Specifically, it is not fully understood which brain processes during simulation-based training will translate to better skill acquisition through practice. Cognitive load theory has been linked to procedural learning during simulations [6], according to which new acquired skill or knowledge is passed through the working memory before being transferred to long-term memory. Unlike the long-term memory, working memory is limited in the amount of new information it can acquire during a single session, meaning that if the cognitive load surpasses the working memory capacity, the learning process is impaired and the simulation becomes ineffective [9]. As the working memory load varies between individuals, objective, and physiologic methods to evaluate the cognitive load during a simulation are of particular importance [10].

The aim of this study was to track brain activity patterns using a small and wearable EEG device while performing a task on a surgical simulator, and to evaluate the relationship between brain activity and the participants’ performance and skill acquisition. We also intended to compare it to the feedback parameters measured by the LAP MENTOR virtual simulator following each laparoscopic exercise, and to test the impact of over-night rest on the perfection of laparoscopic motor dexterity [11-12].

To meet these goals, we used a wearable EEG system with a 3-electrode patch placed on the participant’s forehead (Aurora by Neurosteer® Inc). The system provides 121 Brain Activity Features (BAFs) extracted via harmonic analysis (see Appendix A for full details). The BAFs extraction technique was defined on a large set of EEG recordings (dataset A). Next, the
BAFs were extracted from another dataset (dataset B), which included healthy participants undergoing different cognitive tasks such as auditory detection, auditory discrimination, and resting state tasks. From dataset B, new linear and non-linear combinations of BAFs (e.g. higher-level features) were calculated using machine learning (ML) algorithms. The purpose was to discriminate between the different cognitive tasks and difficulty levels. Specifically, following advanced signal analysis methods, a suitable biomarker (called VC9) was found to be the best discriminator between an auditory detection task and an auditory classification task. VC9 biomarker was recently validated in two controlled experiments using the n-back task [13] and auditory detection task [14-15]. Both studies found that VC9 activity increased with increasing levels of cognitive load within cognitively healthy participants. We were therefore interested in finding out whether VC9 activity will decrease when cognitive load decreases under the surgical simulator (manipulated by simulator trials repetitions), and/or with individual performance (reflecting the reduced need for cognitive capabilities together with improving laparoscopic dexterity). This will help in revealing new and objective information regarding the efficacy of simulation-based training.

Experiment 1

Methods

Participants
This was a prospective single arm study which involved 19 (63% females) healthy medical students from second to sixth year of studying, with mean age of 25.631 (2.532), with no prior experience using a surgical simulator. Ethical approval for this study was granted by the Galilee Medical Center institutional review board.

Procedure
An EEG device (detailed below) with 3 frontal electrodes that were attached to the subject’s forehead was used to record brain activity and calculate real-time brain activity features (BAFs). The participants were then asked to complete a task with a surgical simulator Simbionix LAP MENTOR™ (Simbionix, Airport City, Israel) which involved grasping and clamping of blood vessels using two different laparoscopic arms. The same task was used for all subjects. At the end of the task, the participants were rated by the surgical simulator based on three main parameters: accuracy, economy of movement, and time required to complete the task. The participants repeated the same task 3 times for three consecutive days, one
session per day. These parameters were then compared to the brain activity recorded by the EEG device during the task.

**EEG device**

The EEG signal acquisition system included a 3-electrode patch attached to the subject’s forehead (NS Aurora, Neurosteer®, Herzliya, Israel). The medical-grade electrode patch includes dry gel for optimal signal transduction. The electrodes are located at Fp1 and Fp2 and a reference electrode at Fpz. EEG signal was amplified by a factor of a 100 and sampled at 500 Hz. Signal processing was done in the Neurosteer cloud.

**Brain activity features and biomarkers**

Full technical specifications regarding the construction of BAFs and biomarkers and the extractions of the biomarkers from the BAFs representation are provided in the Supplementary Materials. In brief, the signal processing algorithm interprets the EEG data using a time/frequency wavelet-packet analysis, instead of the commonly used spectral analysis. It is computationally involved and relies on a previously collected large cohort of EEG data from which the features were extracted. One hundred and twenty-one BAFs were created using a variant of the wavelet packet analysis and the best basis algorithm [16-19]. The construction of the biomarkers is based on another large cohort of independent data from healthy subjects performing different tasks, collected with the same device. The labeled data was used in a supervised way to identify biomarkers of equal and nonequal-weight BAFs. This resulted in different biomarkers, of which we used VC9 which is the most relevant to the cognitive task datasets.

**Statistical analysis**

Results of the simulator performance and EEG activity are reported as means and standard deviation. The dependent variables included accuracy, time, and economy for the behavioral measurements. From the EEG device, the VC9 biomarker was included in the analysis, based on a previous validation of the VC9 as a cognitive load biomarker [14-15]. The main analysis included Pearson’s correlation coefficient evaluated the correlation between the mean VC9 activity for each participant and simulator performance per each trial. Repeated-measurement one-way ANOVA was performed to evaluate the differences in performance and EEG activity between the three simulator trials. Two-tailed $p<0.05$ was considered statistically significant. Analyses were performed using R studio version 3.6.3.
Results

Correlation between behavioral performance and EEG activity

There were no significant correlations between the VC9 biomarker and any of the behavioral measurements ($r = -0.19$, $r = -0.18$ and $r = 0.1$ for accuracy, economy of movement, and time respectively, all $p > 0.05$, see figure 1).

![Figure 1: Mean activity of the VC9 biomarker, as function of Accuracy (A), Economy (B) and Time (C). Pearson $r$ and $p$ values presented in the corresponding color of the behavioral measurement.](image)

Behavioral measurements

Behavioral performance was extracted by the virtual simulator after each trial of each participant, including accuracy (in percentage), economy of movement (in percentage) and time to exceed the trial (in second).

For a full description of the ANOVA parameters (Sum of Squares, degrees of freedom, Mean Sum of squares, F values, p values and partial eta squares) for the three ANOVAs performed in this study see table 1.

A significant increase of the participants’ accuracies was observed between the attempts (55.91% on first attempt versus 80.67% on the third attempt, $p<0.001$; Figure 2), as well as a significant increase in the economy of movement (22% versus 40.37%, $p<0.001$). The average time required for the completion of the task was also significantly reduced between the attempts (183.63 sec versus 123.31 sec, $p<0.001$).
**Figure 2:** The mean accuracy, time and economy measures in experiment 1 for trial 1 (blue), trial 2 (red) and trial 3 (grey).

**VC9 Activity**

There was no significant difference in VC9 activity between the trials in consecutive days (54.58 on first attempt versus 57.78 on the third attempt, \(p>0.05\); **Figure 3**)

**Figure 3:** The mean activity of VC9 biomarker in experiment 1, across the first trial (blue), second trial (red) and third trial (grey).
Discussion

In experiment 1, participants’ performance under the simulator improved with trials repetition. However, there was no correlation between VC9 activity and the behavioral measurements, and no significant difference in VC9 activity between the trials. This could be explained with two reasons: first, the overall time for examination in each day was noticeably short (less than five minutes). This might affect the ability of the EEG device to capture sensitive neural changes between the trials. Second, the participants were medical students with different years of studying (from 2nd to 6th year), creating a non-homogenic population. Therefore, a new experiment was conducted, with prolonged session times by running three consecutive trials on the same day with a five-minute break between each trial. In this experiment only medical inters in their first year of internship were enrolled.

Experiment 2

Participants and procedure

A total of 19 participants who did not participate in Exp 1 were enrolled in this study. All participants were healthy medical interns who have never experienced laparoscopic surgery, and with no prior experience using a surgical simulator. The participants’ mean age was 28 (range: 25-36). All participants were monitored by the EEG device and were given 3 attempts to perform the specific task as in Exp. 1. They performed three consecutive trials on the same session, with a five-minute break between the trials. The performance of each participant was graded by the surgical simulator’s algorithm based on their accuracy, economy of movement, and time to complete the task. VC9 biomarker was extracted via Neurosteer®.

Correlation between behavioral performance and EEG activity

VC9 activity significantly correlated with all three behavioral measurements and was found to decrease with better participants performance (e.g. negatively correlated with accuracy and economy of movement and positively correlated with time): r = -0.57, p<0.001, r = -0.56, p<0.001 and r = 0.3, p=0.025 for accuracy, economy of movement and time respectively; see Figure 4).
**Figure 4:** Mean activity of the VC9 biomarker in experiment 2 and 3, as function of Accuracy (A), Economy (B) and Time (C). Pearson R and \( p \) values presented.

**Behavioral measurements**

A significant increase of the participants’ accuracy was observed between the trials (60% on first trial versus 76.9% on the third trial, \( p<0.001 \); **Figure 5**), as well as a significant increase in the economy of movement (24.6% versus 34.3%, \( p<0.001 \)). The average time required for the completion of the task was also significantly reduced between the trials (189 sec versus 142 sec, \( p<0.001 \)).
Figure 5: The mean accuracy, time and economy measures in experiment 2, for trial 1 (blue), trial 2 (red) and trial 3 (grey), in the first session for all participants (n=19).

EEG measurement

VC9 activity was significantly reduced between the first and the third attempts (50.8 versus 47.5, \( p=0.002 \) see figure 6).

Figure 6: The mean activity of VC9 biomarker in experiment 2, across the first trial (blue), second trial (red) and third trial (grey), in the first session including all 19 participants.

Comparison between Exp 1 and Exp 2

To examine differences between the two experiments, four unpaired t-tests were conducted to compare behavioral measurements and VC9 activity in trial 1 of Exp 1 and trial 1 of Exp. 2. The two trials were in the same setup therefore can enable a participant’s comparison. The behavioral performance or trial in trial 1 of Exp. 2 did not differ significantly from trial 1 in Exp 1 for any of the measurements (55.91\% versus 59.99\%, 22\% versus 24.58\%, 183.63 sec versus 188.84 sec, and 48.58 versus 49.45 for accuracy, economy of hand movement, and time, all \( ps>0.05 \), see figure 7). Interestingly, VC9 activity in the trial 1 Exp. 2 was significantly lower than VC9 activity of trial 1 of Exp 1 (54.58 in the first experiment versus 50.121 in the second experiment, \( p=0.034 \)).
Figure 7: The mean accuracy, time, economy (left), and VC9 (right) in the first trial of Exp 1 (dark green) and first trial of Exp 2 (light green).

Discussion

Exp. 2 results exhibited a significant increase in behavioral performance as well as a significant decrease in the VC9 activity between the three trials. In addition, VC9 activity decreased with better individual performance, this was expressed by the significant correlations between the behavioral measures and VC9 activity. These significant correlations and the significant difference in VC9 between the trials, differ from the ones in Exp. 1. This discrepancy could be explained by the prolonged session time. Additionally, analysis comparing behavioral performance and brain activity of the first trial in both experiments revealed a decreased VC9 activity already prominent on the first trial of Exp. 2. This could indicate on inherent differences between the two participants’ groups would did not emerge during the experiment itself.

Next, we aimed to explore the effect of night sleep on the behavioral performance under the simulator and participants’ brain activity. Therefore, a third experiment was conducted including ten participants who participated in Exp. 2. They performed an additional three-trials session in the consecutive day of Exp 2. Since The effect of night sleep was not present on the VC9 biomarker in Exp. 1, aim here was to investigate whether these differences reveal using a longer session (e.g. 3 trials instead of 1).
Experiment 3

Participants and procedure
On the consecutive day of Exp. 2, ten randomly chosen participants performed an additional 3-trials session with the same procedure.

Correlation between behavioral performance and EEG activity
VC9 activity significantly correlated with all three behavioral measurements and was found to decrease with better participants performance (e.g. negatively correlated with accuracy and economy of movement and positively correlated with time): $r = -0.57$, $p<0.001$, $r = -0.42$, $p=0.022$ and $r = 0.4$, $p=0.027$ for accuracy, economy of movement and time respectively; see Figure 8).

Figure 8: Mean activity of the VC9 biomarker in experiment 2 and 3, as function of Accuracy (A), Economy (B) and Time (C). Pearson R and $p$ values presented in the corresponding color of the EEG variable.

Behavioral measurements and VC9
Behavioral performance did not differ between the three trials in this session in any of the measurements (all $p$s >0.05, see Figure 9). Activity levels of VC9 did not differ between the trials of the session, $p>0.05$, see Figure 10.
Figure 9: The mean accuracy, time and economy measures in experiment 3, for trial 1 (blue), trial 2 (red) and trial 3 (grey), in the two session for participants that underwent both sessions (n=10).

Figure 10: The mean activity VC9 biomarker in experiment 3, across the first trial (blue), second trial (red) and third trial (grey), participants included 10 who underwent Exp. 2.

Comparison between Exp. 2 and 3

To compare between Exp. 2 and Exp. 3, behavioral performance and brain activity of the 10 participants who participated in both experiments was taken into the analysis. Four paired t-tests comparing accuracy, economy of movement, time and VC9 activity of the last trial of Exp 2 and the first trial of Exp. 3 were conducted. Both behavioral performance and brain activity were the same in the first trial of Exp 3 relatively to the last trial of Exp 2: 77.6% versus 80.62%, 33.4% versus 36.7%, 136 sec versus 127 sec, and 48.58 versus 49.45 for accuracy, economy of hand movement, time and VC9 activity respectively, all $p$s $>0.05$, see figure 11.
Figure 11: The mean accuracy, time, economy, and VC9 in the third trial of Exp 2 (dark green) and first trial of Exp 2 (light green), averaged over the 10 participants who underwent both experiment (n=10).

| Experiment | Measure | Type III Sum of Squares | df, df error | Mean Square | F    | Sig.     | $\eta^2_p$ |
|------------|---------|--------------------------|--------------|-------------|------|----------|------------|
| Exp 1      | Accuracy| 6005.457                 | 2, 36        | 3002.729    | 14.281 | <0.001   | 0.442      |
|            | Economy | 3388.450                 | 2, 36        | 1694.225    | 35.606 | <0.001   | 0.664      |
|            | Time    | 34565.193                | 2, 36        | 17282.596   | 34.630 | <0.001   | 0.658      |
|            | VC9     | 103.927                  | 2, 36        | 51.963      | 1.719  | 0.194    | 0.087      |
| Exp 2      | Accuracy| 3220.791                 | 2, 36        | 1610.395    | 9.673  | <0.001   | 0.350      |
|            | Economy | 983.193                  | 2, 36        | 491.596     | 13.792 | <0.001   | 0.434      |
|            | Time    | 21019.930                | 2, 36        | 10509.965   | 16.074 | <0.001   | 0.472      |
|            | VC9     | 73.800                   | 2, 36        | 36.900      | 7.719  | 0.002    | 0.300      |
| Exp 3 (2nd session) | Accuracy | 252.285                   | 2, 18        | 126.142     | 0.870  | 0.436    | 0.088      |
|            | Economy | 252.067                  | 2, 18        | 126.033     | 1.716  | 0.208    | 0.160      |
|            | Time    | 2427.800                 | 2, 18        | 1213.900    | 1.543  | 0.241    | 0.146      |
|            | VC9     | 6.590                    | 2, 18        | 3.295       | 1.030  | 0.377    | 0.103      |

Table 1: Type three some of squares, df and df error, mean square, F value and $p$ values for all effects depicted in the three repeated-measures ANOVAs applied in the present study. All
ANOVAs included trial (1/2/3) as a within-participants variable. Exp 1 included 19 participants who underwent three simulator trials in three consecutive days; Exp 2 included additional 19 participants who underwent three trials on the same day; Exp 3 included 10 participants who completed Exp 2, and underwent 3 trials on a consecutive day.

**Discussion**

Exp. 3 results exhibited a clear correspondence between behavioral performance and VC9 activity. First, VC9 activity decreased with better behavioral performance as depicted by significant correlation with all three behavioral measurements. Second, for both behavioral performance and VC9 activity, there were no significant differences between the three trials, meaning that behavioral performance did not improve and VC9 activity did not decrease between the three trials. Finally, the first trial of Exp. 3 was the same in terms of both behavioral performance and VC9 activity as the last trial of Exp. 2. This may indicate that the participants performance improved and VC9 activity decreased throughout the three trials of Exp. 2, and these levels were maintained until the consecutive day when Exp. 3 was conducted.

**General Discussion**

In this study, we evaluated cognitive load levels while performing a task on a surgical simulator with VC9, a cognitive load biomarker measured by a small and wearable EEG device. Exp 1 paradigm included 19 participants repeating the same simulator task in three consecutive days. While participants performance improved through the trials, there was no difference between the VC9 activity. This may suggest that while participants improved their abilities in the simulator task, they were still required for a rather high mental load to complete the task on the consecutive days. After increasing participants homogeneity, we found that while behavioral performance was the same on the first trial of the two experiments, VC9 activity was reduced for the more homogenic group. Together, these two findings together might indicate that VC9 may be a more accurate measurement than behavioral performance.

As a result of prolonging session time to three trials, VC9 activity decreased with higher participants performance both in Exp.2 and in Exp. 3. In addition, behavioral performance improved and VC9 activity decreased during the three trials of Exp. 2 but not throughout the three trials of Exp. 3 which occurred on the consecutive day. Lastly, the behavioral performance and VC9 activity of the first trial on the second day was the same as the last trial of the first day. This may indicate that participants reached their maximum level on the last trial of the first day and maintained it on all trials of the second day. Overall, these findings
support previous finding that as the participant becomes more proficient at a task, which is depicted by the behavioral performance, the pre-frontal activity is reduced [20]. Several methods have been previously described and validated to assess working memory and cognitive load. Traditionally, subjective self-rating scales were proven as reliable assessment tools across several studies [21]. However, as this tool can only be recorded crudely and retrospectively, objective assessment methods with a real-time indication of working memory are in demand. Using such approach, the activity can be broken down to different components that reflect different stages of complex simulations and evaluate the efficacy of each training element. Several biological methods have been reported to successfully assess working memory, such as pupil size [22], eye movement tracking [23], salivary cortisol levels [24], and functional magnetic resonance imaging (fMRI) [25]. Several fMRI studies report conflicting results regarding prefrontal activity in response to training, some showing increased activity due to a higher neuron recruitment rate [26], while others report decreased activity due to improved working efficiency [27-28].

In Exp. 2 we found that VC9 showed a steady downward activation pattern across the trials as the participant’s performance got better and the task became easier to the participant, supporting the second notion presented. Most importantly, when the behavioral improvement was absent throughout the trials in Exp. 3, the second session performed the day after, VC9 levels were also maintained. This activation patterns correlate with working memory load as previously described [29-30]. Altogether, VC9 is found to be an effective biological measurement for the assessment of cognitive load while performing laparoscopic tasks using the surgical simulator.

This study has several limitations. The analyses were performed on young medical internists, which may not accurately reflect the overall population. Additionally, this study was not powered enough to evaluate the differences between the different sessions. Future studies on a larger and more diverse population should further validate the findings presented in this work as well as study the effect of prolonged breaks on the activity of these biomarkers. Moreover, a 24-hour break period between the sessions may not be sufficient to study the effect of long-term memory on the prefrontal brain activity during the simulation. Future studies should evaluate a longer time windows to assess the temporal changes in the activity of the working memory associated biomarkers.

To conclude, in this study we used a previously validated [14-15] cognitive load biomarker extracted via a novel single-electrode EEG using advanced computerized signal analysis, and showed high correlations with the participants’ individual performance using a surgical
As surgical simulations allow to gain important skills and experience needed to perform procedures without any patient risk, it is crucial to fully evaluate and optimize the effect of these simulations on medical staff. This could potentially be expanded to evaluate the efficacy different medical simulations to help medical staff and to measure cognitive and mental load under real laparoscopic surgeries.
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Appendix A: Methodological details

The data analysis methodology is composed of three steps:

1. Creation of a brain activity representation by novel Brain Activity Features (BAFs)
2. Creation of Novel Biomarkers based on the BAFs
3. Examination of the features on previously unseen data

Each of the steps is described below.

Creation of Brain Activity features (BAFs)

The creation of the Brain Activity Features (BAFs) occurs prior to application of the methodology onto the new data to be analyzed. Calculation of the BAFs is based on collecting a large cohort of high dynamic amplitude and frequency range single channel EEG data. The cohort includes multiple subjects that are exposed to different cognitive, emotional, and resting tasks. A schematic representation of the signal processing is depicted in Fig A1. The signal processing module is decomposing the EEG signal input into a large number of components which comprise the Brain Activity Features (BAFs). The output of the module is a Brain Activity Representation which is constructed based on the BAFs for any given EEG signal.

Figure A1. schematic representation of the construction of the Brain Activity Features (BAFs). See text for the description of the different steps.

A: electrophysiological signal input

The EEG cohort described above is the input of the signal processing algorithm presented as the first step of the process.

B: Wavelet Packet Analysis

For a given cohort of EEG recordings, a family of wavelet packet trees is created. For the mathematical description, we follow the notation and construction provided in chapters 5, 6 and 7 of Wickerhauser’s book.

To demonstrate the process; let \( g \) and \( h \) be a set of biorthogonal quadrature filters created from the filters \( G \) and \( H \) respectively. Each of these is a convolution-decimation operator, where in the case of the simple Haar wavelet, \( g \) is a set of averages and \( h \) is a set of differences.

The construction of the full wavelet packet tree is by successive application of these functions (Figure A2), so that at every level, a new full orthogonal decomposition of the original signal \( x \) is created. In the classical wavelet decomposition by Daubechies, only the
marked parts are used and the signal is decomposed into $Gx$, $GHx$ etc., but the full construction of the tree continues recursively, on $Gx$, $GHx$ and so forth, to create a full binary tree. Coifman and Wickerhauser observed that a large number of orthogonal decompositions can be constructed from the full tree by mixing between the different levels and different blocks of the tree, following a simple rule. The recursive construction of the full tree is described next.

![Figure A2. Construction of a Discrete Wavelet Transform Tree (Taken from Wickerhauser).](image)

The top panel represents the classical wavelet construction and the bottom panel extends the construction to a full wavelet packet tree.

Let $\psi_1$ be the mother wavelet associated to the filters $s \in H$, an $d \in G$. Then, the collection of wavelet packets $\psi_n$ is given by:

$$
\psi_{2n} = H\psi_n; \quad \psi_{2n}(t) = \sqrt{2} \sum_{j \in \mathbb{Z}} s(j) \psi_n(2t - j),
$$

$$
\psi_{2n+1} = G\psi_n; \quad \psi_{2n+1}(t) = \sqrt{2} \sum_{j \in \mathbb{Z}} d(j) \psi_n(2t - j).
$$

The recursive form provides a natural arrangement in the form of a binary tree (Figure A2). The functions $\psi_n$ have a fixed scale. A library of wavelet packets of any scale $s$, frequency $f$, and position $p$ is given by:

$$
\psi_{sfp}(t) = 2^{-s/2} \psi_f(2^{-s}t - p).
$$

The wavelet packets $\{\psi_{sfp}: p \in \mathbb{Z}\}$ are an orthonormal basis for every $f$ (under orthogonality condition of the filters $H$ and $G$) and are called orthonormal wavelet packets.
Using this construction, Coifman and Wickerhauser applied the best basis algorithm\(^3\) to search for an orthonormal base that satisfies a specific optimality condition. The optimality condition that was chosen is Shannon’s entropy of the coefficients of each component (or wavelet packet atom). It is a measure that prefers coefficients with a distribution that is far from uniform, in the sense that it prefers a distribution with a small number of high value coefficients and a long tale, namely, a large number with low value coefficients. The full details of the best basis search are described in chapter 7 of Wickerhauser’s book.

The process of creating a best basis from the wavelet packet tree can be further iterated by an optimization on the mother wavelet using a gradient descent in wavelet space as is described in Neretti and Intrator\(^iv\).

\(C:\) Pruning the optimal representation

The outcome of the best basis algorithm is an orthogonal decomposition that is adapted to the stochastic properties of the collection of EEG signals. However, there is a risk that the decomposition is “overfitting” namely it is too adapted to the EEG signals from which it was created. To avoid this phenomenon, we first have to get rid of “small” coefficients. This can be done by the denoising technique of Coifman and Donoho\(^v\). The next step is introducing a validation set, which is another collection of EEG-recordings that was not used in the creation of the best basis. Using this set, we can determine which atoms maintain a high energy (some large coefficients) when decomposing the new signals. These atoms will remain in the representation. At the end of this part, the resulting set of decomposing signal contains only a part of the full orthonormal basis that was found. We then reorder the basis components not based on the binary tree that created them, but based on the correlation between the different components. In this way, we created a brain activity representation in which components that are more correlated to each other, are also geographically close to each other within the representation. This is done for the purpose of improved visualization.

\(D:\) brain activity representation output

The result of the signal processing module is the brain activity representation. Specifically, it is a collection of 121 energy components, emanating from the wavelet packets as well as standard frequency bands which are updated each second. The representation (D) shows a color heatmap of each of the 121 X time matrix, so that the x axis represents time and the y axis represents the different components.

Creation of Novel features based on the BAFs

The signal components, which we termed BAFs, were constructed from single EEG channel recordings in an unsupervised manner, namely, there were no labels attached to the recordings for the purpose of creating the decomposition. To create biomarkers based on the BAFs, task labels are used, indicating the nature of cognitive, emotional, or resting challenge the subject is exposed to during the recording.

Given labels from a collection of subjects, and the corresponding high-dimensional BAF data, a collection of models attempting to differentiate between the labels based on the BAF activity can be used. In the linear case, these models are of the form:

\[
V_k(w, x) = \psi \left( \sum_i w_i x_i \right),
\]
where \( \mathbf{w} \) is a vector of weights, and \( \Psi \) is a transfer function that can either be linear, e.g., \( \Psi(y) = y \), or sigmoidal for logistic regression \( \Psi(y) = 1/(1 + e^{-y}) \).

Figure A3. Supervised construction of different features from labeled brain activity representation of different cognitive and non-cognitive tasks.

For each predictor, which we term biomarker, a standard machine learning procedure is applied as follows:

1. Choose a labeled data set with at least two different tasks (e.g. cognitive, emotional, or resting challenge). The data set may include the same challenge but for a non-homogenous group.

2. Separate the data into three sets: training, validation, and test.

3. Choose a model to train on from a family of models that includes linear regression, linear regression with binary constrains (zero and one values for the weights), linear regression with only positive values, logistic regression, discriminant analysis and principal components analysis. In the non-linear models, use neural networks, support vector machine and the like.

4. Train each model on several sets of train/test and validation to best estimate internal model such as the variance constraints, on the ridge regression, the kernel size and number of kernels in a support vector machine, or the weight constraints in a neural network model.

5. From the above models, obtain predictors to be tested on other data with potentially other cognitive, emotional and rest challenges.

6. The last step in the process includes testing the biomarkers using a test data labeled set that was not used in the creation of these features. This allows removal of features that were overfitting to the training data, namely, they do not produce high significant difference on the validation data. This is still part of the model creation and not part of the model testing that is done on new data and is described in step 3.

All above steps are described in the scheme on Figure A3.
Examination of the features on previously unseen data

Following the creation of BAFs and the creation of features as described above, the features relevance can be tested on various cognitive or emotional challenge. The testing scheme is described in Figure A4. Specifically, data is collected with the sensor system and sent to the cloud for creation of a BAF representation using the previously determined wavelet packet atoms. The BAF representation is provided to previously determined ML models, which convert the BAF activity into features. Statistical tests are then applied to determine the quality of the predictions and the correlation of the features to the cognitive and emotional challenges that the participants undergo. This may include single subject analysis as well as group analysis.

Figure A4: Testing the relevance of the previously found features on the data.

In the process of testing the features on new data, we may want to get an upper bound to the performance of the feature, by seeking an overfitting biomarker on the currently tested data. This is only done to get an idea of the potential upper bound on prediction abilities from the existing data, and indirectly can tell us more about the optimality of the actual features that were constructed from a different data set and are assumed to be more general in this sense.

Appendix References

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