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Approximate Entropy as a Measure of Cognitive Fatigue: An EEG Pilot Study

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Abstract:
Nonlinear analysis of electroencephalogram (EEG) activity can provide a better understanding of brain signal dynamics during cognitive fatigue. The aim of this study was to analyse the regularity of EEG time series of healthy participants undergoing a series of cognitive tasks to test the hypothesis whether the irregularity of EEG signals changes through increasing time on performing cognitive task. EEG activities were recorded from two scalp loci of the international 10-20 system (that are F_z *and* P_z *electrodes representing the midline frontal and parietal lobes of the brain respectively) in twelve participants from which Approximate Entropy (ApEn) values were computed. ApEn is a nonlinear method which quantifies the irregularity of a time series whereby larger ApEn corresponds to more irregularity. ApEn values were found to be significantly different among the six time intervals of a series of 5-minutes cognitive tasks (*$p<0.01$*). Moreover, there was a significant positive correlation between ApEn at the* P_z *electrode and measured mental fatigue visual analogue scale (*$p<0.01$*). Therefore, the irregularity found in the participants' EEG signals across the time intervals of performing cognitive task demonstrate that EEG regularity analysis with ApEn might be a useful tool in increasing our insight into the characteristics of the brain processes involved while performing fatiguing cognitive task and in quantifying cognitive fatigue.*
Keywords: *approximate entropy, attention, cognitive fatigue, EEG analysis, nonlinear method*

1. Introduction

The brain's reticular activating system (RAS) is thought to regulate the perception of mental fatigue. Mental fatigue is the temporary incapability to sustain optimal cognitive performance. During any cognitive activity, the onset of fatigue starts gradually and relies on an individual's cognitive ability. Mental fatigue can manifest itself as decreased attention which occurs when there is depletion of limited resources from the self-regulatory capacity [1].

1.1 Electroencephalogram (EEG) (Fz and Pz)

The electroencephalogram (EEG) has been used as a tool for investigating brain functions for several decades. Various cognitive attention-related studies [2], [3] revealed that both fronto-midline and parietal-midline are associated to focused attention and somatosensory information processing [4]. Moreover, researchers [5] found increased frontal theta power is associated with cognitive task complexity and focused attention, while decreased parietal alpha power is related to increased information processing in a cognitive and visuomotor task. Therefore, in this research, EEG activities were recorded from the frontal midline and the parietal midline areas of the brain.

1.2 Nonlinear Methods

Recent progress in nonlinear dynamics theory has provided new methods for the study of EEG [6]. Nonlinearity is found in many dynamical systems. For instance, nonlinearity is introduced even at cellular level of the brain as the neurons dynamical behaviour is controlled by saturation and threshold phenomena. Nonlinear studies of the brain were successful in making relative comparisons of different physiological states and in forming part of possible medical applications techniques [7].

So far, few authors have analysed EEG in healthy participants with nonlinear methods in the cognitive fatigue context by estimating the underlying nonlinear dynamical complexity of physiological data employing correlation dimension and largest Lyapunov. These measures were problematic as the amount of data required for meaningful results in their computation is beyond the scope for experimental possibilities for physiological data [8], [9]. Furthermore, these nonlinear metrics assume the time series to be stationary, and this is generally not true with physiological data. Thus, the study of the EEG background activity with more suitable nonlinear methods becomes apparent.

1.3 Approximate Entropy

One alternative solution lies in computing the approximate entropy of the EEG. Approximate Entropy (*ApEn*) is a recently introduced family of statistics that quantifies regularity in the data without any *apriori* knowledge about the system generating them[10],[11]. Approximate Entropy is a measure of complexity and it quantifies the unpredictability of fluctuations in a time series[12]. A time series containing many repetitive patterns has a relatively small *ApEn* whereas a less predictable process has a higher *ApEn* and less system order. Given N data points from a EEG time series $\{x(n)\} = x(1), x(2), \ldots, x(N)$, the following steps were used to compute *ApEn* [9], [11]:

Step 1: Form N-m+1 vectors $X(1)\ldots X(N-m+1)$ defined by: $X(i) = [x(i), x(i+1),\ldots x(i+m-1)]$, $i = 1\ldots N-m+1$. Fix m, an integer, and r, a positive real number. The value of m represents the window length of compared run of data, and r specifies a filtering level [11].

Step 2: Define the distance between $X(i)$ and $X(j)$, $d[X(i),X(j)]$, as the maximum norm:

$$d[X(i), X(j)] = \max_{k=1,2,\ldots,m} |x(i+k-1) - x(j+k-1)| \qquad (1)$$

The variable d represents the distance between the vectors *x(i)* and $x(j)$, given by the maximum difference in their respective scalar components.

Step 3: For a given $X(i)$, count the number j ($j = 1\ldots N-m+1$) so that $d[X(i), X(j)] \le r$, denoted as $N^m(i)$. Then, for $i=1\ldots N-m+1$,

$$C_r^m(i) = N^m(i)/(N-m+1) \qquad (2)$$

$C_r^m(i)$ measures, within a tolerance r, the frequency of patterns similar to a given window of length m.

Step 4: Compute the natural logarithm of each $C_r^m(i)$ and average it over i,

$$\phi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln C_r^m(i) \qquad (3)$$

Step 5: Increase the dimension to m+1. Repeat steps (1) to (4) and find $C_r^{m+1}(i)$ and $\phi^{m+1}(r)$.

Step 6: *ApEn* is defined by:

$$ApEn(m,r,N) = \phi^m(r) - \phi^{m+1}(r) \qquad (4)$$

Although the selection of m and r are critical in computing *ApEn*, there are no proper guidelines to optimise these values. For smaller r values, poor conditional probability estimates are achieved whereas for larger r values, detailed system information is lost. To avoid a significant contribution of noise in an *ApEn* computation, value of r should be chosen such that it is larger than most of the noise present in the signal [12]. It was suggested to estimate *ApEn* with parameter values $m = 2$ and $r = 0.2*SD$ where *SD* represents the standard deviation of the original data sequence $\{x(n)\}$ [9], [11]. Couple with that, it was shown that these input parameters produce good reproducibility for *ApEn* especially for time series of data length $N \geq 60$ [11]. Also, previous study [9] showed that these values were good choices especially for time series of data length $N = 3000$ which was applied in this research study [9], [11].

2. Materials and Methods

2.1 Participants Details

Twelve healthy and right-handed participants comprising of 6 males and 6 females were recruited from the research participant database. The participants' mean age was 29.6 ± 3.7 years old, and they were moderately to highly mentally active as they were required to complete a series of 5 minute-block of cognitive task for a total duration of thirty minutes. Using a health questionnaire, participants reported no history of neurological or musculoskeletal pathology that might affect their cognitive and motor performance. Subjects signed an informed consent form approved by the School ethics committee board.

2.2 Hardware and software resources

The Research Power lab, and Octal Bio Amp systems (Power lab, AD Instruments, Australia) were used for the recording of the electroencephalogram (EEG) data. The electro-caps (small, medium or large) consist of Ag/AgCl electrodes embedded in the elastic electro-cap fabric to record EEG activities from the scalp, and these EEG data were transmitted to the Power lab systems via an electro-cap interface (Electro-Cap International, Inc., USA). Moreover, the ECI electro-gel was used to ensure the impedance between the EEG electrodes and the scalp was less than 5kΩ which was verified using a digital multi meter (Draper 52320, UK). The software that were utilised in this study were Chart 5 software for Windows to record and process the physiological signals, the E-Prime software version 2.0 to implement and conduct the cognitive tasks, and Matlab software R2009b for computation of *ApEn*.

2.3 Description of the cognitive tasks

The rapid visual information processing (RVIP) and modified stroop (MST) tasks were used in this research study, so that the psychological strain which was placed by these tasks on the participants was mostly cognitive [13]. For, the modified stroop task (MST), the participants had to respond to the colour of the word appearing at the centre of a computer screen (Red, Yellow, Green and Blue) by pressing quickly the numerical keys associated to these colours on the keyboard. Moreover, if the word that appeared on the screen was written in grey colour, they were required to respond to the word. For instance, if the word RED was written in grey colour, then the participants would need to press the keyboard numerical key which was associated to red colour. The duration of the MST cognitive task was 5 minutes. As for the rapid visual information processing (RVIP) task, the participants were required to respond to a specific sequence (odd or even) of integer numbers from 0 to 9 which appeared at a rate of 600 milliseconds on the computer screen. For instance, when they noticed three consecutive numbers (*e.g.* 5 3 7) or three consecutive numbers (*e.g.* 2 6 8), they had to press the 'spacebar' on the keyboard as quickly and accurately as they could. The duration of this cognitive task was also 5 minutes. These cognitive tasks were alternately presented to the participants for a duration of 30 minutes so that there were in all three RVIPs and three MSTs which represented the cognitive battery task.

2.4 EEG data recording and processing

EEG activities were recorded continuously from the midline placements F_z and P_z according to the international 10-20 system electrode placement (See Figure 1). The cortical EEG activities were amplified, digitized, sampled at a frequency rate of

400Hz which was sufficient to capture the EEG activities based on Nyquist's criterion. Then these EEG activities were online filtered using a pass band of 0.1Hz to 100Hz using the Power Lab systems. The EEG signals were then digitally low pass filtered with a cut-off frequency of 30 Hz, and online reduced to a sample frequency of 100 Hz to analyse the EEG frequency bands of interest [14]. Moreover, artefacts such as blinking and fast eye movements were removed from the recorded signals based on any amplitude greater than ±70 µV [15]. Eventually, these processed EEG signals were used to compute and average the approximate entropy over 3000 EEG data points for each 5 minute block of cognitive task (See illustration Figure 2).

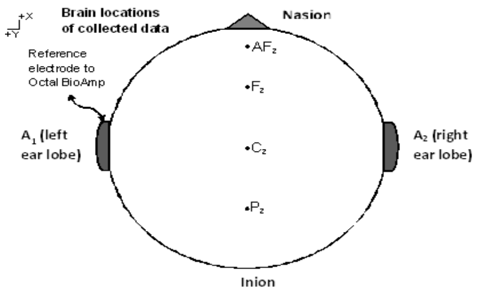

Figure 1: The 10-20 international system electrode placement showing the EEG electrode placement, the reference electrode (A_1 - left earlobe) and the ground electrode (AF_z), F_z (Frontal midline electrode), C_z (central midline electrode) and P_z (parietal midline electrode).

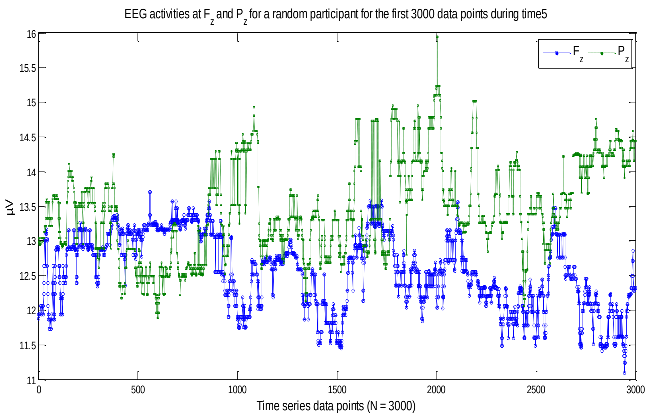

Figure 2: EEG activity (measured in microvolts) for the first 3000 data points for the first cognitive task presented (RVIP) for a randomly chosen participant.

2.5 Study protocol and procedures

On the first visit to the Neurophysiology laboratory, the participants completed the health questionnaire and then, they were each assigned an identification number to protect their anonymity. The right size electro cap was identified for each participant, and then they were given each a practice session on the cognitive tasks that they would need to complete during their second visit. This first visit allowed the participants to get accustomed with the laboratory environment and procedures. One week later, during their second visit, the participants sat comfortably facing the computer monitor at a distance of about 60 cm and the appropriate EEG electro-cap was fitted. Then, EEG activities at the frontal midline (F_z), and parietal midline (P_z) were recorded while the reference Ag/AgCl electrodes were attached to A_1 representing the left ear lobe, and the ground electrode was located at AF_z representing the Anterior Frontal of the scalp [14] (Figure 1).

As precautions, the participants were requested to try not to blink while responding to the visual cues, during the cognitive experiments, to reduce interference of the electrooculogram (EOG) activities [16] to the measured EEG signals. Also, just after each 5 min-block of cognitive task, they had to complete a mental fatigue visual analogue scale (VAS) so that their perceived mental fatigue was monitored during the trial. They were required to mark in-between the horizontal scales that consisted of two extreme marks '0' and '10' signifying low and high mental fatigue respectively.

2.6 Statistical Analysis

Firstly, all the recorded and computed data were tested for normality using Kolmogorov-Smirnov (K-S) test [23]. A Two-way factorial ANOVA (Analysis of Variance) was used (2 Brain Locations x 6 time intervals) to analyse the dependent variable *ApEn* across the brain regions and time on task [17]. The two brain locations are P_z and F_z while the six time intervals are (time5, time10, time15, time20, time25, time30). The notations time5 represents 5 minutes have elapsed, time10 represents 10 minutes had elapsed and so on. When the main analysis indicated a significant interaction ($p < 0.05$) between the factors, follow-up analysis were achieved, adjusting error rates according to Bonferroni correction. Also depending on the normality of the data, appropriate correlation analysis method was employed to find out the relationship between the mental fatigue VAS and computed *ApEn*.

3. Results

Firstly, all measured and computed data were found to be normally distributed and hence appropriate parametric tests were used.

3.1 Mental fatigue Visual Analogue Scale

Table 1: Subjective measure of mental fatigue scale (mean and standard deviation) for the twelve participants during the 6 time intervals

	Time 5	Time 10	Time 15	Time 20	Time 25	Time 30
Mean (±*SD*)	49.2 ± 1.3	44.1 ± 1.9	49.1 ± 1.2	45.3 ± 2.6	50.9 ± 3.1	45.3 ± 2.6
Median	49.3	43.8	49.0	45.0	51.3	45.0

Table 1 shows that the mean and median of mental fatigue scale measures decreased and increased for the different time intervals. Statistical analysis using paired *t*-test showed that there was a significant difference between the perceived mental fatigue scales for these two types (RVIP and MST) of cognitive tasks (Paired *t*-test, *t*-value = 10.046, $p < 0.0001$). Participants felt more mentally fatigued while completing the RVIP (49.7±2.2) as compared to MST (44.9 ± 2.4).

3.2 *ApEn* data

Based on the statistical analysis tests of between-subjects effects with *ApEn* as dependent variable (*DV*), there was a significant difference in *ApEn* values for the factor Time Interval (2-way Factorial ANOVA, $F(5, 11) = 22.684$, $p < 0.0001$, partial $\eta^2 = 0.462$) (See Figure 3) but there was no significant difference in *ApEN* values for the factor brain location. Also there was no significant interaction between brain location and time interval. In addition, there was a significant correlation between *ApEn* at P_z electrode and Mental fatigue scale which means that as the irregularity of the EEG activity increases, the mental fatigue VAS also increases (Pearson's Correlation Coefficient $r = +0.328$, $p = 0.005$). The correlation between *ApEn* for F_z and mental fatigue was positive with $r = +0.118$ but it was not significant with statistical $p > 0.05$.

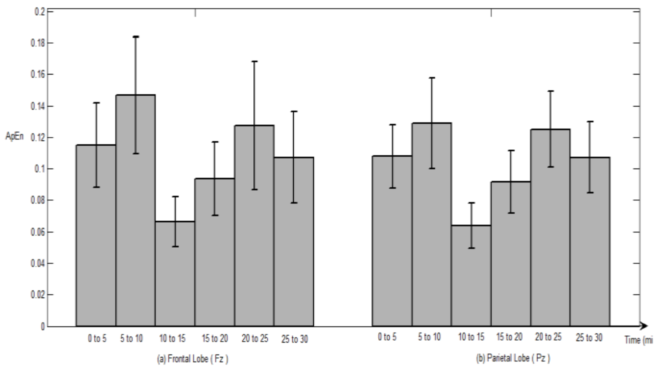

Figure 3: Computed average (±SD) *ApEn* values for the two brain locations (F_z and P_z) for the six time intervals of 5 minutes each.

4. Discussions

The advantage of using the approximate entropy nonlinear metric was that it considers the total information content of the EEG signal across the brain regions under investigation [18]. ApEn involved low computational demand and it took in average about 2.7 minutes to compute *ApEn* for data length $N= 3000$ data points and it is robust to noise. Based on the results, it appeared that *ApEn* is successfully detecting changes in the irregularity of EEG signals among the different time intervals of performing and completing the cognitive trials. In addition, ApEn studies had successfully classified EEG in psychiatric diseases [7] and here ApEn could distinguish well the different time intervals of performing the cognitive tasks. Mathews and Desmond (2002) stated that prolonged cognitive task exposure and multiple task demands could induce a great level of information processing which subsequently increased the mental workload. Such increments in mental workloads caused a depletion of the cognitive system's energy resources that were available for task completion and consequently promoted the development of fatigue [19, 20] as felt by the participants especially while completing the RVIP task over the MST task. Also, *ApEn* at P_z electrode showed positive associations with mental fatigue VAS which insinuates that this nonlinear metric could be used to reflect cognitive fatigue levels. So results found in this study support previous cognitive attention-related studies [4] where they found that EEG activities at P_z electrode had strong associations with attention and information processing as the EEG irregularity changes were clearly observed at the midline parietal lobe region.

5. Conclusion

Approximate entropy at the midline parietal (P_z) region of the brain reflects positively the perceived mental fatigue. Also it distinguishes well the regularity of the EEG signals among the different time intervals of performing cognitive tasks and thus, *ApEn* is a promising tool to distinguish the well the brain signal irregularity dynamics involved during increasing time on task of performing cognitive activities. Future studies could investigate changing the *ApEn* parameter, the filtering level *r*, and see whether there may be stronger or weaker associations with perceived mental fatigue scale measurements and also involve only one type of cognitive task for the same duration of 30 minutes.

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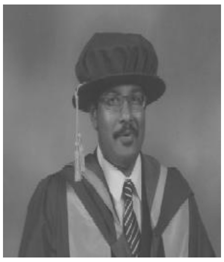
Author Profile



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