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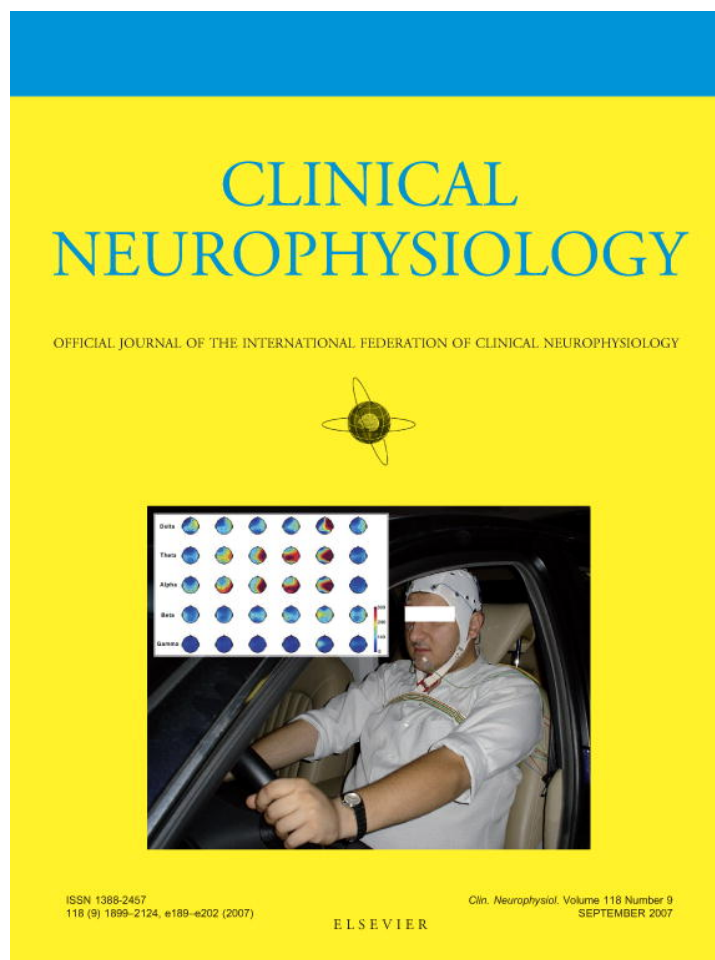


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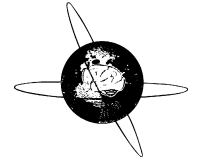
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Clinical Neurophysiology 118 (2007) 1906–1922



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Monitoring sleepiness with on-board electrophysiological recordings for preventing sleep-deprived traffic accidents

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See Editorial, pages 1899–1900

Abstract

Objective: The objective of this study is the development and evaluation of efficient neurophysiological signal statistics, which may assess the driver's alertness level and serve as potential indicators of sleepiness in the design of an on-board countermeasure system.

Methods: Multichannel EEG, EOG, EMG, and ECG were recorded from sleep-deprived subjects exposed to real field driving conditions. A number of severe driving errors occurred during the experiments. The analysis was performed in two main dimensions: the macroscopic analysis that estimates the on-going temporal evolution of physiological measurements during the driving task, and the microscopic event analysis that focuses on the physiological measurements' alterations just before, during, and after the driving errors. Two independent neurophysiologists visually interpreted the measurements. The EEG data were analyzed by using both linear and non-linear analysis tools.

Results: We observed the occurrence of brief paroxysmal bursts of alpha activity and an increased synchrony among EEG channels before the driving errors. The alpha relative band ratio (RBR) significantly increased, and the Cross Approximate Entropy that quantifies the synchrony among channels also significantly decreased before the driving errors. Quantitative EEG analysis revealed significant variations of RBR by driving time in the frequency bands of delta, alpha, beta, and gamma. Most of the estimated EEG statistics, such as the Shannon Entropy, Kullback–Leibler Entropy, Coherence, and Cross-Approximate Entropy, were significantly affected by driving time. We also observed an alteration of eyes blinking duration by increased driving time and a significant increase of eye blinks' number and duration before driving errors.

Conclusions: EEG and EOG are promising neurophysiological indicators of driver sleepiness and have the potential of monitoring sleepiness in occupational settings incorporated in a sleepiness countermeasure device.

Significance: The occurrence of brief paroxysmal bursts of alpha activity before severe driving errors is described in detail for the first time. Clear evidence is presented that eye-blinking statistics are sensitive to the driver's sleepiness and should be considered in the design of an efficient and driver-friendly sleepiness detection countermeasure device.

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Keywords: Sleepiness; Fatigue; Driving; EEG; EOG; Eye blinks

1. Introduction

Sleepiness at the wheel has been identified as the reason behind fatal crashes and highway accidents caused by car or truck drivers (Philip, 2005; Connor et al., 2001; Hakkanen and Summala, 2000). Boredom, fatigue, monotony,

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disturbed or deprived sleep may induce sleepiness and drowsiness. Deprived sleep is one of the most important factors of sleepiness that affects various aspects of performance (Bocca and Denise, 2006). Sleep deprivation can reduce attention and vigilance by 50%, decision-making ability, communication skills, and memory (Killgore et al., 2006; Raidy and Scharff, 2005; Harrison and Horne, 2000). The most sensitive tasks are those that are long, monotonous, and boring such as driving (especially during night) that becomes very vulnerable to the effects of sleep deprivation (see Dinges and Kribbs, 1991, for a review). During sleepy conditions, decreased attention, impaired information processing, and the reduced decision-making capability can all diminish driver's ability to respond effectively to unusual or emergent situations (Mascord and Heath, 1992). Specifically, Williamson and Feyer (2000) affirmed that sleep-deprived drivers are just as dangerous as drunk drivers. Recent studies presented evidence that driver sleepiness accounts for 6% of crashes, 15% of fatal crashes, and 30% of fatal crashes on rural roads (The Parliament of the Commonwealth of Australia, 2000). Since sleepiness impairs cognitive skills and therefore can adversely affect drivers' ability to monitor and assess their own fitness to continue driving safely, serious care should be taken for the implementation of sleepiness technological countermeasures, which might be used to provide drivers with useful feedback about the onset of sleepiness and to improve road safety.

The importance of developing driver sleepiness countermeasure devices has been identified in recent studies, mainly for the purpose of preventing driving accidents and errors (Lal and Craig, 2001b). The basic idea behind vehicle-based detection is to monitor the driver unobtrusively by means of an on-board system that can detect when the driver is impaired by sleepiness and drowsiness. Such a device might possibly be based on physiological measurements which are sensitive to the driver's alertness. Numerous physiological indicators are possible to assess the sleepiness and alertness level. The electroencephalographic (EEG) signal may be one of the most predictive and reliable measurements since it reflects directly human brain activity (Artaud et al., 1973; Volow and Erwin, 1973).

Driver sleepiness research has received increased interest in the last few decades. A number of studies have been performed in drivers concerning the EEG alterations due to sleepiness. A review of this literature can be found in Lal and Craig (2001b). In most studies, the EEG data were subjected to Fourier spectral analysis and alterations in alpha and theta bands were generally reported (Torsvall and Åkerstedt, 1983; Åkerstedt et al., 1982; Lal and Craig, 2000). In a pioneer study of night driving, sleep intruded while the drivers still had their eyes open, and it was accompanied by theta waves, sleep bursts and K-complexes (O'Hanlon and Kelley, 1977). Interestingly, the drivers had not been aware that they had been driving the car while asleep. Later, Torsvall and Åkerstedt (1987) recorded

ambulatory EEG and electrooculogram (EOG) from train drivers during a night and day trip and they observed that alpha power increased during night driving relative to the daytime levels for the sleepy group. Higher alpha power during night trips was also observed in this sleepy group in comparison with the alert group (Torsvall and Åkerstedt, 1987). Later, in another study of night driving, Lal and Craig (2000) found, in a laboratory-based simulator setup, consistent increases in delta, theta, and alpha activities during transition to sleepiness from an awake and alert state. These authors focused their attention on the appearance of delta waves during sleepiness and confirmed that delta rhythm may become a reliable and simple indicator of sleepiness.

A few authors have attempted further to establish a link between the alertness and performance by correlating EEG alterations and the driving task's performance. Specifically, Khardi and Vallet (1994) presented a significant positive correlation between the number of steering wheel reversals and the EEG's activities in the theta and alpha bands. More recently, Horne and Baulk (2004) established correlations between the (alpha + theta) EEG power and the incidents (a car wheel crossing the lateral lane marking) in a simulated driving task. In agreement with these results, Campagne et al. (2004) also established correlations between the lower-frequency EEG changes and the driving errors. In the independent driving simulator studies, it was reported that the driving duration but not sleep deprivation was found to have an effect on (alpha + theta) EEG power (Otmami et al., 2005), or that the driving performance was positively correlated with log sub-band (<20 Hz) power spectrum (Lin et al., 2005). However, all these results have been obtained using driving simulators. Consequently, subjects knew that the consequences of their driving errors would not affect their safety. Thus, from a psychological point of view, it is necessary to perform further studies with experimental paradigms in more realistic or field environments.

The main goal of our study is the development of a reliable and driver-friendly neurophysiological fatigue countermeasure device that may detect sleepiness, and that can provide drivers with useful feedback and alert them about the onset of sleepiness and consequently may assist in the prevention of sleep-deprived car accidents. In our study, EEG and peripheral physiological measurements were collected from healthy sleep-deprived subjects during realistic night driving conditions in an experimental car on the road. The data analysis was performed in two main dimensions: (a) macroscopic analysis, which monitors or estimates the on-going temporal evolution of physiological measurements during the driving task, assuming that sleep deprivation together with the duration of driving would attenuate gradually the driving performance as well as the subjective sleepiness; and (b) microscopic event analysis, which focuses on physiological measurements' alterations before and during driving incidents or serious driving errors. The EEG data were analyzed by using both

standard linear techniques and the more advanced non-linear analysis tools.

2. Materials and methods

2.1. Subjects

Twenty-one subjects (20 males and 1 female) participated in the present study with a mean age of 33.04 ± 10.7 (mean \pm SD) years. The subjects had average driving experience (i.e., with possession of their driving license) for 12.28 ± 8.66 (mean \pm SD) years. All the drivers reported that they drove more than 10,000 km/year. They were medically evaluated prior to the study and were found to be in good physical condition. All subjects had normal vision or corrected to normal (20/20). One subject was excluded from the subject pool before the experiment due to severe hypertension. Alcohol, caffeine, tea, and chocolate consumption were prohibited for one day prior to the measurements. All subjects were free of any kind of medication, and did not possess any personal or family history of neuropsychiatric disorder. Each subject signed an informed consent agreement prior to his/her participation and completed a short questionnaire. All subjects were paid for their participation. Written instructions explaining to the subjects the complete experiment procedure were provided. This investigation has obtained an approval from the Local Ethics Committee.

2.2. Experimental protocol

The experiments were performed at CERTH-HIT (Center for Research and Technology, Hellenic Institute of Transport) in Thessaloniki, Greece, from 6 June up to 27 July 2005. The participants were supervised to ensure that they remained awake for at least 24 h prior to the experiment, and then to arrive at the CERTH-HIT around 8.00 pm. Upon arrival and after passing the standard medical examination, the subjects' level of sleepiness was estimated in a 20-min recording at rest position by using the Maintenance of Wakefulness Test (MWT) (Doghramji et al., 1997). The EEG, EOG, electromyogram (EMG), and electrocardiogram (ECG) measurements were collected during this stage. The subjects were asked to relax in a lean-back armchair in a quite, dark room and try not to sleep while keeping their eyes open during the measurements. An experienced sleep medical doctor conducted the on-line monitoring of the EEG traces, and estimated subject's sleepiness level according to the MWT scale (1–20, with 1 being most sleepy and 20 being most awake). Their sleep behavior was also scaled by using the Epworth Sleepiness test such that the pathological sleep disorders were excluded. All subjects were found free of any pathological sleep disorder.

The on-board measurements were conducted in the CERTH-HIT experimental car (LANCIA™ Thesis, 2.4 Emblema, 5 cylinders, 2446 cm³, 170 HP). The vehicle is

equipped with double support pedals that are accessible to the driver's instructor and are equipped with advanced driver assistance systems and sensors, such as the Lane Detection System (LDS), and the Eye Leads Sensors (ELS). The LDS (CRF, FIAT Center of Investigations) consists of a CCD camera and a processing unit that recognizes lane borders and estimates the position and orientation of the experimental vehicle with respect to them (with a temporal resolution of 1 s). The ELS system (Siemens, Germany) detects the eye blinks and consists of a CCIR camera with two near infrared lighting units that enable night measurements (see the inset of Fig. 1), and a personal computer supporting the ELS software. The ELS system outputs the following data: timestamp in seconds, eye blink duration of both eyes in millisecond, and the per minute averaged blink duration (PERCLOS).

The subject was seated at the driver seat and the attached electrodes were connected to an ambulatory monitoring system (Brain Products GmbH, Germany) (Fig. 1). Eight-channel EEG, four-channel EOG, EMG, and ECG recordings were collected simultaneously during the experiment. An experienced driving instructor was seated at the co-driver's seat. At the back a technician monitored the functioning of the recording equipment, and a medical doctor monitored the on-going EEG and the other physiological measurements. A CCIR camera was placed behind the wheel that also monitored the subjects. The camera display was shown on a LCD screen in the back seat. The driving data collected by the LDS system were used for marking the driving error events. Only the driving errors identified by the driver instructor and verified by the LDS system were used for the final quantitative analysis.

The same route was followed during each measurement from CERTH-Thessaloniki to Veria (approximate distance: 100 km) and then back to Thessaloniki. It is a monotonous motorway with light traffic during the exper-



Fig. 1. One of the experimental subjects in front of the wheel wearing the EEG cap before the on-road experiment. The inset of the figure shows the Eye Leads Sensors (ELS) system, which consists of a CCIR camera and two near infrared lighting units that enable the night measurements.

iment's time. Subjects were asked to drive at their own pace while observing the usual driving rules that are to drive in the right lane except for overtake and not to exceed the motorway speed limit (in Greece: 120 km/h). They were also required to drive as much as possible in the center of the right lane and to avoid overtakes. The task was monotonous enough to promote hypovigilance. In four cases, subjects' sleepiness levels were very high during the driving task, and the driver instructor stopped the measurements after two consecutive severe sleepiness incidents (e.g., unintentionally crossing the lane border). During the experimental procedure, a total of nine severe driving errors occurred. All severe errors occurred during the last 15-min of the experiment. Seven out of nine events were observed during the last 10-min. There were also minor driving error events during the task. These events were observed only by the driver instructor and not confirmed by the LDS system. We excluded these minor driving error events from our analysis in order to ensure that these observations were not just driver instructor's subjective observations avoiding a possible bias in our analysis.

2.3. Physiological recordings

Physiological recordings were measured during the pre-experimental stage (20-min recordings in a dark room) and during the actual experiment (measurements in the research car on the motorway) by means of a digital ambulatory data acquisition system (Brain Products, Inc.). An Electro-Cap connected to the recording device was used to collect EEG data from positions Fp1, Fp2, C3, C4, P3, P4, O1, and O2. The active sites on the scalp were referenced to linked mastoids, and all impedances were maintained less than 10 k Ω . The EOG signal was also monitored via four Ag/AgCl electrodes positioned one above, and one below the right eye, one at the outer canthus of the right eye and one at the nasion. EOG channels were connected, one for horizontal (HEOG) and one for vertical (VEOG) eye-movements. Electrodes for heart activity were positioned on the sternum and the fifth intercostal space on the left side of the body. The EMG signal was also collected from two Ag/AgCl electrodes positioned on the chin. A 50-Hz hardware notch filter was also applied to all measurements to remove power interference. Sampling frequency was 200 Hz for all channels. Two test measurements were performed before the whole experimental procedure in order to assure that there was no noise contamination from the vehicle electrical or mechanical parts.

2.4. Artifact rejection

The EEG recordings were first band-pass filtered (2nd order Butterworth filter, low-pass filter cut-off frequency: 40 Hz, high-pass filter cut-off frequency: 0.5 Hz), and then the Infomax Independent Component Analysis (ICA) algorithm was used, in order to remove the artifacts from the

data (e.g., [Jung et al., 2000](#)). The analysis and extraction of artifacts were performed off-line on a PC by means of the EEGLAB software ([Delorme and Makeig, 2004](#)). The ICA decomposition was performed on the entire multi-channel waveforms (eight EEG channels plus two EOG channels). After the separation of the independent components, all the abnormal components such as eye blinks, eye-movements, and muscle activity were eliminated. Components contaminated by artifacts were rejected, and the remaining components were mixed and projected back onto the scalp-channels.

The peripheral physiological data were also band-passed filtered (EOG: 2nd order Butterworth filter, low-pass filter cut-off frequency: 13 Hz, high-pass filter cut-off frequency: 1 Hz; ECG: 2nd order Butterworth filter, low-pass filter cut-off frequency: 40 Hz, high-pass filter cut-off frequency: 1 Hz; EMG: 2nd order Butterworth filter, low-pass filter cut-off frequency: 100 Hz, high-pass filter cut-off frequency: 20 Hz). For two subjects no EMG data could be taken because of the removal of electrodes during the experiment.

2.5. Statistical data analysis

The quantitative analysis was performed on the artifact-free EEG and peripheral physiological data in two main dimensions: macroscopic and microscopic. At the macroscopic analysis, we estimate the on-going temporal evolution of physiological measurements during the driving task, assuming that sleep deprivation together with the increased duration of driving would attenuate the driving performance and subjective sleepiness would increase. At the microscopic event analysis, we focus on the physiological measurements' alterations before, during, and after the driving errors. The analysis was performed on the recorded data that satisfied the following two criteria: (a) the subject's MWT score before the experiment was less than 10, and (b) the subject managed to accomplish one hour driving task such that all subjects have comparably equal duration of recordings. The EEG traces were visually interpreted by two independent sleep-specialized neurophysiologists who kept notes on the traces. The specialists were not aware of the possible driving errors, or the subject's MWT score. The visual interpretation of the data revealed the occurrence of high-amplitude 'alpha bursts' synchronization events before the driving errors, which will be analyzed in detail in the next section of the paper.

In the macroscopic event analysis, EEG recordings were divided into one-second segments. For each channel, the relative band ratio (RBR) of the classic EEG frequency bands (delta: 0.5–4 Hz, theta: 4–8 Hz, alpha: 8–12 Hz, beta: 12–30 Hz, and gamma: 30–40 Hz) was calculated. The RBR is estimated by the relative ratio of the power of specific frequency bands against the total frequency power, and it is a unit-less value in the range between 0 and 1. The Shannon Entropy (SE) ([Appendix A](#)), the Kullback–Leibler (K–L) Relative Entropy ([Appendix B](#)), and the

Approximate Entropy (ApEn) (Appendix C) were also calculated for each EEG segment and each channel. As reference segment for the K–L entropy, an EEG segment from the first minute of each recording was used. These quantitative EEG statistics were then averaged in 5-min periods.

Based on the observations of the two neurophysiologists who visually analyzed the signals, we applied both linear and non-linear statistical tools to our measurements in order to detect and quantify the multichannel synchronization of ‘alpha spindles’ events that were identified as crucial indicators of sleepiness. To quantify the synchrony among pairwise channels, we use the common linear coherence measure and the non-linear Cross-ApEn (Appendix D). Coherence was calculated for the classic EEG frequency bands per one-second segment between all possible combinations of the EEG channels. As an information-theoretic measure, Cross-ApEn describes the pattern similarity between two time series. It can be viewed as a generalization of the non-linear dynamic measure of ApEn, which is a statistic that quantifies the complexity (or irregularity) of a single signal (Fusheng et al., 2001). We applied the cross-ApEn with typical setup of $m = 1$ and $r = 0.2$ to the EEG segments of one second for all pairwise combinations of channels. These quantitative EEG statistics were also averaged in 5-min periods.

The eye blinks were detected as peaks in the differentiated EOG signals, and the number of eye blinks was also calculated per minute (Hyoki et al., 1998). The per minute averaged eye blink duration (PERCLOSE) was also calculated from the EOG signal.

We examine the MWT score variation as a function of the driver’s age and driver’s experience by using one-way analysis of variance (ANOVA). Possible correlations between the MWT score and the EEG and eye blink statistics were also examined (Pearson’s bivariate correlation test).

For the macroscopic analysis, we have complete data, available to perform statistical analysis from 10 subjects (EEG data were either missing or were interrupted in four subjects due to technical problems during recordings, and six subjects did not satisfy the inclusion criteria of the present study). One-way ANOVA was applied to the averaged EEG statistics. The independent variables were different time factors (5, 10, and 15-min). The Bonferroni test was used for correction of multiple comparisons. Post hoc analysis was performed using the Tukey HSD test and the means were considered significantly different when the probability of error was less than or equal to 0.05. Correlation between the averaged EEG quantitative statistics and the MWT scores was calculated using the Pearson coefficient correlation. A cut-off correlation coefficient of 0.632 was regarded as a sign of significance.

We also validated the ELS system’s ability to reliably estimate the number of eye blinks per minute and the per minute averaged eye blink duration (PERCLOSE) comparing the system’s outputs with the estimated eye blink statistics derived from the EOG signal.

In the microscopic event analysis, we averaged the corresponding EEG statistics every 5 s; 40 s before, and 10 s after the nine severe driving incidents that occurred during the experiments. Additionally, nine 5-s segments from the first minute of each measurement (from those during which severe driving errors occurred) served as control conditions. We also averaged the eye blink statistics in every minute right before the driving errors. As a baseline, we selected one-minute segments from the first five minutes of each measurement. One-way ANOVA was applied on the averaged EEG and eye blink statistics. The independent variable was the time factor. The Bonferroni test was also used for correction of multiple comparisons. Post hoc analysis was performed using the Tukey HSD test.

For the definition of the exact onset time of a severe driver error, both LDS system and EMG activity were used as markers. When a driver error event was noticed by the driver instructor and confirmed by the LDS system, then the event was defined as severe driver’s error. In all cases, the instructor corrected the driver’s error for safety reasons. During this time, the driver was alerted by his/her mistake and/or instructor’s intervention, leading to a noticeable and measurable EMG activity (Fig. 2). The onset of the driver’s error was defined according to the EMG activity (increase in EMG RMS (in μV) by at least 25% in comparison with the previous 200 ms time window). The EMG patterns were estimated by computing muscles activation level (RMS, root mean square) (Gentili et al., 2006; Papadelis et al., 2007).

In order to analyze the microscopic events of driving accidents, we are also interested in monitoring the short-range (1–2 s) *phase synchrony* between different EEG channels. In the neuroscience literature, phase synchrony is an important phenomenon that might have some relationships with attention, cognition, and memory (Lachaux et al., 1999). In neuroelectric or biomagnetic recordings, a good measure for quantifying the instantaneous phase relationship between two signals is the so-called phase locking value (PLV; Appendix E). Specifically, PLV has some advantages over the common coherence measure (i.e., spectral covariance) since coherence can be applied only to stationary signals and it does not specifically quantify phase relationship (Lachaux et al., 1999). In addition, the PLV statistic calculated from Hilbert transform is a non-linear measure compared with the linear coherence measure; moreover, the PLV is based on the instantaneous phase difference between two signals, while the coherence does not explicitly use the phase information. In this paper, no statistical test was applied to the PLV measure, since we only want to use the PLV for quantifying the specific duration (generally <1 s) of temporally local, synchronized events. Application of such a measure for predicting the synchronized event is the topic of a separate research that will be reported elsewhere. In this paper, we will show by visual illustration the distinction of the PLV statistic during, before, and after the synchronized events.

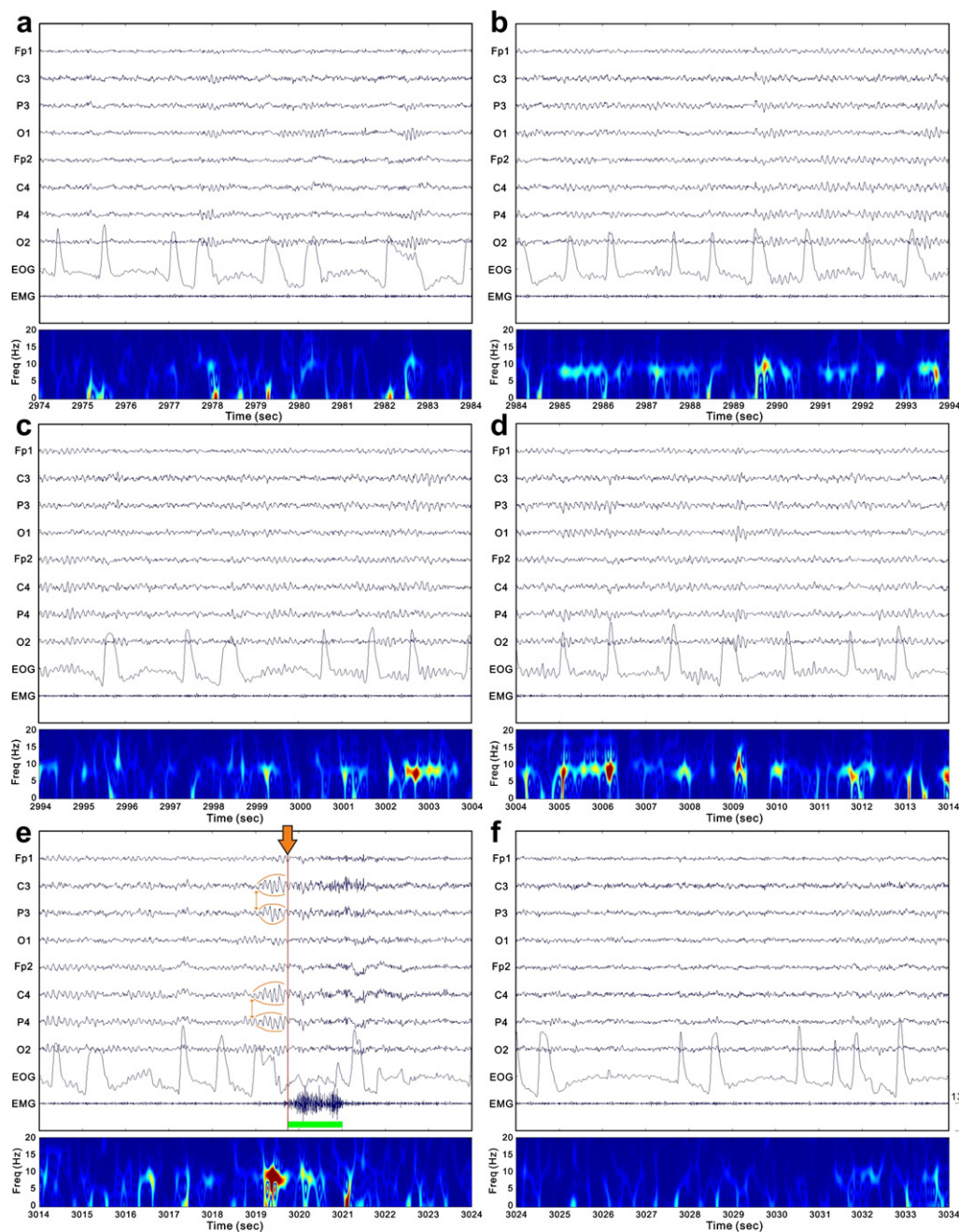


Fig. 2. The traces of eight-channel EEG, EOG and EMG during 45 s before and 13 s after a severe driving error (Subject No. 4, Date: 2 June 2005). The row indicates the onset of the driving error, and the green bar the subject's reaction due to the driving instructor's correction. We observe the frequent occurrence of brief 1–2 s paroxysmal bursts of alpha activity in the central and parietal brain regions (orange highlight) with a frequency component 1–2 Hz slower than the alpha rhythm and an increased synchrony among EEG channels (indicated by small arrows between the bursts) that appears more obvious exactly before the driving error. The alpha bursts just before the error were accompanied by a long-duration eye blink. At the bottom of each time traces panel, the time-frequency map representation of channel C3 is shown. We observe the increase of alpha power before the driving event that appears more dominant almost half second before the driving error onset. After the driving instructor's correction, the alpha rhythm disappears and the brain activity is shifted to higher frequencies.

3. Results

3.1. Visual interpretation of EEG

Two independent sleep-specialized neurophysiologists visually interpreted the measurements. The visual interpretation of the continuous measurements of EEG, EMG, and

EOG revealed the occurrence of 'alpha synchronization bursts' especially just before the driving errors. The occurrence of these bursts was consistent with the nine severe driving error events (before the events). Alpha synchronization bursts were also observed before minor driving errors (in two cases), and additionally two more times independently from any driving error. The bursts were more

prominent in the most sleep-deprived subjects (i.e., subjects with low MWT scores). As to the wave morphology, they had frequency typically between the higher portion of the theta band and the lower portion of alpha bands (7–9 Hz) with gradual increase of amplitude (Fig. 2). They can be characterized by high intra- and inter-hemispheric synchronization among EEG channels. As to the topographical distribution, these bursts were more dominant in the central and parietal areas (Fig. 3).

Within this ‘alpha synchronization bursts’ period, eye blinks of long-duration and sometimes multiple eye blinks were present (Fig. 2). We also noticed that the same observations occurred before an increase of EMG activity in cases where no driving error event was present. This may be interpreted as arousal effort of the driver, which could prevent him/her from the driving error event. During the evaluation process the two neurophysiologists posed six criteria, according to their observations, which can characterize the potential driving error event: (a) at least 10 s before the driving error event, ‘alpha synchronization bursts’ from the lower limit of alpha waves gradually to theta waves; (b) 10 s before the driving error event, at least one eye blink per second and during the driving error event one long-duration eye blink; (c) decrease of eye blinks occurrence right after the driving event; (d) after the driving error event, faster EEG waves and a desynchronization among EEG channels for about 1–2 s; and (e) increased EMG activity during the driving error event. Based on the measurements of the present study, the two neurophysiologists concluded that provided three of those criteria are met, there is a high possibility of an upcoming driving error event.

3.2. MWT score

Before the experiment, MWT score did not vary as a function of driver’s age, or of driver’s experience. There was not any significant correlation between the MWT score and any quantitative EEG statistic of the ten first minutes for any EEG channel. We also did not observe any correlation between the MWT score and the eye blink statistics for the first 10-min of the measurements.

3.3. Relative frequency band power ratio

The Spectral RBR was significantly increased between the first and the last 15-min in delta band for the channels C3, P3, O1, P4, and O2, and the same in alpha band only for the channel P3. Graphical representations of relative alpha power suggested that the alpha power increased between the first and the last 15-min at most sites, but these results failed to reach significance. This was probably due to extreme intersubject variations. A statistically significant decrease between the first and the last 15-min was observed in beta band for all channels except the frontal one, and in gamma band for the channels C3, P3, C4, and P4. Theta RBR did not significantly alter between the first and the last 15-min.

Single-factor ANOVA did not reveal a statistical significant alteration of RBR for theta, alpha, and gamma frequency bands by driving time for any EEG channel. A statistically significant alteration of RBR in the delta band by driving time (15-min periods) was revealed for the following EEG channels: C3 ($F(3, 116) = 3.006$, $p = 0.033$),

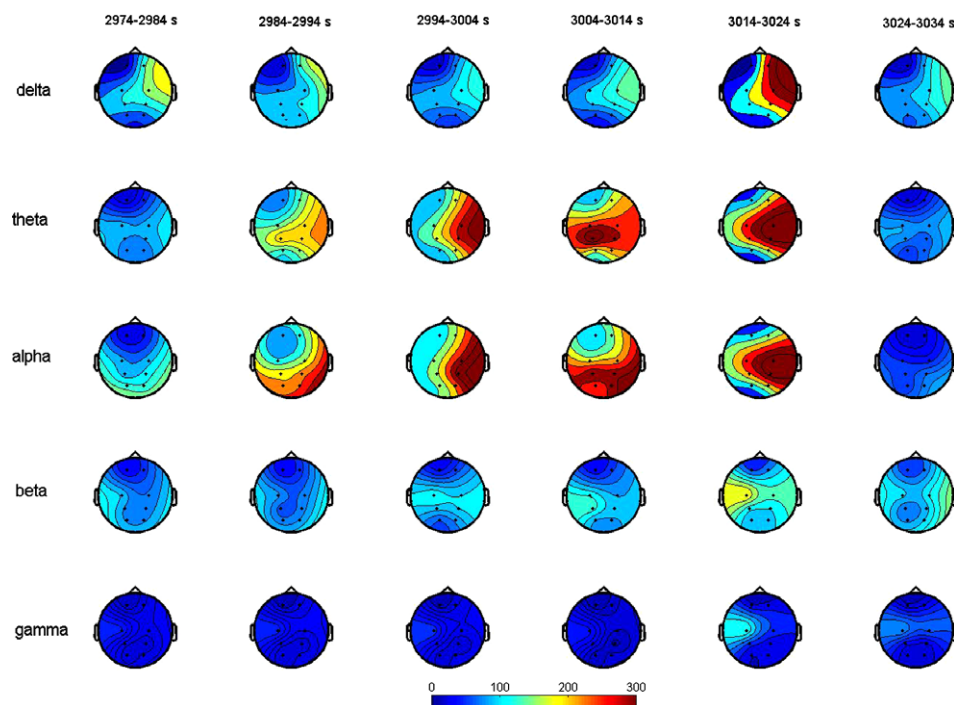


Fig. 3. The absolute power topographical maps for the standard EEG frequency bands before, during, and after the driving error presented in Fig. 2. We observed a significant increase of alpha and theta power before and during the driving event. Delta power is also increased during the driving error. The driving error occurred at 3020 s.

P3 ($F(3, 116) = 5.066, p = 0.002$), and O2 ($F(3, 116) = 3.147, p = 0.028$). For the beta frequency band, we observed a statistically significant alteration of RBR by driving time for the channels: C3 ($F(3, 116) = 3.051, p = 0.031$), P3 ($F(3, 116) = 4.005, p = 0.009$), C4 ($F(3, 116) = 3.309, p = 0.023$), and P4 ($F(3, 116) = 3.373, p = 0.021$). The post hoc analysis by Tukey HSD revealed two homogenous groups for the delta band (channels: C3, P3, and O2), and also two homogenous groups for the beta band (channels: C3, P3, C4, and P4), and two for the gamma band (channels: C4 and P4).

3.4. Shannon Entropy, K–L Entropy, and ApEn Measures

A statistically significant decrease between the first and the last 15-min was observed in Shannon Entropy for all channels except the frontal one. The statistical analysis for Shannon Entropy (one-way ANOVA) revealed a statistically significant alteration by driving time (15-min periods) for all EEG channels except the frontal ones: C3 ($F(3, 116) = 3.77, p = 0.013$), P3 ($F(3, 116) = 5.846, p = 0.001$), O1, ($F(3, 116) = 3.758, p = 0.013$), C4 ($F(3, 116) = 4.451, p = 0.005$), P4 ($F(3, 116) = 5.521, p = 0.001$), and O2 ($F(3, 116) = 3.99, p = 0.01$).

A statistically significant decrease between the first and the last 15-min was observed in K–L Entropy for the channels: P3, O1, P4, and O2. The K–L Entropy was significantly affected by driving time only for the P4 channel ($F(3, 116) = 3.51, p = 0.018$). The post hoc analysis by Tukey HSD revealed two homogenous groups for the Shannon Entropy (all channels except the frontal), and also two homogenous groups for the K–L Entropy only for the P4 channel. We did not observe a statistically significant alteration of ApEn by driving time for any EEG channel.

3.5. Coherence and Cross-ApEn Measures

Coherence increased significantly between the first and the last ten minutes for the EEG between channels C3–C4 ($F(1, 38) = 5.748, p = 0.022$) (Fig. 4). Single-factor ANOVA revealed a statistically significant alteration of coherence by driving time (15-min periods) for the same

combination of EEG channels ($F(3, 116) = 2.712, p = 0.048$). The statistical analysis for coherence revealed also a statistically significant increase for the EEG delta frequency band between the first and the last 10-min between channels C3–C4 ($F(1, 38) = 8.930, p = 0.005$) as well as for the theta frequency band ($F(1, 38) = 7.532, p = 0.009$) (Fig. 4). The increase was also observed for the delta band between channels C3–P3 ($F(1, 38) = 6.275, p = 0.017$). ANOVA revealed a statistically significant alteration of coherence by driving time (15-min periods) for the channels' combination C3–C4, for the delta frequency band ($F(3, 116) = 5.763, p = 0.001$), as well as for the theta frequency band ($F(3, 116) = 5.020, p = 0.003$). By selecting a smaller time period (10-min), single-factor ANOVA revealed also a statistically significant alteration of coherence by driving time for the same combination of channels and the same frequency bands: (delta band: ($F(3, 116) = 3.185, p = 0.010$) and beta band: ($F(3, 116) = 2.827, p = 0.019$)).

Single-factor ANOVA revealed a statistically significant alteration of Cross-ApEn by driving time (15-min periods) for the following EEG channel combinations: P3–P4, P3–C4, C3–P4, C4–P4, C3–C4, and C3–P3 (Supplementary Table 1). For the 10-min periods, significance was reached only for the EEG channel combination P3–P4 ($F(3, 116) = 2.544, p = 0.032$). Cross-ApEn was increased significantly between the first and the last quarters for all the above EEG channel combinations: P3–P4 ($p = 0.003$), P3–C4 ($p = 0.004$), C3–P4 ($p = 0.017$), C4–P4 ($p = 0.019$), C3–C4 ($p = 0.02$), and C3–P3 ($p = 0.033$). The post hoc analysis (15-min periods) revealed two homogenous subsets for these channel combinations.

3.6. Eye blinks

A statistically significant increase between the first and the last 15-min was observed for the per minute averaged eye blink duration (PERCLOSE) ($F(1, 58) = 5.668, p = 0.021$) (Fig. 5). Single-factor ANOVA did not reveal a statistically significant alteration of per minute averaged eye blink duration (PERCLOSE) by driving time ($F(3, 116) = 2.106, p = 0.103$). We did not observe

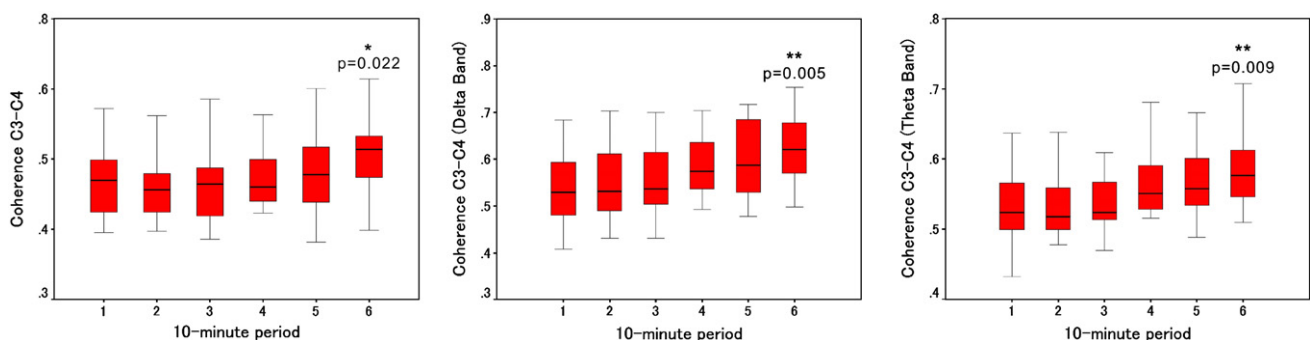


Fig. 4. The averaged (per 10-min) Coherence for the channels combination C3–C4 for the whole frequency range (left panel), for the delta band (middle panel), and for theta band (right panel). The p -values correspond to the results of ANOVA, and the asterisks (*) and **) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the first and last 10-min.

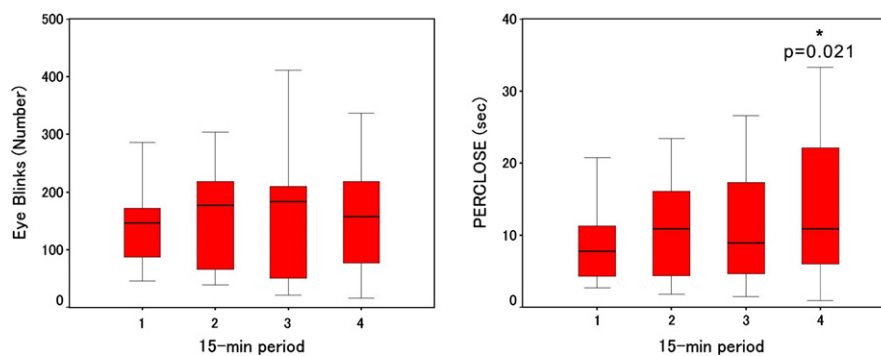


Fig. 5. The averaged (per 15-min) number of eye blinks (left panel) and per minute averaged eye blink duration (PERCLOSE) (right panel). The p -values correspond to the results of ANOVA, and the asterisks (*) and **) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the first and last 15-min.

significant alteration of number of eye blinks by driving time ($F(3, 116) = 0.566$, $p = 0.638$), nor statistically significant differences between the first and the last 15-min ($F(1, 58) = 0.311$, $p = 0.579$).

The ELS system was found to have high reliability in the estimation of both the per minute averaged number of eye blinks (mean \pm SD: $96.3\% \pm 5.2\%$) and per minute averaged eye blink duration (mean \pm SD: $92.8\% \pm 6.12\%$).

3.7. Heart rate variability

We did not observe a statistically significant alteration of heart rate variability by driving time, nor a significant difference between the first or the last quarters of the experiment.

3.8. EEG statistics before, during, and after driving error events

The spectral alpha RBR significantly increased between the control condition and before the driving errors for the following channels: C3 (Fig. 6), P3, O1, C4, and P4 (Fig. 7). The increase was more dominant in the central and parietal channels (Fig. 7). A statistically significant decrease of gamma RBR was also observed (Fig. 7) between the control condition and all the segments before the driving errors for the following channels: Fp1, C3 (Fig. 6), and P3. For the rest of channels, we observed a statistically significant decrease of gamma RBR between the control condition and all the segments before and after the driving errors. For the delta and theta frequency bands, we did not observe differences between the control condition and the segments before the driving errors (Fig. 6). A statistically significant decrease was also observed between the control condition and all the segments before the driving errors for beta frequency band, for channel C4. For the channels Fp1, C3, P3, O1, Fp2, P4, and O2, we observed a significant decrease between the control condition and some of the segments before the driving errors, but these results were not consistent for all EEG segments before the driving event (Fig. 6, for channel C3).

Single-factor ANOVA revealed statistically significant differences between the 11 EEG segments for the RBR of theta, alpha, beta, and gamma frequency bands (Supplementary Table 2). The post hoc analysis revealed three homogenous subsets for alpha band for the channels C3 and C4, including one subset that containing the control condition and the segments after the driving error, one subset that contained the segment after the driving error (9 and 10) and the segments (1, 2, and 4), and another subset that contained all the segments before the driving error. Post hoc analysis revealed three homogenous subsets for theta band for the channels: Fp1, C3, P3, O1, and C4, and two homogenous subsets for the rest of channels. For the beta frequency band, post hoc analysis revealed four homogenous subsets for channels Fp1 and C4, and three subsets for the other EEG channels. The post hoc analysis revealed four homogenous subsets for gamma band for the channels P3, O1, and C4, including one subset that contained the control condition, one subset that contained the segment after the driving error (9 and 10), one segment contained the first segment after the driving event and the first segment before the driving event (1 and 9), and another subset that contained all the segments before the driving error. For the rest of channels, post hoc analysis revealed three homogenous subsets for the gamma frequency band.

The Shannon Entropy was significantly decreased between the control condition and most of the segments before the driving errors for the channels: C3 (Fig. 8), P3, O1, C4, P4, and O2. For the K–L Entropy, we did not observe consistent differences between the control condition and the segments before the driving errors (Fig. 8). Single-factor ANOVA revealed statistically significant differences between the 11 EEG segments in all channels for the Shannon Entropy (Supplementary Table 3), and in all channels except the frontals for the K–L Entropy (Supplementary Table 3). The post hoc analysis revealed four homogenous subsets for the Shannon Entropy for channel C4, with one subset contained the control condition and the segments after the driving error. For the rest of channels, post hoc analysis revealed three homogenous subsets for the Shannon Entropy. For the K–L Entropy, post

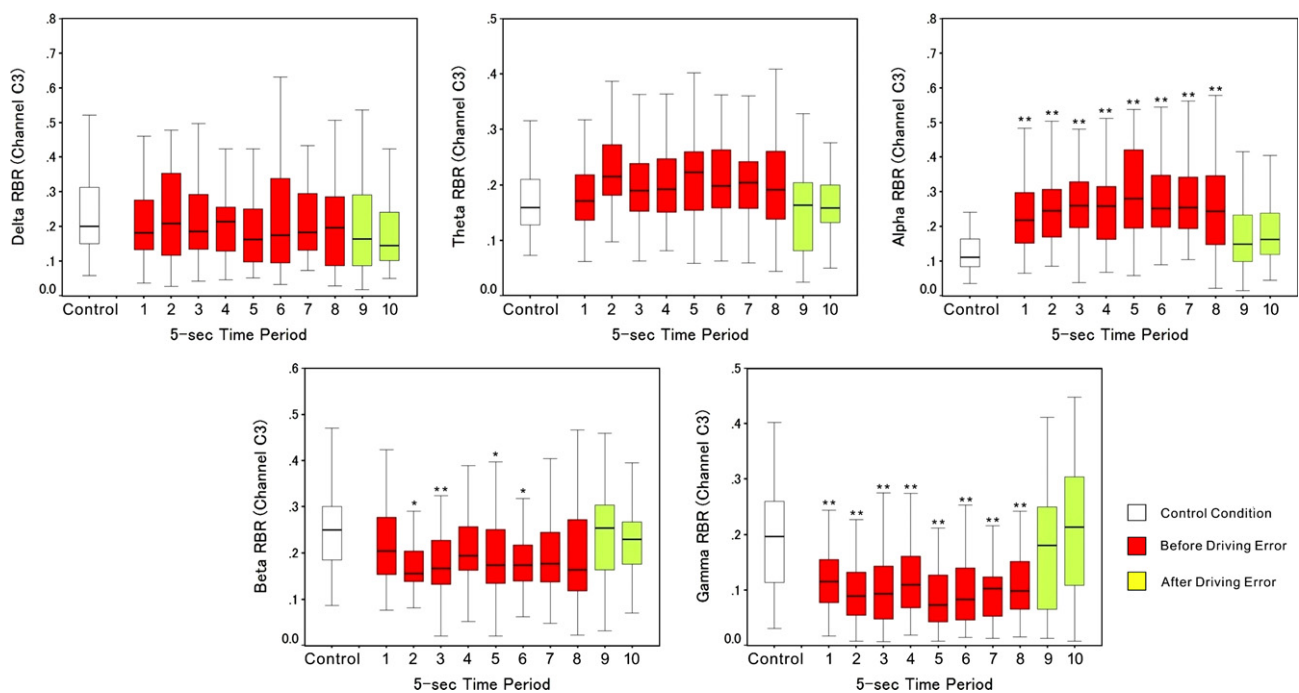


Fig. 6. The averaged (per 5 s among all nine severe driving events occurred in our experiments) relative band ratio (RBR) of all EEG standard frequency bands, 40 s before (on red) and 10 s after (on green) the driving errors' onset. As control condition (on white) we selected EEG segments (5 s duration) from the first minute of each measurement in which driving errors occurred. The p -values correspond to the results of ANOVA, and the asterisks (*) and (**) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the control condition and each time-period.

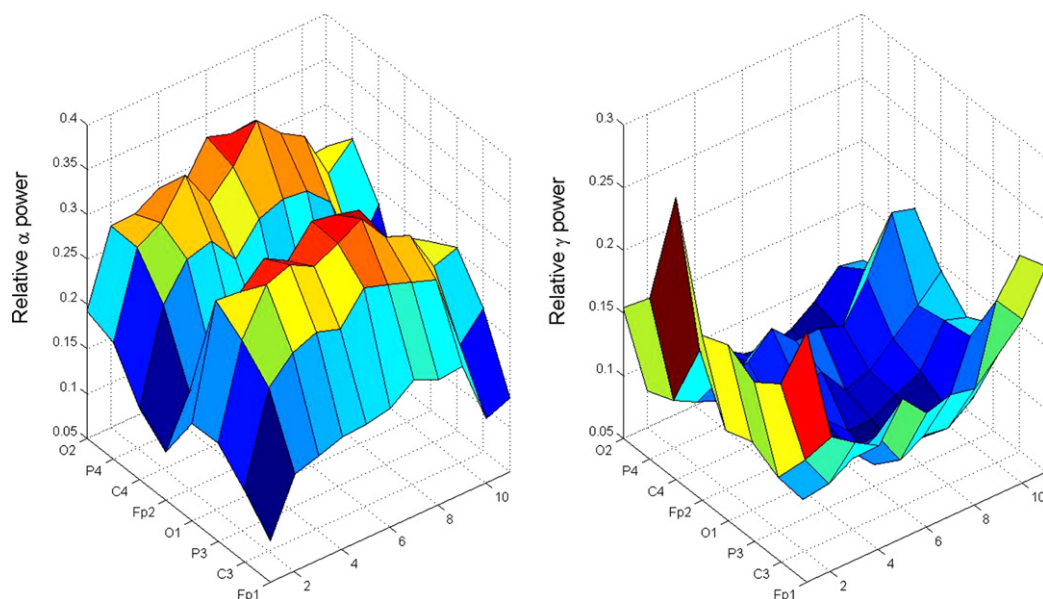


Fig. 7. The relative power of alpha and gamma frequency bands of time evolution (in 5-s segments, averaged over nine driving error events) before, during, and after the driving errors for all eight EEG channels. We observed an increase of alpha and decrease of gamma RBR before the driving error onset, which is more dominant at the central and parietal channels. The segments correspond to 40 s before (1–8) and 10 s after (9–10) the driving errors' onset. As the control condition, we selected an EEG segment (5 s duration) from the first minute of each measurement where driving errors occurred.

hoc analysis revealed three subsets for channels C4 and P4, two subsets for channels: C3, P3, O1, and O2, and one subset for the frontal channels. We did not observe statistically significant differences of Approximate Entropy between the control condition and the segments before the driving errors for any channel.

Coherence increased significantly before driving events in comparison with the control condition for the frequency band 7–9 Hz (channels combination C3–C4) (Fig. 9), and for the gamma frequency band (channels' combination: C3–C4, C3–P3, C3–P4, C4–P4, P3–C4, and P3–P4). Single-factor ANOVA revealed statistically significant

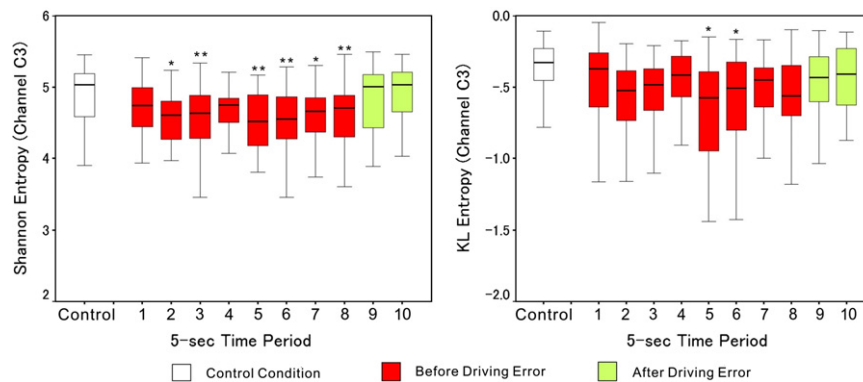


Fig. 8. The averaged (per 5 s among all nine severe driving events occurred during our experimental procedure) Shannon Entropy and K–L Entropy of channel C3, 40 s before (on red) and 10 s after (on green) the driving errors' onset. As control condition we selected EEG segments (5 s duration – on white) from the first minute of each measurement in which driving errors occurred. The p -values correspond to the results of ANOVA, and the asterisks (*) and **) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the control condition and each time-period. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

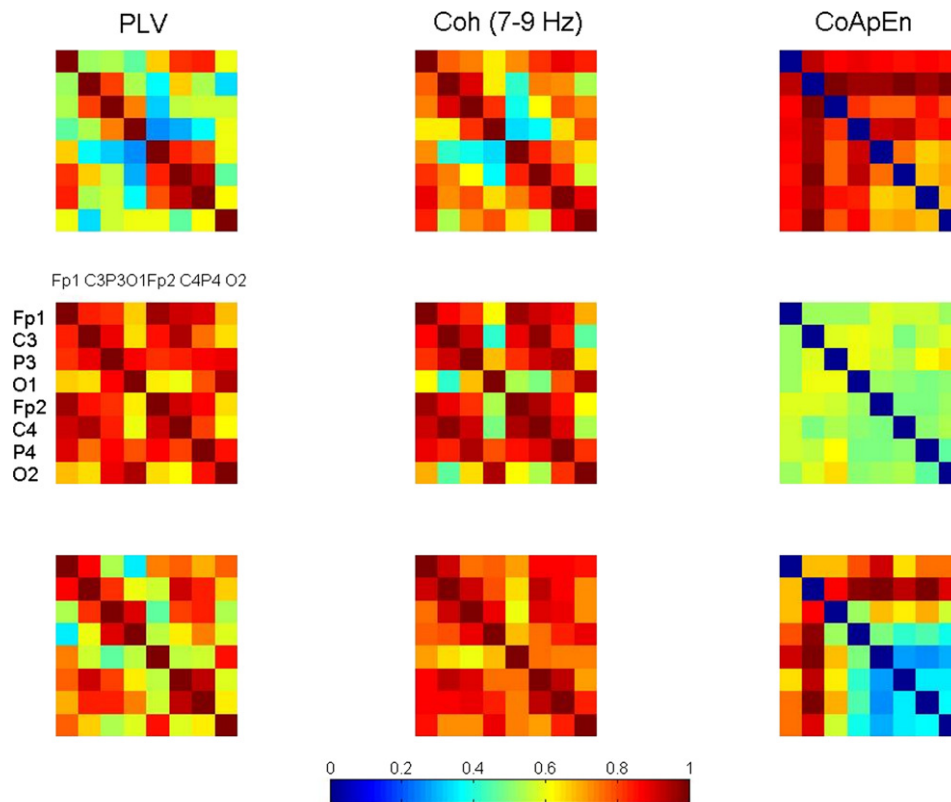


Fig. 9. The PLV (7–9 Hz), Coherence (7–9 Hz), and Cross Approximate Entropy between all EEG pairwise channel combinations during the control condition (first row), before (second row), and after (third row) of a severe driving error.

differences of coherence between the 11 EEG segments for the alpha band (channels combination C3–C4), and for the gamma band (channels' combination: C3–C4, C3–P3, C3–P4, C4–P4, P3–C4, and P3–P4) (Supplementary Table 4). The post hoc analysis revealed three homogenous subsets for coherence in the gamma band (channels' combination: C3–C4, C3–P4, C4–P4, P3–C4, and O1–O2).

The Cross-ApEn significantly decreased before the driving errors in comparison with the control condition

for all the EEG segments for the following channels' combinations: C3–C4, C3–P3, C3–P4, C4–P4, P3–C4, P3–P4, and O1–O2 (Fig. 10). Single-factor ANOVA revealed statistically significant differences between the 11 EEG segments in all previously mentioned channels' combinations for the Cross-ApEn (Supplementary Table 5). The post hoc analysis revealed three homogenous subsets for Cross-ApEn for all these channels' combinations.

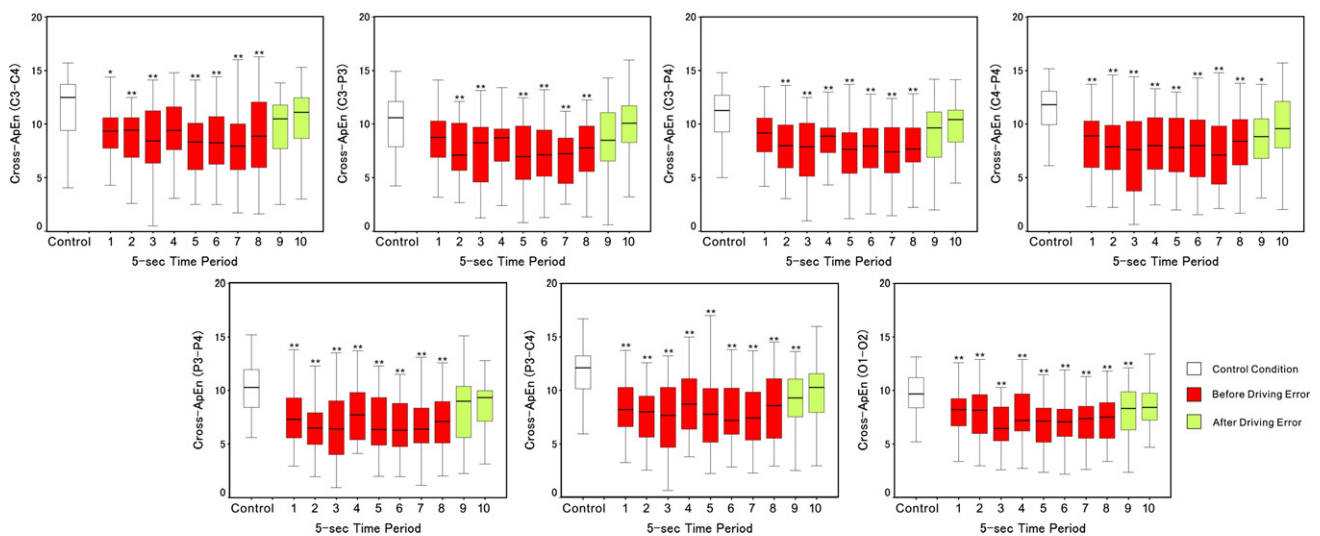


Fig. 10. The averaged (per 5 s among all nine severe driving events occurred during our experimental procedure) Cross Approximate Entropy for different EEG channel combinations, 40 s before (on red) and 10 s after (on green) the driving errors' onset. As control condition we selected EEG segments (5 s duration – on white) from the first minute of each measurement in which driving errors occurred. The p -values correspond to the results of ANOVA, and the asterisks (*) and (**) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the control condition and each time-period. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

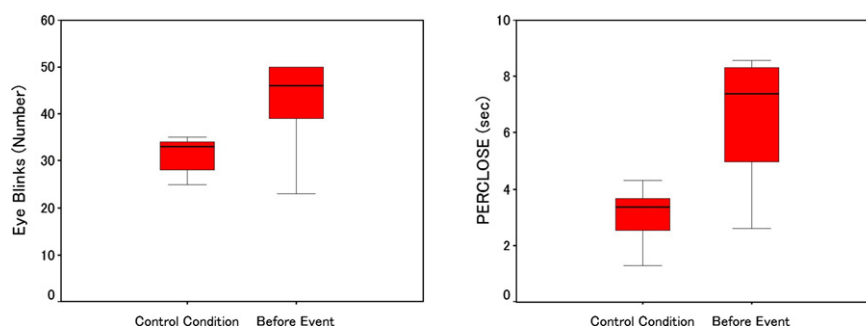


Fig. 11. The averaged (per one-minute) number of eye blinks (left panel) and, per minute averaged eye blink duration (PERCLOSE) (right panel) (among all nine severe driving error events occurred in our experiments) in control condition and before severe driving errors. As control condition we selected EOG segments (one-minute duration) from the first minute of each measurement in which driving errors occurred. The p -values correspond to the results of ANOVA, and the asterisks (*) and (**) indicate statistically significant differences ($p < 0.05$ and $p < 0.01$) between the control condition and the minute before driving errors.

3.9. Eye blink statistics before and after the driving error events

Both the number of eye blinks and the per minute averaged eye blink duration (PERCLOSE) significantly increased during the minute right before the driving errors in comparison with the control condition (number of eye blinks: $F(1, 16) = 5.632$, $p = 0.030$; PERCLOSE: $F(1, 16) = 17.821$, $p = 0.001$) (Fig. 11).

4. Discussion

Driving is a complex task that requires an optimum level of alertness to guarantee the security of the driver and other road users. Driver's sleepiness has been recognized as one of the most significant safety hazards in the transportation industry (Lal and Craig, 2005). The development

of an on-board countermeasure system that provides drivers with useful feedback about the onset of their sleepiness can essentially contribute to the prevention of sleep-deprived traffic accidents.

In the last few decades, there is an increasing interest in the scientific community on the evaluation of electrophysiological indicators for the detection of sleepiness. While numerous physiological indicators are available for assessing the level of alertness, the EEG signal has been recognized as the most predictive and reliable one (Artaud et al., 1973; Lal and Craig, 2002). In a number of driving simulator studies, significant alterations in EEG frequency bands were observed as a result of fatigue or sleepiness (Horváth et al., 1976; Torsvall and Åkerstedt, 1987; Gillberg et al., 1996; Lal and Craig, 2000). In general, an increase in the power of alpha and theta frequency bands was the consistent finding in the majority of these studies.

Notably, we shall not forget that these results have been obtained in driver simulators, and therefore the subjects knew that the consequences of their driving errors would not affect their safety. Moreover, driving simulator produces results that may not be generalized to real-life driving, and calibrations have been suggested against real driving for the driving simulators in various conditions (Philip et al., 2005).

In the present study, we used an experimental paradigm that involves neurophysiological measurements in real driving conditions to assess the driving task in a more realistic way. We obtained peripheral physiological measurements and we examined the effectiveness of eye blink statistics as potential indicators of sleepiness.

It is well known that increased driving time would impair the alertness and the driving performance (Otmani et al., 2005). Total sleep restriction during the night prior to the experiment combined with the effect of time on the driving task would amplify the decrease in the level of alertness and induce severe sleepiness. Based on this assumption, we estimated the on-going temporal evolution of physiological measurements during the experiment. We extended this analysis by also focusing on some well-defined severe driving errors. Although the idea of introducing a link between the alertness and driving performance is not new (Broukhuis and de Waard, 1993; Campagne et al., 2004), the recorded neurophysiological measurements are rarely linked with specific driving errors. In order to use EEG for the development of a sleepiness countermeasure device, the EEG signal should be free of both environmental and biological artifacts that occur frequently in the real field measurements. Artifact rejection pre-processing techniques were rarely applied to EEG data recorded from sleep-deprived drivers prior to the quantitative analysis. Gevins et al. (1995), in an operational environment experiment, reported advances in on-line reduction of muscle and eye-movement artifacts based on low-pass filtering with variable cut-off frequencies. In our study, we used a widely accepted signal processing technique, known as independent components analysis (ICA), in order to remove eye-blinking and muscle activity artifacts (Jung et al., 2000). In the current data analysis, we used the ICA algorithm for off-line EEG analysis; however, the ICA method can be adapted for real-time processing in an on-line setup for the development of practical devices.

Our quantitative EEG analysis revealed significant variations of RBR by driving time in the frequency bands of delta, alpha, beta, and gamma. These alterations were more prominent in the central and parietal areas, and less prominent in the occipital areas. We did not observe RBR alteration by driving time in frontal electrodes for any frequency band. More specifically, an increase of RBR was observed in the delta and alpha bands, and a significant decrease in the beta and gamma frequency bands by driving time. Most of our observations concerning the EEG frequency bands (increase in delta and alpha bands) are in agreement with previous findings reported in the lit-

erature. Lal and Craig (2000) found consistent increases in the delta, theta, and alpha activities during transition to fatigue from an awake state. Torsvall and Åkerstedt (1987) reported that the alpha activity was clearly the most sensitive to sleepiness, while the delta and theta bands were also affected by driving time but to a lesser extent. In a field study, Kecklund and Åkerstedt (1993) recorded EEG continuously during evening/night driving in a group of truck drivers, and found increased alpha and theta burst activities during the last few hours of driving. Although theta power increase due to sleepiness is a frequent observation in most of the studies, we did not find a significant alteration of theta RBR as a function of driving time. The observed beta band RBR decrease is in accordance with results reported by Lal and Craig (2005), while it is the first time that the gamma frequency band is investigated, which has a statistically significant alteration by driving time. The differences in frequency bands between our results and the findings of previous studies could be due to the fact that we estimated RBR instead of the absolute spectral power. In light of Parseval's theorem (e.g., Arfken and Weber, 2001), the sum of the square of signal is equal to the sum of the square of its Fourier transform. Hence, the spectral power of frequency bands strongly depends on the EEG signal's amplitude, and therefore also depends on the electrode's impedance; while relative power disregards the total power of the signal, focusing on the ratio of frequency components of the EEG signal.

Although considerable progress has been made for the detection of sleepiness onset, we know of no published studies that analyze the EEG data obtained from sleep-deprived drivers by using more advanced signal processing techniques than the standard Fourier analysis. In an attempt to develop and validate more sensitive and reliable statistics for sleepiness detection, we also applied several entropy measures to our EEG data. The concept of entropy is defined as the rate of information loss over time (Stam, 2005). The non-linear entropy measures quantify successfully the cortical function at different sleep stages (Fell et al., 1996; Acharya et al., 2005). Entropy showed a very high statistically alteration by driving time in almost all EEG channels. However, the ApEn was not affected by driving time, although it seemed to be sensitive to the classification of sleep stages (Burioka et al., 2005).

Compared to other qualitative descriptive studies, the finding of Santamaria and Chiappa (1987) unquestionably provided the most detailed description available for the EEG events during the sleepiness onset. These authors confirmed many earlier observations and stressed that the EEG changes during drowsiness are often rapid, with some states lasting from less than a second to a few seconds. Therefore, the macroscopic temporal event analysis of the on-going brain activity may not be able to capture these transient EEG alterations, and important information might be lost concerning the sleepiness' onset. For the same reason, a microscopic event analysis focusing on driving errors is more desirable.

The visual interpretation of our EEG measurements revealed the occurrence of ‘alpha bursts’ especially right before the driving errors (Fig. 2). The occurrence of these bursts was a consistent finding during all measurements but was more frequent at the end of the measurements, and more prominent before the errors. Although, these alpha bursts did not occur exclusively just before the severe driving errors, the fact that before all nine severe errors alpha synchronization bursts occurred shows that the occurrence of brief paroxysmal bursts of alpha activity and the increased synchrony among EEG channels are strongly linked with an upcoming driving error. The alpha bursts all had the same frequency content (in the lower portion of alpha band). These EEG alterations were observed in previous laboratory sleepiness-onset studies as first described by Santamaria and Chiappa (1987) and latter confirmed by Broughton and Hasan (1995) about EEG alterations during sleepiness onset. Mano et al. (1995), in their real field driving experiment, observed a diffuse slower alpha activity when the drivers closed their eyelids as the driving time went on. Although it seems difficult to identify if the observed alpha bursts correspond to one of the two types of alpha activity related with sleepiness as they have been described by Broughton and Hasan (1995), their duration (1–2 s) and their spatial distribution lead us to believe that this phenomenon may correspond to the paroxysmal bursts of alpha activity (Broughton and Hasan, 1995). Furthermore, the fact that they occurred more frequently in the EEG recordings of the most-deprived subjects confirms our notion that they are strongly related with high levels of sleepiness. The spectral RBR of alpha activity was also significantly increased almost one minute before the driving errors, and such an increase was more dominant in the central and parietal channels. However, the alpha RBR presented statistically significant alteration by driving time only in one channel in the macroscopic analysis of our EEG data. This can be explained by the fact that these paroxysmal bursts of alpha waves occurred in brief groups of 1–2 s duration, and thus their overall frequency power was not strong enough at all channels to increase significantly the alpha RBR in the macroscopic event analysis.

The visual interpretation of our recorded data revealed an increase of EEG signal synchronization among different channels before the driving errors, which led us to examine if we can quantify this phenomenon by using both linear and non-linear signal processing techniques. In the last decade, the notion of EEG synchronization has attracted the attention of many researchers and it has led to a whole new range of quantitative EEG measures as well as a number of emerging applications for monitoring of sleep (Stam, 2005). In macroscopic analysis, we calculated the frequency-domain based linear coherence measure and the time-domain based non-linear Cross-ApEn (Fusheng et al., 2001) in order to quantify the synchrony among the EEG channels. It was found that coherence increased significantly between the first

and the last 10-min for the channels’ combination C3–C4, which corresponds to the central areas of the brain. In the microscopic analysis of our data, coherence increased significantly before driving events in comparison with the control condition for both alpha and gamma frequency bands. The Cross-ApEn was more sensitive in detecting the sleepiness onset since it significantly decreased before the severe driving errors for the majority of EEG channel combinations, and moreover it was significantly affected by the driving time for these channel combinations. In addition, we also used PLV to measure the short-range (1–2 s) phase synchronization while examining the pairwise channel synchronization before the severe driving errors.

Our study provides further evidence that a variety of quantitative EEG statistics are reliable for the detection of sleepiness and therefore they can be used as sleepiness indicators in an on-board countermeasure device. However, this approach encounters several practical problems. Even if we assume that a reliable EEG-based sleepiness indicator is available, there are other technical problems that need be solved. We should not be remiss of the fact that the system would work reliably in a real environmental condition where the EEG signal is highly contaminated with noise. Even if this problem can be solved by the usage of some on-line artifact rejection techniques, such as the ICA, the usability of such a device should be reconsidered for more practical than technical reasons. Our group believes that it will be difficult for the drivers to place jelly electrodes on their scalp before every driving session, and especially on hairy areas (such as the central or parietal regions) that appear to be the most sensitive on the EEG alterations due to sleepiness. More recently, advanced electrodes have been developed that allow to amplify the EEG signal in the scalp-electrode, and some groups (Lal and Craig, 2001a) also conducted research on the development of miniaturized dry electrodes. However, other approaches using peripheral neurophysiological measurements, which can be obtained with some driver-friendly techniques, should also be considered and studied more intensively.

Eye blinks are sensitive to high visual attention demands. Fewer and shorter duration blinks are often associated with situations that require intake of important information such as reading (Ponder and Kennedy, 1928), city driving (Lecret and Pottier, 1971), and formation flying (Wilson et al., 1987). Blink closure duration has also been shown to be sensitive to high overall task demand. Blink patterns have also been used to provide information about the operator’s responses to the environmental stimuli and thus the situational awareness (Fogarty and Stern, 1989; Wilson, 1992).

Since Aserinsky and Kleitman (1955) reported changes in spontaneous eye movement patterns not only in sleep but also in the hypnagogic state, EOG has been used for assessing alertness, often together with EEG (Isse et al., 1978; Hori, 1982; Santamaria and Chiappa, 1987; Ota

et al., 1990; Hyoki et al., 1998). Furthermore, EOG has been widely applied to clinical evaluations, such as drug effects on alertness (Shigeta et al., 1993), and arousal levels in psychiatric disorders (Toyoshima, 1991). However, the relationship between the EOG and EEG measures had not been clarified at various stages of alertness until Hyoki et al. (1993). In their study, a significant correlation between the number of eye movements and EEG powers at alpha and beta frequency bands was found (Hyoki et al., 1993).

Mano et al. (1995) first reported in their real field highway driving experiment that blinking of eyelids increased as the driving time went on; and recently, EOG measurements have been obtained (Lal and Craig, 2005) in a simulator study of driver's sleepiness. However, there is still a lack of research on the systematic evaluation of EOG-based statistics as potential indicators for the driver's sleepiness. Indeed, Mano et al. (1995) restricted their observations on a macroscopic evaluation of the on-going eye-blinking activity, and Lal and Craig (2005) used the EOG signal for eye blink artifact identification without presenting any results concerning the eye-blinking activity. We analyzed the eye-blinking statistics in both a macroscopic and microscopic way. We found a statistically significant alteration of eye-blinking duration by driving time. More specifically, the eye-blinking duration and the number of eye blinks both increased as the driving time went on, but only eye-blinking duration reached significance. Moreover, the number of eye blinks and the per minute averaged eye blink duration (PERCLOSE) statistics were significantly increased during the minute right before the driving errors in comparison with the control condition. Our study presented clear evidence that the eye-blinking statistics are sensitive to the driver's sleepiness and they should be considered in the design of a future sleepiness detection countermeasure device. Since advanced technological systems, such as the ELS system used in our experiment, are available and reliable in measuring the eye-blinking activity, the EOG-based approach seems to be more driver-friendly and efficient than an EEG-based system, and therefore this technology should attract more attention from the researchers in industry.

In this paper, we evaluated the effectiveness of a plethora of neurophysiological statistics in detecting driver's sleepiness in a real environment experimental paradigm. We can conclude that the occurrence of brief paroxysmal bursts of alpha activity (with frequency 1–2 Hz slower than the conventional alpha rhythm) in the central and parietal brain regions, as well as an increased synchrony among the EEG channels, indicates a high level of sleepiness and a high possibility of an upcoming severe driving error. The EEG statistics that quantify the signal's complexity and synchronization between channels can serve as potential indicators of driver's sleepiness. However, we would like to emphasize that the most important finding of the present study is the sensitivity of the peripheral physiological measurements, such as the eye blink statistics, to the driver's

sleepiness. Further research is anticipated for developing and testing the applicability of a neurophysiological sleepiness countermeasure device in real field driving situations, which should be based on peripheral physiological measurements. It is noteworthy that we have conducted several multiple tests (each with omnibus hypothesis) on the level of a single ANOVA and made appropriate corrections of significance level, a potential remaining pitfall of this procedure is the existence of falsely claimed significance; in the literature, it is known the level of false discoveries can be controlled by false discovery rate (Benjamini and Hochberg, 1995).

5. Conclusion

The quantitative EEG and EOG statistics are both promising neurophysiological indicators of sleepiness and have the potential for monitoring sleepiness in an occupational setting as well as being used in a sleepiness countermeasure device. In the present study, we describe in detail for the first time, the occurrence of brief 1–2 s paroxysmal bursts of alpha activity (with a frequency concept 1–2 Hz slower than the conventional alpha rhythm) in the central and parietal brain regions and an increased synchrony among the EEG channels before severe driving errors. We also interpret our findings based on some early published neurophysiological studies regarding the sleepiness onset. The occurrence of these alpha wave bursts indicates a high level of sleepiness and a high possibility of an upcoming severe driving error. Finally, we present clear evidence that eye blink statistics are sensitive to the driver's sleepiness and should be considered in the design of a future sleepiness detection countermeasure device, considering the fact that advanced technological systems are now available that can reliably measure eye-blinking activity. The EOG-based sleepiness detection approach seems to be more driver-friendly and efficient than an EEG-based system, and we expect it will attract more attention from the researchers in the near future.

Acknowledgements

The research was supported by the SENSATION Project of the Information Society Technologies (IST) Program (507231) of European Union (EU). We would like to acknowledge Dr. G. Strikis (IASI Medical Centre, Thessaloniki, Greece) for his work on the visual interpretation of the EEG data. Dr. C. Papadelis would like to thank his students from the Technological Institute of Thessaloniki, Department of Automation, who participated as subjects in the present study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.clinph.2007.04.031](https://doi.org/10.1016/j.clinph.2007.04.031).

References

- Acharya UR, Faust O, Kannathal N, Chua T, Laxminarayan S. Non-linear analysis of EEG signals at various sleep stages. *Comput Methods Programs Biomed* 2005;80(1):37–45.
- Åkerstedt T, Torsvall L, Gillberg M. Sleepiness and shiftwork: field studies. *Sleep* 1982;5(Suppl. 2):95–106.
- Arfken GB, Weber HJ. *Mathematical methods for physicists*. Harcourt: San Diego; 2001.
- Artaud P, Planque S, Lavergne C, Cara H, de Lepine P, Tarriere C, et al. An on-board system for detecting lapses of alertness in car driving. In: 14th ESV conference, session 2, intelligent vehicle highway system and human factors, Munich, Germany; 1973.
- Aserinsky E, Kleitman N. Two types of ocular motility occurring in sleep. *J Appl Physiol* 1955;8:1–10.
- Benjamini Y, Hochberg Y. controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc* 1995;57(1):289–300.
- Bocca ML, Denise P. Total sleep deprivation effect on disengagement of spatial attention as assessed by saccadic eye movements. *Clin Neurophysiol* 2006;117:894–9.
- Broughton R, Hasan J. Quantitative topographic electroencephalographic mapping during drowsiness and sleep onset. *J Clin Neurophysiol* 1995;12(4):372–86.
- Broukhuis KA, de Waard D. The use of psychophysiology to assess driver status. *Ergonomics* 1993;36:1099–110.
- Burioka N, Miyata M, Cornelissen G, Halberg F, Takeshima T, Kaplan DT, et al. Approximate entropy in the electroencephalogram during wake and sleep. *Clin EEG Neurosci* 2005;36(1):21–4.
- Campagne A, Pebayle T, Muzet A. Correlation between driving errors and vigilance level: influence of the driver's age. *Physiol Behav* 2004;80:515–24.
- Connor J, Whitlock G, Norton R, Jackson R. The role of driver sleepiness in car crashes: a systematic review of epidemiological studies. *Accid Anal Prev* 2001;33:31–41.
- Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods* 2004;134:9–21. (EEGLAB software available from: <http://scn.ucsd.edu/eeGLAB>).
- Dinges DF, Kribbs NB. Performing while sleepy: effects of experimentally induced sleepiness. In: Monk TH, editor. *Sleep, sleepiness and performance*. Chichester: Wiley; 1991. p. 97–128.
- Doghramji K, Mitler MM, Sangal RB, et al. A normative study of the maintenance of wakefulness test (MWT). *Electroencephalogr Clin Neurophysiol* 1997;103(5):554–62.
- Fell J, Roschke J, Mann K, Schaffner C. Discrimination of sleep stages: a comparison between spectral and nonlinear EEG measures. *Electroencephalogr Clin Neurophysiol* 1996;98(5):401–10.
- Fogarty C, Stern JA. Eye movement and blinks: their relationship to higher cognitive processes. *Int J Psychophysiol* 1989;8:35–42.
- Fusheng Y, Bo H, Qingyu T. Approximate entropy and its application in biosignal analysis. In: Akay M, editor. *Nonlinear biomedical signal processing. Dynamic analysis and modeling* 2001;vol. II. New Jersey, USA: IEEE Press Series on Biomedical Engineering; 2001.
- Gentili R, Papaxanthis C, Pozzo T. Improvement and generalization of arm motor performance through motor imagery practice. *Neuroscience* 2006;137:761–72.
- Gevens A, Leong H, Du R, Smith ME, Le J, DuRousseau D, et al. Toward measurement of brain function in operational environments. *Biol Psychiatry* 1995;43:145–52.
- Gillberg M, Kecklund G, Åkerstedt T. Sleepiness and performance of professional drivers in a truck simulator – comparisons between day and night driving. *J Sleep Res* 1996;5:12–5.
- Gray R. *Entropy and information theory*. New York: Springer; 1990.
- Hakkanen H, Summala H. Sleepiness at work among commercial truck drivers. *Sleep* 2000;23:49–57.
- Harrison Y, Horne JA. The impact of sleep deprivation on decision making: a review. *J Exp Psychol Appl* 2000;6(3):236–49.
- Hori T. Electrodermal and electro-oculographic activity in a hypnagogic state. *Psychophysiology* 1982;19:668–72.
- Horne JA, Baulk SD. Awareness of sleepiness when driving. *Psychophysiology* 2004;4:97–110.
- Horváth M, Frantik E, Kopriva K, Meissner J. EEG theta activity increase coinciding with performance decrement in a monotonous task. *Activitas Nervosa Superior (Prague)* 1976;18:207–10.
- Hyoki K, Shigeta M, Nishikawa Y, Kawamuro Y, Soda K. The correlation between changes of EEG and eye movements (EOG) accompanied by lowered arousal level. *Jpn J Clin Pathol* 1993;41:813–8.
- Hyoki K, Shigeta M, Tsuno N, Kawamuro Y, Kinoshita T. Quantitative electro-oculography and electroencephalography as indices of alertness. *Electroencephalogr Clin Neurophysiol* 1998;106:213–9.
- Isse K, Kojima T, Ando H, Shimazono Y, Ando K. A study of the relationship between eye movements (EOG) and arousal levels (EEG). *Seishin Igaku* 1978;20:537–44.
- Jung TP, Makeig S, Humphries C, Lee TW, Mckeown MJ, Iraqui V, et al. Removing electroencephalographic artifacts by blind source separation. *Psychophysiology* 2000;37:163–78.
- Kecklund G, Åkerstedt T. Sleepiness in long distance truck driving: an ambulatory EEG study of night driving. *Ergonomics* 1993;36:1007–17.
- Khaldi S, Vallet M. Drivers vigilance. Analysis of differences in vigilance states assessments by physiological and mechanical indicators. In: *Proceedings of the 1st World Congress on applications of transport telematics and intelligent vehicle-highway systems*. 30 November–3 December, Paris, France; 1994.
- Killgore WD, Balkin TJ, Wesensten NJ. Impaired decision making following 49 h of sleep deprivation. *J Sleep Res* 2006;15(1):7–13.
- Lachaux J-P, Rodriguez E, Martinerie J, Varela FJ. Measuring phase synchrony in brain signals. *Human Brain Mapp* 1999;8:194–208.
- Lal SKL, Craig A. Psychophysiological effects associated with drowsiness: driver fatigue and electroencephalography. *Int J Psychophys* 2000;35:39.
- Lal SKL, Craig A. Electroencephalography activity associated with driver fatigue: implications for a fatigue countermeasure device. *J Psychophysiol* 2001a;15:183–9.
- Lal SKL, Craig A. A critical review of the psychophysiology of driver fatigue. *Biol Psychol* 2001b;55:173–94.
- Lal SKL, Craig A. Driver fatigue: electrophysiology and psychological assessment. *Psychophysiology* 2002;39:1–9.
- Lal S, Craig A. Reproducibility of the spectral components of the electroencephalogram during driver fatigue. *Int J Psychophysiol* 2005;55:137–43.
- Lecret F, Pottier M. La vigilance, facteur de securite dans la conduite automobile. *Le Travail Humain* 1971;34:51–68.
- Le Van Quyen M et al.. Comparison of Hilbert transform and wavelet methods for the analysis of neuronal synchrony. *J Neurosci Methods* 2001;111:83–98.
- Lin C-T, Wu R-C, Jung T-P, Liang S-F, Huang T-Y. Estimating driving performance based on EEG spectrum analysis. *EURASIP J Appl Signal Process* 2005;19:3165–74.
- Mano T, Shiozawa Z, Amino A, Nagasaka T, Shindo K, Nagasaki H, Kobayashi T, Mihara K. EEG findings for drivers during driving in a highway. *Electroencephalogr Clin Neurophysiol* 1995;97(4):149 (1).
- Mascond DJ, Heath RA. Behavioral and physiological indices of fatigue in a visual tracking task. *J Safety Res* 1992;23:19–25.
- O'Hanlon SF, Kelley GR. Comparison of performance and physiological changes between drivers who perform well and poorly during prolonged vehicular operation. In: Mackie RR, editor. *Vigilance*. New York: Plenum; 1977. p. 189–202.
- Ota T, Ohshima H, Toyoshima R, Yamauchi T. Arousal level measurements by biphasic changes of the mean alpha amplitude. *Jpn J EEG EMG* 1990;18:258–67.
- Otmani S, Pebayle T, Roge J, Muzet A. Effect of driving duration and partial sleep deprivation on subsequent alertness and performance of car drivers. *Physiol Behav* 2005;84:715–24.
- Papadelis C, Kourtidou-Papadeli C, Bamidis P, Albani M. Effects of imagery training on cognitive performance and use of physiological measures as an assessment tool of mental effort. *Brain Cogn* 2007;64(1):74–85.

- Philip P. Sleepiness of occupational drivers. *Ind Health* 2005;43:30–3.
- Philip P, Sagaspe P, Taillard J, Valtat C, Moore N, Åkerstedt T, et al. Fatigue, sleepiness, and performance in simulated versus real driving conditions. *Sleep* 2005;28(12):1511–6.
- Pincus SM. Approximate entropy (ApEn) as a complexity measure. *Proc Natl Acad Sci USA* 1991;88:110–7.
- Ponder E, Kennedy WP. On the act of blinking. *Q J Physiol* 1928;18:89–110.
- Raidy DJ, Scharff LF. Effects of sleep deprivation on auditory and visual memory tasks. *Percept Mot Skills* 2005;101(1):451–67.
- Santamaria J, Chiappa KH. The EEG of drowsiness in normal subjects. *J Clin Neurophysiol* 1987;4:327–82.
- Shannon CE. A mathematical theory of communication. *Bell Syst Tech J* 1948;27:379–423.
- Shigeta M, Nishikawa Y, Shimuzu M, Usui M, Hyoki K, Kawamuro Y. Horizontal component of electro-oculogram as a parameter of arousal in dementia: relationship between intellectual improvement and increasing arousal under pharmacotherapy. *J Clin Pharmacol* 1993;33:741–6.
- Stam CJ. Nonlinear dynamical analysis of EEG and MEG: review of an emerging field. *Clin Neurophysiol* 2005;116(10):2266–301.
- Takens F. Detecting strange attractors in turbulence. In: Rand DA, Young LS, editors. *Dynamical systems and turbulence. Lecture notes in mathematics* 1981;vol. 898. Berlin: Springer; 1981. p. 366–81.
- The Parliament of the Commonwealth of Australia. Beyond the midnight oil. Managing fatigue in transport. House of Representatives Standing Committee on Communications, Transport and the Arts, Australia; 2000.
- Torsvall L, Åkerstedt T. Sleepiness and irregular work hours. *Sleep Res* 1983;12:376.
- Torsvall L, Åkerstedt T. Sleepiness on the job: continuously measured EEG changes in train drivers. *Electroencephalogr Clin Neurophysiol* 1987;66:502–11.
- Toyoshima R. Arousal level in schizophrenia: measurements by biphasic changes of the mean alpha amplitude and frequencies of eye movements. *Jpn J EEG EMG* 1991;19:364–73.
- Williamson AM, Feyer AM. Moderate sleep deprivation produces impairments in cognitive and motor performance equivalent to legally prescribed levels of alcohol intoxication. *Occup Environ Med* 2000;57:649–55.
- Wilson GF. Applied use of cardiac and respiratory measures: practical considerations and precautions. *Biological Psychol* 1992;34:163–78.
- Wilson GF, Purvis B, Skelly J, Fullenkamp P, Davis I. Physiological data used to measure pilot workload in actual flight and simulator conditions. In: *Proceedings of the human factors society, 31st annual meeting*; 1987, p. 779–83.
- Volow MR, Erwin CW. The heart rate variability correlates of spontaneous drowsiness onset. *International Automotive Engineering Congress*; Detroit MI, USA, 1973.