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Improving the saccade peak velocity measurement for detecting fatigue

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ABSTRACT

The aim of the study was to compare saccadic peak velocity (SPV) values measured with video based Fitness Impairment Tester (FIT) and electro-oculography (EOG) during prolonged wakefulness. We tested different numbers of saccades and two saccade paradigms to improve the EOG measurements for detecting fatigue. The SPVs were measured from 11 fast patrol boat navigators with FIT and EOG every sixth hour until 54 h. Subjective sleepiness was assessed with the Karolinska Sleepiness Scale.

EOG was measured using an overlap and a gap paradigm and the data was divided into sequential five 20-saccade blocks and cumulative blocks of 20, 40, 60, 80, and 100 saccades. Compared to the gap paradigm, the overlap paradigm produced a higher number of analyzable saccades for a given measurement time. The shorter measurements (20–40 saccades) appeared to be more sensitive for fatigue, whereas the longer measurements (60–100 saccades) were more sensitive to time spent on the task. Thus, the optimal number of saccades varies also depending on the research question. The EOG method was more sensitive to fatigue than FIT. The FIT values measured after 30 and 36 h of wakefulness did not differ significantly from the baseline values, while subjective sleepiness and the EOG values showed that the participants were significantly less alert at these time points.

The EOG measurements can be improved for detecting fatigue by using the overlap saccade paradigm. The SPV values measured with the EOG method appear to be somewhat more sensitive in detecting fatigue than the FIT method.

1. Introduction

Fatigue caused by sleep deprivation has a negative impact on human performance (Harrison and Horne, 2000; Dorrian et al., 2008), thus increasing the possibility of accidents and human errors (Horne and Reyner, 1995; Russo et al., 1999; Dorrian et al., 2008). A monitor of fatigue, applicable also to field studies, would be highly welcome e.g. in safety critical occupations (Gevins et al., 1995; Hancock and Szalma, 2007).

Fatigue affects eye movements, especially the saccadic peak velocity (SPV) (De Gennaro et al., 2000, 2001; Ferrara et al., 2000; Russo et al., 2003; Thomas et al., 2003; Caldwell et al., 2004; Rowland et al., 2005; Zils et al., 2005). SPV values have also been reported to decrease as a function of time-on-task, which has been proposed to be caused by motivational factors (App and Debus, 1998). The decrease of SPV has been suggested to be caused by a possible dysfunction at the level of reticular formation of the brain stem (Zils et al., 2005).

Electro-oculography (EOG) (Porcu et al., 1998; De Gennaro et al., 2000, 2001; Ferrara et al., 2000; Zils et al., 2005; Bocca and Denise, 2006; Schleicher et al., 2008) and video based Fitness Impairment Tester (FIT 2000-3, Pulse Medical Instruments Inc., Rockville, MD) (Russo et al., 1999, 2003; Thomas et al., 2003; Caldwell et al., 2004; Rowland et al., 2005) have shown to be reliable methods for measuring saccadic eye velocity in sleep deprivation studies. The methods vary considerably in set-up time and measurement time requirements. However, to our knowledge, these two methods have not been compared in a single study.

The video-oculography based FIT measurement lasts from 30 to 90 s and needs no preparation before the measurement. The EOG signal is measured with Ag/AgCl electrodes attached around the subject's eyes. In addition, the number of saccades varies in EOG based measurements from 20 up to 100, and may result in measurement times lasting up to several minutes (Ferrara et al., 2000; Zils et al., 2005). In sleep deprivation studies where electroencephalography (EEG) is used as an objective measure of sleepiness, the EOG electrodes are always attached (Åkerstedt and Gillberg, 1990; Caldwell et al., 2004; Sallinen et al., 2004). Thus additional preparation time for the saccade task is not needed. One of the advantages of the EOG method is that it can also be measured with a lightweight ambulatory device, allowing measurements to be

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done during normal work (Gevins et al., 1995). In addition, the EOG measurement alone has been used in recent studies for automatic detection of slow wave sleep (Virkkala et al., 2007b), unintentional sleep (Virkkala et al., 2007a), and sleepiness detection during a multiple sleep latency test (MSLT) (Fabbri et al., 2009). These findings suggest that the EOG method could be a promising online monitor for detecting increased fatigue during a work task in real life situations and field studies.

The aim of this study was to compare the EOG and FIT methods in a study where subjects had to stay awake for 60 h. Our goal was to improve the EOG measurement in such a way that it can be used as a handy and low cost oculomotor test in prolonged wakefulness studies. In order to improve the EOG measurements, we focused on three main points; (1) measurement method (saccade paradigm), (2) measurement time (number of saccades), and (3) the comparison between the EOG method and the FIT device.

(1) The saccade task paradigm affects the saccadic latencies (Fischer and Weber, 1997). Bocca and Denise (2006) found that the effect of sleep deprivation on saccadic latencies was greater in the overlap than in the gap paradigm (Bocca and Denise, 2006). However, Bocca and colleagues had two measurement points, before and after 24 h of time-awake. In our study, the saccade paradigms are studied in greater detail, since the measurements are done every sixth hour. Our hypothesis is that the overlap paradigm is more appropriate to use in fatigue studies than the gap paradigm.
(2) The number of saccades should be optimized so that a reliable SPV value is achieved in a reasonable measurement time. The FIT measurement SPV value is averaged from four saccades. However, in sleep deprivation studies where EOG has been used to measure saccade variables, the number of saccades has varied from 20 (Zils et al., 2005) to 100 (Ferrara et al., 2000).
(3) The method should be sensitive to the measured phenomenon. The previous findings suggest that EOG might be more sensitive than FIT to the decrease of SPV values under fatigue. For example, Caldwell et al. (2004) found that the SPV values measured with FIT first differed from the baseline after 21 h of time-awake (Caldwell et al., 2004). In the De Gennaro et al. (2000, 2001) studies, EOG was used and the SPV values seemed to decrease after 16 h of time-awake (De Gennaro et al., 2000, 2001). In our study, we compare FIT and EOG, in order to evaluate which of the methods is more sensitive in detecting fatigue. In addition, the SPV results are compared with subjective sleepiness evaluations obtained with the Karolinska Sleepiness Scale (KSS) (Åkerstedt and Gillberg, 1990).

2. Materials and methods

2.1. Participants and research ethics

Eleven male navigators from the Royal Norwegian Navy volunteered for this study. The age of the participants was 23–30 years (mean = 26.6 years, SD 2.2). The measurements were made on two occasions, separated by three months. Five of the subjects participated in both measurement weeks. In the eye movement analysis we treated measurement occasions as separate measurements, and therefore we had altogether 16 observations in the statistical analysis. We chose to use the maximum amount of SPV data because the nature of the saccade task is involuntary and confounding due to learning effects is likely to be small. In addition there was a three-month washing period between the measurement occasions.

The participants were screened for somatic and psychiatric health problems (including sleep disorders or abnormal sleep habits), and they did not report any current use of medication. Two of the participants used correction lenses for visual myopia. The participants reported normal sleep length (before working days: mean 6.9 h, range 6–8, SD 0.7), and were all classified as "intermediate" types using the Composite Morningness Questionnaire (Smith et al., 1989). One participant had an Epworth Sleepiness Scale (Johns, 1991) score of 11, indicating slightly excessive daytime sleepiness, while the rest of the participants had normal scores between 4 and 9.

This study adhered to the Declaration of Helsinki and all participants gave written informed consent. A physician was on call at all times throughout the sleep deprivation periods. The study protocol was approved by the Regional Committee for Medical Research Ethics, Western Norway, and the Norwegian Social Science Data Services. The participants were paid for their participation.

2.2. Study design

Eye movement measures were conducted as part of a larger research project in which the effect of sleep deprivation on performance in two high-speed navigation systems was studied (Gould et al., 2009). The study was carried out in ship simulators at the Royal Norwegian Navy (RNoN) Naval Academy, Bergen.

Two weeks before the measurements the participants received a letter with detailed information about the study together with an Actigraph (ActiwatchTM, Cambridge Neurotechnology Inc., Cambridge, UK) and a sleep diary. They were instructed to go to bed between 23:00 and 24:00, and to awake between 7:00 and 8:00 on the last seven days before the study. They were also requested not to consume any alcoholic beverages 48 h prior to the study start, as well as not to drink any caffeinated beverages on the morning of the first day of the study.

On the first study day, the participants arrived at 8:00 a.m. and the first navigation session started at 10:00 a.m. (see Fig. 1). A single navigation session lasted 2.5 h in total, including preparation and rest breaks. After navigation the participants were brought into a separate (illuminated) room for 25 min where they filled out the questionnaires on PDAs (Portable Digital Assistant) (e.g. KSS). After this, an 80-min period followed where the participants underwent eight vision tests in a darkened test laboratory, including the saccade tasks measured with FIT and EOG, and e.g. contrast vision. (The data from the other vision tests will be published in the forthcoming articles.) The test cycle (preparation–simulator navigation session–questionnaires–vision tests) was repeated 10 times. Each test cycle, including breaks, took six hours. At the completion of each test cycle, the participants were allowed 90 min to eat and rest, but not to sleep, before the next test cycle started. The same test cycle was followed throughout the study. The eye movement data from the first nine test cycles is presented in this article, since the saccade task measured with EOG was not measured during the 10th test cycle due to the practical reasons. The subjects were really tired and the saccade task was practically impossible to carry out.

During their rest breaks, the participants were allowed to read, watch films, use the Internet, and walk (but not run). Participants showing signs of falling asleep were prompted to stay awake by a research assistant. In order to recreate realistic operation conditions, the participants were allowed to use caffeine and tobacco; this was limited to the number of units consumed on an ordinary workday (this information was obtained at the time of recruitment). Caffeine units were administered in the form of 4 g instant coffee sachets. None of the subjects smoked, but three used snuff during the measurements.

2.3. Measures

2.3.1. Karolinska Sleepiness Scale (KSS)

Subjective sleepiness was measured using a PDA-based version of the KSS (Åkerstedt and Gillberg, 1990). The KSS data was col-

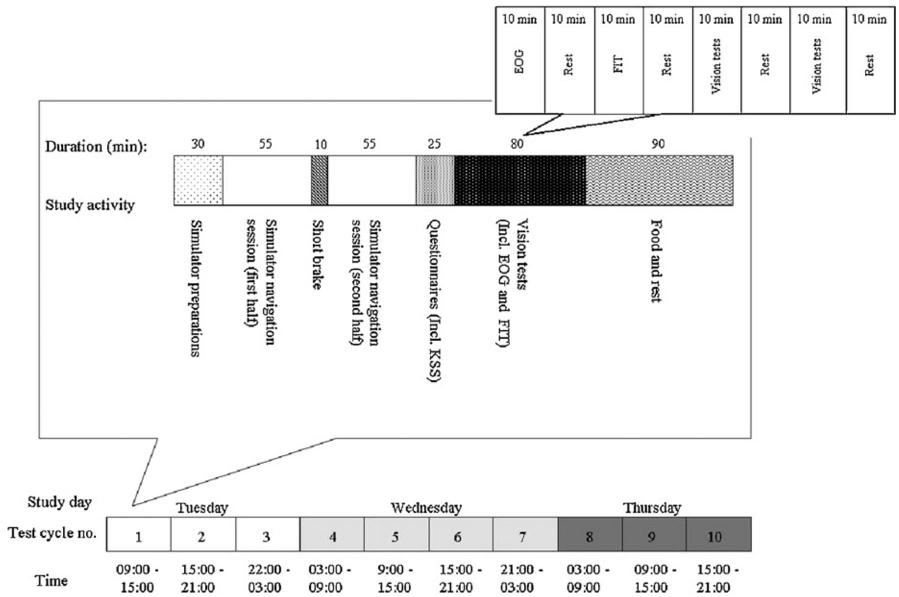

Fig. 1. The test cycle. During the 80 min vision test-set eight different vision tests was performed e.g. saccade task measured with EOG, FIT measurements, and contrast vision measurement.

lected during every measurement cycle, just before the vision tests (Fig. 1).

2.3.2. Fitness impairment test

The mobile FIT machine is a commercially available, computer based eye-tracker. The FIT measurement lasts from 30 to 90 s depending on how quickly the FIT recognizes the eye. During a single measurement the FIT measures SPV, initial pupil diameter, pupil-constriction latency, and pupil-constriction amplitude. Before the FIT test was begun, the subjects were instructed to avoid head movements and blinking during the test. The test was performed with the dominant eye and the head was supported with a forehead rest.

The FIT defines the SPV value by tracking the eye with a 600 Hz sampling rate and a 0.1 mm resolution. The subject is instructed to follow a green light, which moved on the horizontal axis from left to right. The SPV value (mm/s) is the mean value of four 20° (degrees of visual angle) saccades that are performed during a test.

2.3.3. FIT data

In the 80-min vision test-set (Fig. 1) 10 min was reserved for the FIT measurement. During that time the FIT measurement was intended to be measured three times. If the measurement time ended before three measurements were obtained, the recording was aborted and the subject moved to the next vision test. The numbers of needed FIT measurements before the three measurements were carried out and the percentages of missing data are presented in Table 1. The missing data points increased as a function of measurement repetitions. This could be due to eye strain and eye drying since the subject has to avoid blinks during the measurement. The first measurement block (FIT1) includes the mean peak velocity value from four saccades, which were obtained during a single FIT measurement. The FIT2 is the averaged peak velocity value of the two sequential FIT measurements (first and second). Whereas the FIT3 is averaged peak velocity value of three sequential FIT measurements (first, second and third).

Table 1
Repetition times and percentages of missing data in FIT measurements.

Measurement block	Repetition times (SE)	Missing data (%)
FIT1	1.27 (0.06)	1.39
FIT2	2.29 (0.11)	2.08
FIT3	3.55 (0.11)	7.64

2.3.4. Saccade task measured with electro-oculography (EOG)

The saccade task was implemented using Presentation software (Neurobehavioural systems, Albany, CA, version 9.70). The EOG signal was measured with Embla A10 (Medcare, Reykjavik, Iceland) with a sampling rate of 200 Hz and a bandwidth 0.5–90 Hz. The saccade task sent online triggers to the Embla's trigger channel on the central fixation point and the target stimuli. Horizontal and vertical electro-oculography (EOG) was measured with four electrodes from the outer canthi of both eyes, and from above and below of the right eye. The measurements were performed using bipolar coupling and the electrodes were grounded to the left mastoid (A2).

The subjects were placed in a chair at a 70 cm distance from the computer screen. The distance was confirmed before every measurement. Participants were instructed to stay still, avoid blinks, and look at the location of the central fixation point until the target stimulus appeared, after which they should move their gaze as quickly as possible to the target stimulus. When the stimulus disappeared, they were instructed to move their gaze back to the central fixation point. The size of the saccade was 10° (degrees of visual angle) and the sizes of the fixation point and the target stimulus were one degree of visual angle.

The saccade task consisted of alternating overlap and gap blocks (Fischer et al., 1997). Both paradigms are depicted in Fig. 2. In the

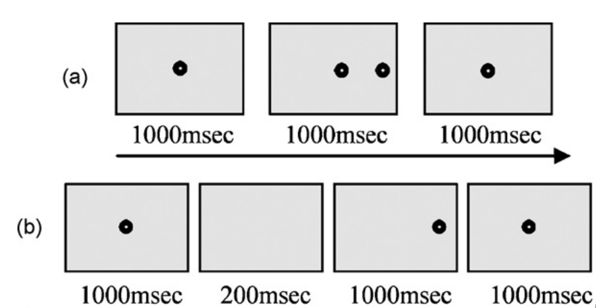

Fig. 2. Saccade paradigms: (a) the overlap sequence and (b) the gap sequence.

overlap condition the central fixation point was visible all the time. The task sequence started with the central fixation point. After 1000 ms the target stimulus appeared on either the left or the right side of the screen. The target stimulus disappeared after 1000 ms and the next trial started with a central fixation point. In the gap condition the fixation point disappeared 200 ms before the target stimulus appeared.

The saccades were presented in 20-saccade overlap or gap condition blocks and there were 5-s rest pauses between the blocks, during which the subjects were instructed to blink repeatedly to lessen the need to blink during the stimulus blocks, and thus reducing blinking artefacts in eye movement recordings. One 20-saccade block lasted 45 s, which included the 5-s rest pause. In each 8-min measurement session 200-saccade stimuli, 100 per condition were presented.

2.3.5. EOG data

The EOG data was analyzed with custom made Matlab-software (Matlab R2007a, The MathWorks Inc., Natick, Massachusetts). The saccades made towards the stimulus were detected offline from the horizontal EOG signal. The saccades were identified from the differentiated eye movement signal. If the eye velocity was greater than 20°/s, the movement was identified as a saccade. The highest velocity of each saccade was registered as the peak velocity (°/s) of the saccade.

If a blink was detected or the amplitude of the vertical EOG signal was higher than 100 μV in a 250 ms window around the saccade (corresponding to an oblique saccade), the saccade was rejected from the analysis. Otherwise correctly performed saccades were rejected from the analysis if they were detected outside of the window between 100 and 700 ms after the target stimulus appearance. The earlier literature suggests that the minimum reaction time for the visually guided saccade is 100 ms (Kalesnykas and Hallett, 1987; Wenban-Smith and Findlay, 1991; Fischer and Weber, 1993).

Five correctly made saccades per direction (left/right) were chosen from the first test cycle to obtain a calibration constant between saccade amplitude and visual angle. The average amplitude of these five saccades was taken to match 10° of visual angle. This calibration was made separately for each subject in each measurement occasion.

The overlap and gap saccades were separated, and the data was divided into five sequential 20-saccade blocks (first 20 1_20, second 20 saccades: 2_20, third 20 saccades: 3_20, fourth 20 saccades: 4_20, and fifth 20 saccades: 5_20) and cumulative blocks of 20, 40, 60, 80, and 100 saccades (resulting measurement time of 45, 90, 135, 180, and 225 s respectively).

The data was defined as missing if there were less than five correctly performed saccades in the measurement block, or the eye movement signal was not available (e.g. from loose electrodes). The percentages of missing data are presented in Table 2.

Table 2
The percentages of missing data in the gap (GAP) and overlap (OVER) conditions and the specifications for data loss.

Measurement block	Technical problems (%)	No correct saccades (%)	Σ (%)
GAP20	5.65	72.82	78.47
GAP40	5.65	40.18	45.83
GAP60	5.65	22.13	27.78
GAP80	5.65	13.10	18.75
GAP100	5.65	11.02	16.67
OVER20	5.65	27.68	33.33
OVER40	5.65	3.38	9.03
OVER60	5.65	2.68	8.33
OVER80	5.65	2.68	8.33
OVER100	5.65	1.99	7.64

2.3.6. Overlap and gap conditions

The percentages of correctly classified saccades in the five different measurement blocks are presented in Fig. 3. In the gap condition, the percentages of correctly made saccades were lower compared to the overlap condition. In the overlap condition, the percentage of correctly made saccades decreased as a function of time-awake whereas there was no such decrease in the gap condition (Fig. 3). The number of correct saccades in the different blocks was tested with the Kruskal–Wallis test, and the results showed that the overlap and gap condition differed significantly from each other in every measurement block. Since the number of correctly made saccades was significantly lower in the gap condition compared to the overlap condition, and the data was also limited as regard to the number of correct saccades in the gap condition, we decided to use only data from the overlap condition in the statistical analysis.

2.3.7. Statistical analyses

All the statistical analyses were made with SPSS 15. In the saccade task (EOG) the mean SPV was calculated from the correctly performed saccades. If the number of correct saccades in a given session was less than five, the value was omitted, and the missing data point for a subject was replaced with the mean value calculated from all valid values of that time-awake class (12, 18, 24, 30, 36, 42, 48, 54), in all datasets. One subject had suspiciously low values (compared to the other subjects and the subject's other measurement values) in the 6-h measurement. In addition, correctly made saccades were detected only during the first block. This suggests that the measurement has been erroneous, and the odd values were omitted and replaced with the mean value of the time-awake class.

The first measurement after 6 h of time-awake was used as a baseline measurement, and was set to 100%. The velocity values of all time-awake classes were changed to percentage changes from the individual baseline of each subject.

The Mann–Whitney *U* test was used to compare the difference between baseline and each consequential time-awake data point. The comparisons were made for the KSS scores and for all the SPV measurement blocks (FIT1-3, OVER1-5_20, and OVER20-100). The Bonferroni corrections were applied to all baseline vs. time-awake classes, with *p* set 0.006 (0.05/8).

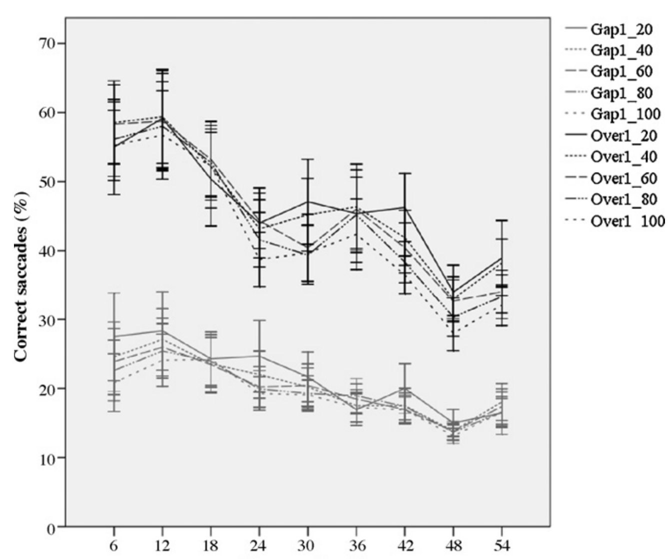

Fig. 3. The mean percentages of correctly made saccades to presented stimuli. In the overlap condition the number of correctly made saccades was significantly higher than in the gap condition. All the measurement blocks are presented and the error bars are standard error of mean.

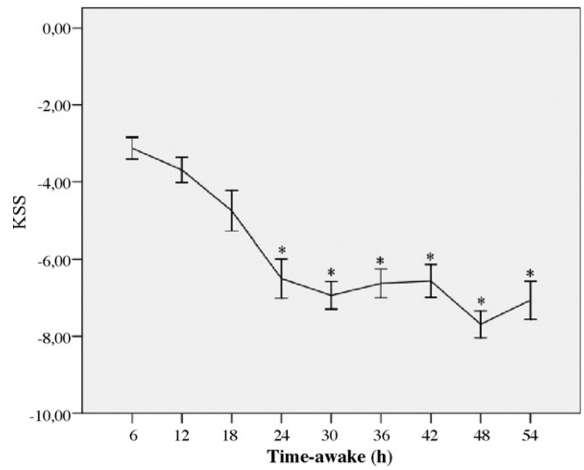

Fig. 4. The KSS results during the study. The values are presented with a negative scale. The error bars are standard error of mean.

3. Results

3.1. Subjective sleepiness

The KSS values differed significantly from baseline after 24 h of time-awake (12 h: $Z = -1.285$, $p = 0.199$, 18 h: $Z = -2.158$, $p = 0.035$, 24–54 h $Z < -3.75$, $p < 0.001$,) indicating that the participants rated themselves as significantly more sleepy from this data point onward (Fig. 4).

3.2. FIT: SPV value's ability to recognize fatigue caused by time-awake

The SPV values in the FIT1 and FIT2 measurements decreased significantly for the first time after 24 h of time-awake (FIT1: $Z = -3.867$, $p < 0.001$, FIT2: $Z = -4.512$, $p < 0.001$) (Fig. 5). However, in the FIT1 measurement the SPV measured after 30 and 36 h of time-awake did not differ from the baseline (30 h: $Z = -2.578$, $p = 0.010$, 36 h: $Z = -2.578$, $p = 0.010$) and in the FIT2 measurement the 36 h measurement did not differ from the baseline ($Z = -2.578$, $p = 0.010$), whereas the rest of the FIT1 and FIT2 measurements did differ significantly from the baseline. The FIT3 measurements showed significant differences from the baseline after 18 h of time-awake (Fig. 5).

3.3. EOG: SPV value's ability to recognize fatigue caused by time-awake

The first and second 20-saccade block differed for the first time from the baseline after 12 h of time-awake (OVER1_20: $Z = -4.512$, $p < 0.001$, OVER2_20: $Z = -4.512$, $p < 0.001$) (Fig. 6). After that, the SPV value in these blocks stayed lower than the baseline value. In the third and fourth 20-saccade blocks the SPV differed for the first time from the baseline after 18 h of time-awake (OVER3_20: $Z = -3.223$, $p = 0.001$, OVER4_20: $Z = -3.867$, $p < 0.001$) and remained below baseline throughout the subsequent measurement points. The fifth 20-saccade block value differed from baseline for the first time at 24 h of time-awake and onward (OVER5_20: $Z = -4.516$, $p < 0.001$).

In the cumulative measurement blocks the results were quite similar to those in sequential 20-saccade blocks (Fig. 7). In the OVER20-60 measurement blocks the SPV value differed for the first time from the baseline after 12 h of time-awake, whereas in the OVER80-100 measurement blocks the first measurement that differed from the baseline was the 18-h measurement.

4. Discussion

The SPV is one of the most sensitive oculomotor parameters for assessing fatigue (De Gennaro et al., 2001; Thomas et al., 2003; Caldwell et al., 2004). In the present study we compared SPV values measured with FIT and EOG methods during prolonged wakefulness. We also attempted to determine the optimal number of saccades, and compared the gap and overlap paradigm in order to improve the EOG measurements.

In the first hypothesis we argued that the overlap paradigm would be more appropriate for detecting fatigue than the gap paradigm. Our results showed that the error rate in the gap paradigm was significantly higher than in the overlap paradigm. In further analysis we found that in the gap paradigm subjects had a statistically higher number of anticipatory responses (saccades latencies with <100 ms), direction errors, and blinks. The number of anticipatory responses decreased slightly as a function of time-awake in the gap paradigm whereas in the overlap paradigm the trend was the opposite. The number of missed targets and blinks increased in both paradigms whereas the number of direction errors stayed at the same level through the measurements. Based on these findings we suggest that in prolonged wakefulness studies, the overlap paradigm yields more data in a shorter measurement time.

Based on previous studies, we hypothesized that the ideal saccade number would be between 20 and 100 (Ferrara et al., 2000; Zils et al., 2005). The saccade measurements were first divided into sequential 20-saccade blocks and then into five cumulative blocks of 20, 40, 60, 80, and 100 saccades. The results of the first two 20-saccade blocks were quite similar and the third and fourth blocks resembled each other quite nicely. The fifth block differed from the third and fourth blocks in the 18 h of time-awake measurement. A similar trend was observed in the cumulative saccade blocks; the

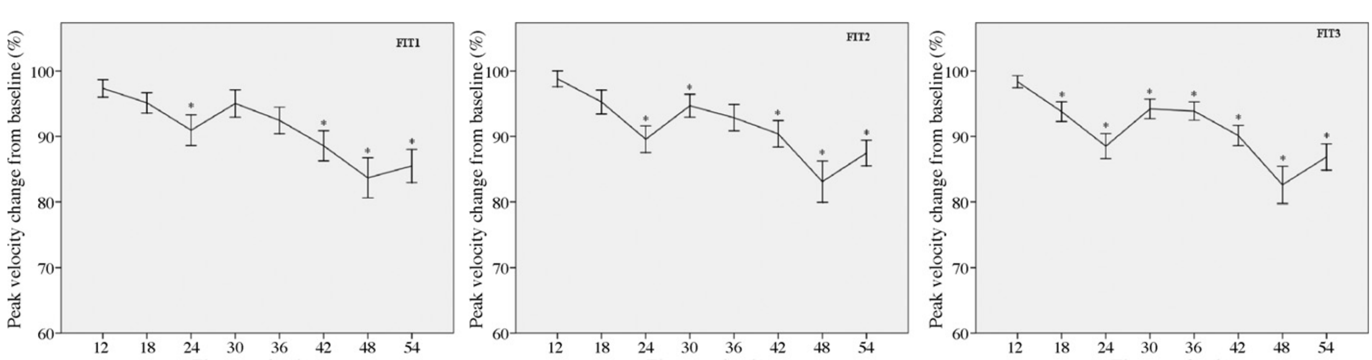

Fig. 5. The peak velocity change percentages from the baseline (set as 100%) as a function of time-awake hours. The peak velocities were measured with FIT (FIT1-3). ($^{*}p < 0.006$).

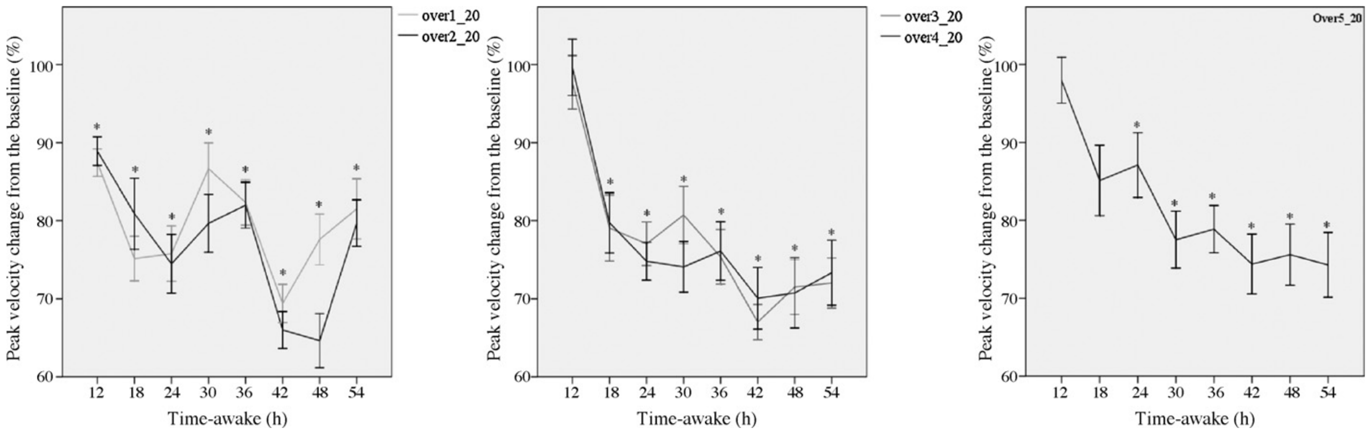

Fig. 6. The peak velocity change percentages from the baseline (set as 100%) as a function of time-awake hours. The SPV values from the sequential 20-saccade blocks are divided into three different figures by the results of statistical analysis to visualize the behaviour of the SPV values as a function of time-awake. ($^* p < 0.006$).

20, 40, and 60 saccade blocks were quite similar whereas 80 and 100 saccade blocks resembled each other. Results suggest that shorter measurement blocks are more sensitive to time-awake, whereas in the longer measurements the time spent on the task has a stronger influence on the SPV values resulting in a lower baseline value. Thus the first measurement which differs from the baseline is at 18 h of time-awake. Our results indicate that no strict threshold value for the number of saccades can be set. However, our results suggest that SPV values can be used to detect both time-awake and time-on-task effects depending on the length of the measurement.

Our third hypothesis was that the EOG method would be more sensitive than FIT to the decrement of the SPV in a prolonged wakefulness situation. This hypothesis was derived from the De Gennaro et al. studies (2000, 2001) and Caldwell et al. (2004) study. In these studies the SPV measured with EOG decreased after 16 h of time-awake (De Gennaro et al., 2000, 2001) and SPVs measured with FIT decreased after 21 h of time-awake (Caldwell et al., 2004). In our study the FIT3 block (average of the three sequential FIT measurements) differed significantly from the baseline after 18 h, whereas FIT1 and FIT2 differed for the first time from the baseline at 24 h of time-awake. In contrast, all the OVER measurement blocks differed from the baseline after 18 h of time-awake, and the shorter measurement blocks even after 12 h of time-awake. Our results suggest that the SPVs measured with EOG are more sensitive to prolonged time-awake than the FIT measurement.

We used the Karolinska Sleepiness Scale (Åkerstedt and Gillberg, 1990) to evaluate subjective sleepiness. The KSS has been validated against EEG and shown to have high validity in measuring sleepiness (Kaida et al., 2006). We compared the KSS results with the SPV values since a good physiological variable should detect the decrease of alertness at the same time, or preferably even earlier than a subjective sleepiness measure. In the Greneche et al. (2008) study, the KSS was measured every hour, and increased from the baseline after 21 h. In our study, the KSS results indicated that the subjects felt significantly less alert after 24 h compared to the baseline. Our participants were a selected sample, which may partially explain this difference. However, previous studies suggest that significant decrements in alertness occur even earlier than after 21 h of awake (Dawson and Reid, 1997). This indicates that KSS may not be sensitive enough to detect early signs of fatigue, and thus cannot be considered as an established reference to which our EOG and FIT results should be compared to. We need additional studies on different sub-populations to be able to give firm answers to the ecological and convergent validity of our findings.

The measurement frequency affects the resolution of the SPV sensitivity for detecting increasing fatigue. This means that the changes in SPV values that take place between the measurement points are not detected. In our study the measurements were carried out every sixth hour. In the studies by De Gennaro et al. (2000, 2001), the measurements were done every other hour and Caldwell et al. (2004) measured oculomotor functions every fifth hour. In

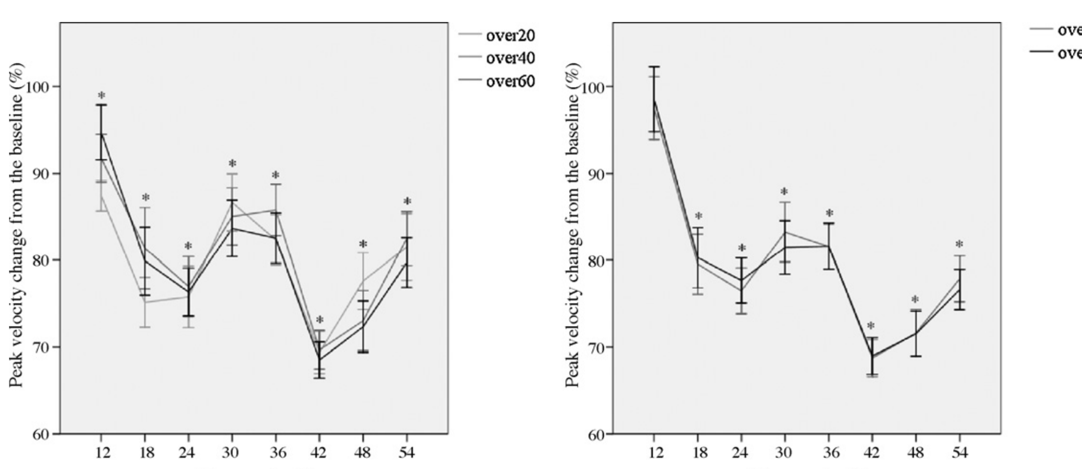

Fig. 7. The peak velocity change percentages from the baseline (set as 100%) in a five cumulative blocks of 20, 40, 60, 80, and 100 saccades are presented as a function of time-awake hours. ($^* p < 0.006$).

addition, the analysis of circadian rhythm is dependent on measurement frequency. The circadian effect is always present in total sleep deprivation studies. De Gennaro et al. (2001) reported that the eye velocity approximated the circadian curve. The circadian curve is also clearly visible in both methods' SPV values (Figs. 5–7). The SPVs measured with EOG stayed below the baseline once the value dropped below it, in every measurement block. This indicates that SPVs measured with the EOG are not as affected by the circadian effect. However, the SPV values measured with FIT increased to the same level with the baseline after 30 (FIT1) and 36 (FIT1-2) h of time-awake. Caldwell et al. (2004) achieved similar results with FIT measurements in a 37-h sleep deprivation study (Caldwell et al., 2004).

The optimization of the number of saccades means balancing between the measurement length and the accuracy of the achieved value. App and Debus (1998) reported that the SPV values decreased as a function of time-on-task. They also suggested that this may be due to motivational factors. In an animal study, the knowledge of a reward has been found to increase the SPVs (Takikawa et al., 2002). In our study the number of saccades in EOG measurements was far higher than in the FIT and the participants had to spent a longer time on the task. We therefore believe that the difference between FIT and EOG findings might be due to the number of saccades performed rather than the intrinsic properties of the measurement methods. The decrease of the SPV value was greater in the EOG method, possibly because of a time-on-task effect and decreased motivation. This was seen in the difference between the sequential 20-saccade blocks of EOG measurements. The changes in the SPV values were smaller in the third, fourth, and fifth 20-saccade blocks compared to the earlier 20-saccade blocks (the first and second). This means that the time spent in the task has an influence on baseline measurement in the last three blocks, which may result in a slower SPV baseline value for these blocks. This could mean that the shorter EOG measurements (20–40 saccades) can detect fatigue due to the time-awake and changes in alertness because of the circadian effect while longer measurements (60–100) could be used to detect overall fatigue caused by e.g. a long working hours and time-awake.

One of the limitations in this study is that we have not been able to address the repeatability of our results; since there to our knowledge no other studies have been published using the same parameters and study design. In order to optimize the minimum number of saccades, the measurements should have been carried out by recording all 100 saccades successively using a single paradigm. An additional limitation of the study is that the measurements were done only every sixth hour. In order to obtain more accurate information about the circadian rhythm influences and the point where the SPV drops significantly below the baseline value for the first time, more frequent measurements are needed (De Gennaro et al., 2000, 2001). Unfortunately, the overall study protocol did not permit this in our study. It would also be desirable to study the relation between the SPV values and navigation performance, to assess the ecological validity of the results.

The strength of this study was the long duration (60 h sleep deprivation) which ensured that all the participants became fatigued. In this study we used a selected population of soldiers, who were accustomed to staying awake for long periods of time. In the future the individual variability in the normal population should be studied, and also the need of a baseline correction, requires further investigation.

Lightweight portable, field and real life study-compatible EEG and EOG devices are currently being developed (Bulling et al., 2009). Recent studies have shown that the EOG method alone can be used in automated detection of slow wave sleep (Virkkala et al., 2007b), unintentional sleep (Virkkala et al., 2007a), and sleepiness detection during a MSLT (Fabbri et al., 2009). These findings together with our results suggest that EOG can be further developed for detecting fatigue in real life situations in the near future.

Conflict of interest

This was not an industry supported study. The authors have indicated no financial conflicts of interest.

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References

App E, Debus G. Saccadic velocity and activation: development of a diagnostic tool for assessing energy regulation. Ergonomics 1998;41:689–97.

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.

Bulling A, Roggen D, Tröster G. Wearable eog goggles: eye-based interaction in everyday environments. In: Conference on Human Factors in Computing Systems (CHI). Boston, MA, USA: ACM; 2009.

Caldwell JA, Caldwell JL, Brown DL, Smith JK. The effects of 37 hours of continuous wakefulness on the physiological arousal, cognitive performance. Self-reported mood, and simulator flight performance of F-117A pilots. Mil Psychol 2004;16:163–81.

Dawson D, Reid K. Fatigue alcohol and performance impairment. Nature 1997;388:235.

De Gennaro L, Ferrara M, Curcio G, Bertini M. Visual search performance across 40 h of continuous wakefulness: measures of speed and accuracy and relation with oculomotor performance. Physiol Behav 2001;74:197–204.

De Gennaro L, Ferrara M, Urbani L, Bertini M. Oculomotor impairment after 1 night of total sleep deprivation: a dissociation between measures of speed and accuracy. Clin Neurophysiol 2000;111:1771–8.

Dorrian J, Tolley C, Lamond N, van den Heuvel C, Pincombe J, Rogers AE, Drew D. Sleep and errors in a group of Australian hospital nurses at work and during the commute. Appl Ergon 2008;39:605–13.

Fabbri M, Provini F, Magosso E, Zaniboni A, Bisulli A, Plazzi G, Ursino M, Montagna P. Detection of sleep onset by analysis of slow eye movements: a preliminary study of MSLT recordings. Sleep Med 2009;10:637–40.

Ferrara M, De Gennaro MFL, Bertini M. Voluntary oculomotor performance upon awakening after total sleep deprivation. Sleep 2000;23:801–11.

Fischer B, Gezeck S, Hartnegg K. The analysis of saccadic eye movements from gap and overlap paradigms. Brain Res Brain Res Protoc 1997;2:47–52.

Fischer B, Weber H. Effects of stimulus conditions on the performance of antisaccades in man. Exp Brain Res 1997;116:191–200.

Fischer B, Weber H. Express saccades and visual attention. Behav Brain Sci 1993;16:553–610.

Gevins A, Leong H, Du R, Smith ME, Le J, DuRousseau D, Zhang J, Libove J. Towards measurement of brain function in operational environments. Biol Psychol 1995;40:169–86.

Gould KS, Hirvonen K, Koefoed VF, Roed BK, Sallinen M, Holm A, Bridger RS, Moen BE. Effects of 60 hours of total sleep deprivation on two methods of high-speed ship navigation. Ergonomics 2009;52:1469–86.

Greneche J, Krieger J, Erhardt C, Bonnefond A, Eschenlauer A, Muzet A, Tassi P. EEG spectral power and sleepiness during 24 h of sustained wakefulness in patients with obstructive sleep apnea syndrome. Clin Neurophysiol 2008;119:418–28.

Hancock PA, Szalma JL. Stress and neuroergonomics. In: Parasuraman R, Rizzo M, editors. Neuroergonomics: The Brain at Work. New York: Oxford University Press; 2007. p. 430.

Harrison Y, Horne JA. Sleep loss and temporal memory. Q J Exp Psychol A 2000;53:271–9.

Horne JA, Reyner LA. Sleep related vehicle accidents. BMJ 1995;310:565–7.

Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540–5.

Kaida K, Takahashi M, Akerstedt T, Nakata A, Otsuka Y, Haratani T, Fukasawa K. Validation of the Karolinska sleepiness scale against performance and EEG variables. Clin Neurophysiol 2006;117:1574–81.

Kalesnykas RP, Hallett PE. The differentiation of visually guided and anticipatory saccades in gap and overlap paradigms. Exp Brain Res 1987;68:115–21.

Porcu S, Ferrara M, Urbani L, Bellatreccia A, Casagrande M. Smooth pursuit and saccadic eye movements as possible indicators of nighttime sleepiness. Physiol Behav 1998;65:437–43.

Rowland LM, Thomas ML, Thorne DR, Sing HC, Krichmar JL, Davis HQ, Balwinski SM, Peters RD, Kloeppel-Wagner E, Redmond DP, Alicandri E, Belenky G. Oculomotor responses during partial and total sleep deprivation. Aviat Space Environ Med 2005;76:C104–13.

Russo M, Thomas M, Sing H, Thorne D, Balkin T, Wesensten N, Redmond D, Welsh A, Rowland L, Johnson D, Cephus R, Hall S, Krichmar J, Belenky G. Saccadic velocity and pupil constriction latency changes in partial sleep deprivation, and correlations with simulated motor vehicle crashes. Sleep 1999; 22:297.

Russo M, Thomas M, Thorne D, Sing H, Redmond D, Rowland L, Johnson D, Hall S, Krichmar J, Balkin T. Oculomotor impairment during chronic partial sleep deprivation. Clin Neurophysiol 2003;114:723–36.

Sallinen M, Harma M, Akila R, Holm A, Luukkonen R, Mikola H, Muller K, Virkkala J. The effects of sleep debt and monotonous work on sleepiness and performance during a 12-h dayshift. J Sleep Res 2004;13:285–94.

Schleicher R, Galley N, Briest S, Galley L. Blinks and saccades as indicators of fatigue in sleepiness warnings: looking tired? Ergonomics 2008;51:982–1010.

Smith CS, Reilly C, Midkiff K. Evaluation of three circadian rhythm questionnaires with suggestions for an improved measure of morningness. J Appl Psychol 1989;74:728–38.

Takikawa Y, Kawagoe R, Itoh H, Nakahara H, Hikosaka O. Modulation of saccadic eye movements by predicted reward outcome. Exp Brain Res 2002;142: 284–91.

Thomas ML, Sing HC, Belenky G, Holcomb HH, Mayberg HS, Dannals RF, Wagner HN, Thorne DR, Popp KA, Rowland LM, Welsh AB, Balwinski SM, Redmond DP. Neural basis of alertness and cognitive performance impairments during sleepiness: II effects of 48 and 72 h of sleep deprivation on waking human regional brain activity. Thalamus Relat Syst 2003;2:199–229.

Wenban-Smith MG, Findlay JM. Express saccades: is there a separate population in humans? Exp Brain Res 1991;87:218–22.

Virkkala J, Hasan J, Varri A, Himanen SL, Harma M. The use of two-channel electro-oculography in automatic detection of unintentional sleep onset. J Neurosci Methods 2007a;163:137–44.

Virkkala J, Hasan J, Varri A, Himanen SL, Muller K. Automatic detection of slow wave sleep using two channel electro-oculography. J Neurosci Methods 2007b;160:171–7.

Zils E, Sprenger A, Heide W, Born J, Gais S. Differential effects of sleep deprivation on saccadic eye movements. Sleep 2005;28:1109–15.

Åkerstedt T, Gillberg M. Subjective and objective sleepiness in the active individual. Int J Neurosci 1990;52:29–37.