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THE INFLUENCE OF SLEEP DEPRIVATION ON THE CONTINGENT NEGATIVE VARIATION

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ABSTRACT

The physiological functions (contingent negative variation (CNV), critical flicker fusion frequency (CFF), oral temperature, blood pressure and heart rate) of five subjects were measured every three hours in 36-hour sleep deprivation and twice after the recovery night. The subjects were given tasks (Uchida-Kraepelin test, etc.) and were made to fill out a self-rating questionnaire of subjective symptoms and the Stanford sleepiness scale (SSS) before every measurement. The CNV area decreased sharply at and after 3:00 of the second day, and dropped to its minimum at 9:00 of the same day and still did not increase after the recovery night. The number of subjective symptoms reached its maximum at 6:00 and 9:00 of the second day. A close correlation was found between the number of subjective symptoms and the CNV area during sleep deprivation. The SSS was at its maximum at 6:00 of the second day and a good correlation was found between the SSS and the CNV area. The correlation between the CNV area and CFF and between the CNV area and oral temperature was slight. The CNV is meaningful as an index which objectively indicates the drop in arousal level caused by sleep deprivation.

Keywords: CNV, CFF, Subjective symptom, Sleep deprivation.

INTRODUCTION

In some industries, e.g., manufacturing, service, construction, transportation, etc., nightshift workers often work continuously through the day following their night shift under the condition of sleep deprivation due to unavoidable circumstances. In such cases, since the arousal level is lowered, a critical situation is very likely to occur and to cause an accident.

In the analysis of such events, the carelessness of the worker is often emphasized and the significance of the natural decline of the physiological function is ignored. An analysis overemphasizing the former and neglecting the latter is inadequate from a disaster-prevention point of view. Because such inadequate analysis is common, there have been few physiological studies about night-work problems of this type.

The critical flicker fusion frequency (CFF) has often been utilized until now in the studies of night-work problems. However, with the CFF, which has been considered to reflect the level of brain wakefulness, a recovery phenomenon is observed at dawn when drowsiness increases; the cause of this phenomenon remains a question. In order to settle this question, an electroencephalographic study method has recently been introduced. Endoh, for instance, explained by observing the brain waves of a long-distance truck driver at this low level of

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arousal concluded, that the driver's unnecessary act of passing the car ahead of him was an effort to urge arousal by excessive action.[1] Ohkuma reported that the alpha-component of brain waves of truck drivers for long distance increases, even with eyes open, when driving an automobile during the middle of the night.[2]

The present authors planned an experiment using the contingent negative variation (CNV) in order to promote a study of the night-work problem. CNV, first reported by W.G.Walter et al. in 1964,[3] has come to be considered a part of the event related potential (ERP), together with the readiness potential and the P_{300}, as a result of subsequent studies. In studies of the relation between CNV and every day human behavior, it was reported that CNV has a close correlation with attention, expectancy, motivation and arousal and that the CNV amplitude drops after total sleep deprivation.[5] We kept in mind the results of these studies and made an experimental study to clarify the fluctuation of CNV in the state of sleep deprivation for 36 h and to examine the correlation between CNV and subjective symptoms in sleepiness and physiological indices measured at the same time as the CNV.

MATERIALS AND METHODS

Subjects

Before our main experiment was planned, a preliminary experiment was made with two healthy subjects.[6] The results of the preliminary experiment suggested that there were individual differences in the drop of the CNV amplitude caused by sleep deprivation as well as large differences in the value of CNV amplitude depending on the measuring conditions. For that reason, 11, healthy, male college student volunteers, aged 21 to 25 were first measured for CNV in the same manner as in the main experiment. Five students with relatively high CNV amplitude were then chosen as subjects for the main experiment.

Measured items and measuring time period

Fig. 1 shows the procedures for applying the work load, for measuring physiological functions, and for providing rest with lapse of time. The measured physiological functions were the oral temperature, blood pressure, heart rate, CFF (Kawasaki-Electronica; Railway Labor Science Research Institute Type) and CNV, as shown in Table 1. Each item was measured before work began and every three hours there after. Just before the measurement of physiological functions, subjects were made to fill out their own self-rating questionnaire of subjective symptoms (according to Japanese Association of Industrial Health)[7] and the Stanford sleepiness scale (SSS)[8] (in Japanese). The work load consisted of four kinds of tasks: the Unida-Kraepelin test, the "a,m,e,f,u,r,i" letter cancellation test (Institute of Science of Labor), signal detection with a spare-capacity measuring apparatus (Kawasaki Electronica) and the dual task performance.

Restrictions of the subjects' behavior

The experimental subjects were made to eat every meal in the presence of monitoring persons insuring that the subjects were continuously monitored for 36 h and deprived of sleep. Except for meal times, the subjects were made to stay in the electroencephalograph room of the central laboratory. Work, such as the Uchida-Kraepelin test and the cancellation test, also had the purpose of preventing the optional behavior of each subject.

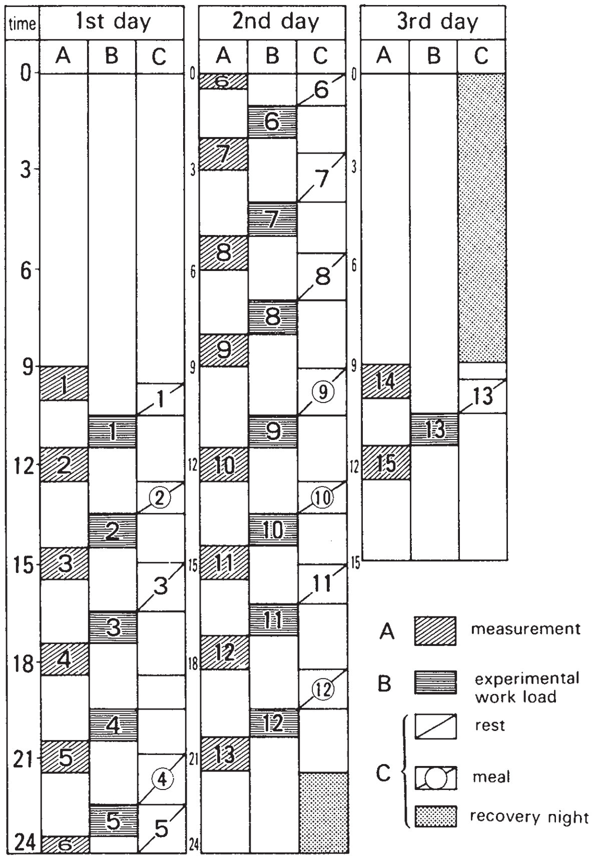

Fig. 1 Timetable of the experiment

Table 1. Tasks and Examinations

1. Work load
a. Uchida-Kraepelin Test
b. Cancellation Test
c. Signal Detection Test
d. Dual Task Performance
2. Measured Physiological Functions
a. Oral Temperature
b. Blood Pressure
c. Heart Rate
d. CFF
e. CNV

Measurement of CNV

After the subjects were given the first stimulus S_1, they were given the second stimulus S_2 at regular interval. The subjects were instructed to make a motor response (MR) as soon as the second stimulus was given. The slow surface negative shift in the baseline of the electroencephalogram[4] appears during the period between the first and the second stimuli (inter-stimulus interval: ISI). This shift is the CNV. In the S_1-S_2-MR paradigm, S_1 and S_2 are called the warning stimulus and the imperative stimulus, respectively. For the motor response, the pressing of a button is generally used. If the second stimulus S_2 is terminated by the motor response, i.e., an operant action, the CNV amplitude increases. Even if the button is pressed by only one hand, the CNV comes out to be bilaterally symmetrical over the two hemispheres.[4]

For the CNV paradigm in the main experiment, the procedures mentioned below were used. The red light-emitting-diode (LED) was used as the stimuli S_1 and S_2. The LED was fixed at a distance of 1 m from the eyes of the supine subjects. Stimulus S_2 was given with an ISI of 1,000 msec after stimulus S_1. The MR was the act of pressing a button which whould terminate the stimulus S_2. The subject was instructed to press the button with his more skilled hand as soon as possible after S_2 had been given. The process from giving S_1 to the termination of S_2 was regarded as one trial. After an inter-trial interval (ITI) of 10 to 15 sec, a second similar trial was carried out. A series of 25 trials was regarded as one CNV measuring test.

For EEG recordings, an electroencephalograph (NEC-SANEI 1A75) was used and the time constrant was set at 3 sec. The electrodes were placed according to the method of Nakamura et al..[9] The electrodes were Ag-Agcl electrodes. The active electrode and the reference electrode were fitted on the vertex (Cz in 10-20 method) and the left ear lobe (A_1), respectively. The forehead was grounded.

It is known that eye movement affects CNV.[3,4] The electroencephalograph was set to draw an electrooculogram (EOG) and an EEG at the same time. When the baselines of the EEG and the EOG were stable, the CNV was measured. The CNV was recorded each time together with the S_1, S_2 and MR on a four-channel data recorder (TEAC A-704). The data on the CNV were processed by a data processor (Nihonkohden ATAC-450) to eliminate inappropriate trials from the 25 trials and to average 20 appropriate trials. The trial was considered inappropriate if an artifact level over 1.5 times the calibration level appeared during the period between 500 msec before the S_1 and the S_2. Programming was carried out so that the mean amplitude of the EEG between 500 msec before the S_1 and S_1 was used as the baseline. The CNV pattern obtained by averaging the 20 trials was plotted on an x-y recorder (WATANABE SOKKI). The CNV area (unit: μV·msec) for the period of 550 msec from the point of 450 msec after the S_1 to the S_2 was measured[10,11] with a planimeter. The CNV area was used as a concrete numerical value indicating the CNV amplitude.

In order to analyze the measured values, the FACOM M-382 at the Computation Center of Nagoya University was used.

RESULTS

CNV

The CNV patterns at the time of measurement are shown with lapsed time in Fig. 2. The upper patterns at each time of measurement are the superimposition of the CNV of all the subjects; the lower pattern is the mean wave-form of CNV in these subjects.[12] In the lower pattern at 9:00 of the first day, the CNV area is indicated by the shaded part of the mean wave-form. The CNV amplitude was reduced with increasing sleep deprivation. Although small differences were observed in the CNV amplitude among the subjects, the CNV amplitude of the subjects as a whole tended to drop sharply after 3:00 of the second day. The average of the five subjects showed a minimum value at 9:00 of the second day and continued to be low thereafter. The CNV amplitude at 9:00 of the third day after the recovery night showed the second lowest value. CNV patterns in two subjects appeared under the baseline as "contingent positive variation (CPV)" from 3:00 of the second day (Fig. 2).

Fig. 3 shows changes in the mean value of the CNV area together with those changes in the other measurement results. The mean value of the CNV area was 4,422 μV·msec at 9:00 of the first day, 880 μV·msec at 9:00 of the second day, 1,198 μV·msec at 21:00 of the second day and 916 μV·msec at 9:00 of the third day. The latter three values were significantly lower than the former and had a significance of $P<0.05$ in the t-test.

Physiological function

Fig. 3 shows the measured values of items against lapsed time. The mean value of the critical flicker fusion frequency (CFF) increased from 32.3 Hz at 9:00 of the first day and reached a maximum of 34.9 Hz at 21:00 of the same day. After that, the mean value of the

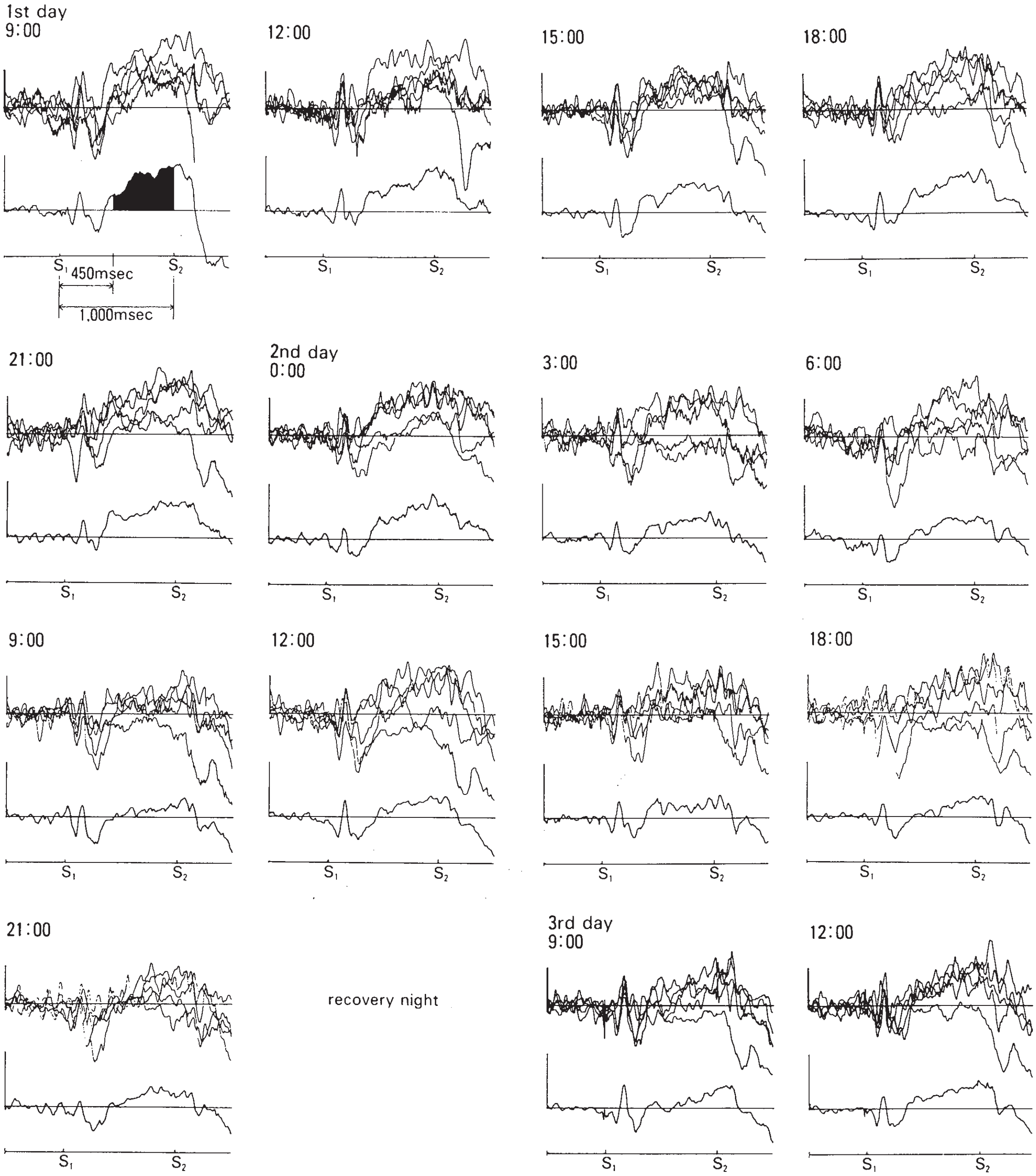

Fig. 2. Change of CNV-pattern with lapsed time
upper patterns: superimposition
lower patterns: mean wave-form
CNV area: shaded part of the mean wave-form, 1st day, 9:00
calibration: $10\mu V$

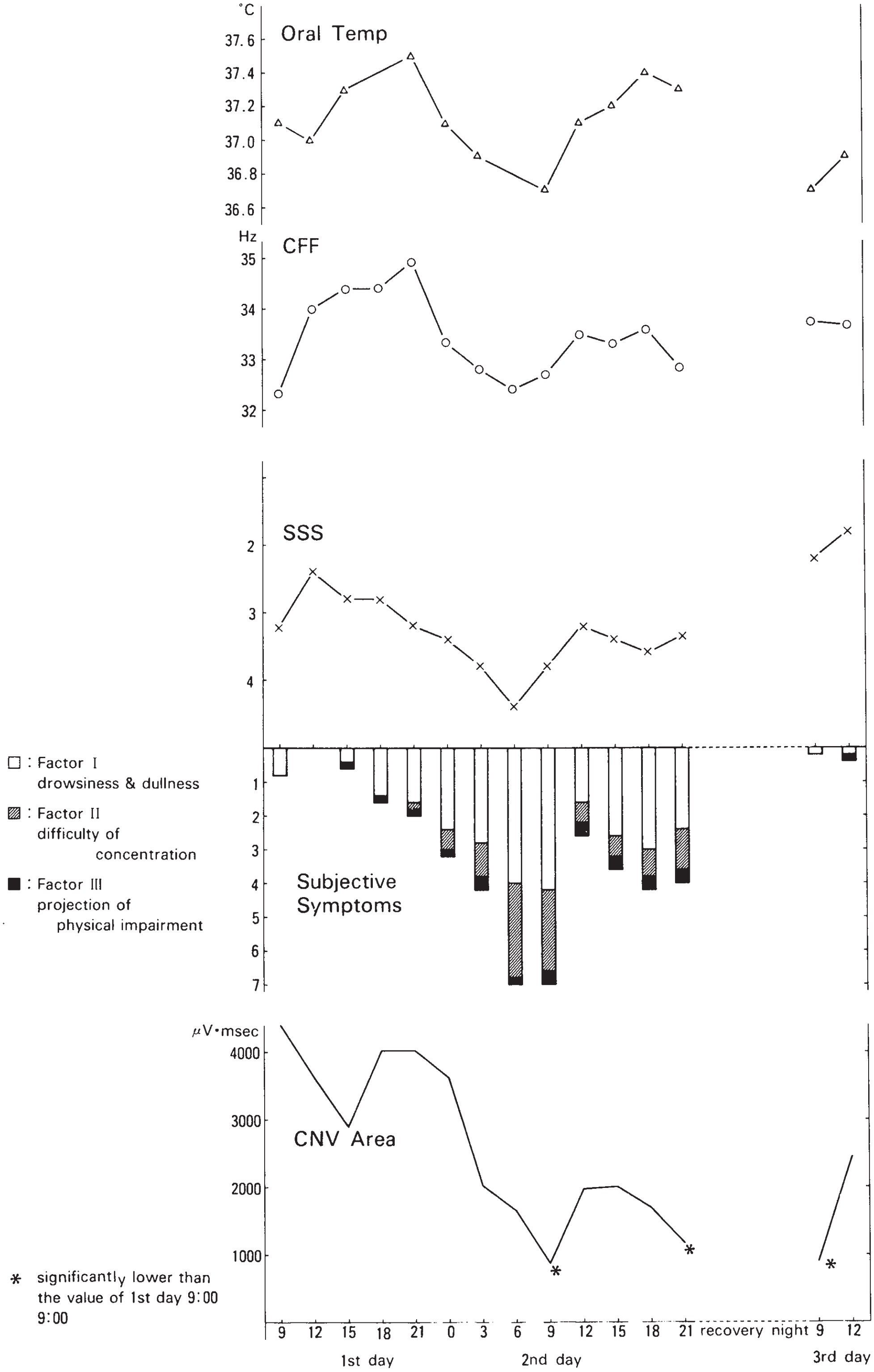

Fig. 3. Serial variation of oral temperature, CFF, SSS, subjective symptoms, and CNV area.

CFF decreased and was 32.4 Hz at 6:00 of the second day, which was the second lowest value from the beginning of the measurement. After 6:00 of the second day, the mean value rose but remained lower than that on the first day. The value was lower than 34 Hz on the third day after the recovery night.

The mean value of the oral temperature was 37.1°C at 9:00 of the first day and reached a maximum of 37.5°C at 21:00 of the same day; it reached its minimum of 36.7°C at 9:00 of the second day but rose to 37.4°C at 18:00 of the same day. On the third day, it had relatively low values of 36.7°C and 36.9°C at 9:00 and 12:00, respectively.

The blood pressure and heart rate fluctuated within their normal ranges.

Subjective symptoms and Stanford sleepiness scale

The mean values of the number of complaints written in the self-rating questionnaire of subjective symptoms was 0.8 at 9:00 of the first day but sharply increased to 3.2 at 0:00 of the second day and rose to a maximum of 7.0 at 6:00 and 9:00 of the next day. The value once decreased to 2.6 at 12:00 of the second day but increased thereafter. On the third day, the value dropped to 0.2 and 0.4 at 9:00 and 12:00, respectively, close to the value at the beginning of the experiment.

According to the proposal of the Industrial Fatigue Research Committee of the Japanese Association of Industrial Health, the thirty subjective symptoms were divided into 3 groups: the first group, 1 to 10, related to drowsiness and dullness (Factor I); the second group, from 11 to 20, concerned with difficulty of concentration (Factor II); and the third group, from 21 to 30, related to projection of physical impairment (Factor III). Most of the complaints made by the subjects were in Factor I. However, the number of complaints in Factor II also increased at and after 21:00 of the first day. There were only a few complaints from Factor III (Fig. 3).

The mean value of the Stanford sleepiness scale (SSS) was 3.2 at 9:00 of the first day and dropped once thereafter. The value then gradually rose to 3.2 at 21:00 of the same day and reached a maximum of 4.4 at 6:00 of the second day. After that, the value decreased slightly but remained higher than 3.2. The values were 2.2 and 1.8 at 9:00 and 12:00, respectively, on the third day after the recovery night (Fig. 3).

Correlation between CNV and the other results

The coefficients of correlation between the CNV amplitude (CNV area) and the other measured values at the thirteen measuring times of the first and the second day during sleep deprivation were calculated. The CNV amplitude and the number of complaints of the self-rating questionnaire of subjective symptoms showed a close correlation ($r = -0.79$). The correlation between the CNV amplitude and the SSS was good ($r = -0.63$). The correlation between the CNV amplitude and the CFF and between the CNV and the oral temperature was slight ($r = 0.46$ and $r = 0.41$).

DISCUSSION

About the method

According to the CNV paradigm standards of the Research Committee for Examination of Evoked Potential of the Japanese Society of EEG & EMG, it is appropriate to use relatively strong and short sounds such as pure tone and a click sound as the first stimulus S_1 and to use light, which differs in modality from the first stimulus, as the second stimulus S_2. In our main experiment, light was used for both stimuli S_1 and S_2 in order to restrict the eye movement likely to produce an artifact in measuring the CNV, as mentioned earlier. The subjects were made to move their eyes adequately (opening, closing and blinking) during the ITI. After that, each trial was carried out when the EEG and the EOG were stable.

In averaging the trials, a program was utilized to reject trials in which the EEG amplitude became excessively large under the influence of the EOG artifact. Such measures for preventing the CNV from being contaminated by the EOG were useful in clarifying the CNV pattern.

The above-mentioned standards of the Research Committee for Examination of Evoked Potential were proposed after the present experiment and prescribed that the ISI be 2 sec or more, that the time constant be three to four times that of the ISI, and that the recording sports be Fz, Cz and Pz. In our experiment, the paradigm and recording spots were adopted according to the method of Nakamura et al. because of the specification of our equipment and the limited measuring time. Our method should be evaluated according to the results of the present experiment.

Effects of sleep deprivation on CNV and on physiological functions

It has been known that the fluctuations in functions such as attentiveness,[3] expectancy,[3,13] conation,[10] motivation[14] and attention[4] affect the CNV amplitude. We expected the CNV amplitude to drop if these functions fell due to sleep deprivation. Naitoh et al. reported that the CNV amplitude does not drop below that of the baseline days after partial sleep deprivation in the stages of slow wave sleep and REM sleep, but drops significantly after total sleep deprivation. In our experiment, the CNV amplitude dropped significantly at 9:00 of the second day after total sleep deprivation similarly to that in Naitoh et al.'s report. Although they reported that the CNV amplitude after the recovery nights was significantly higher than that of baseline days, our experiment showed that the CNV amplitude at 9:00 of the third day after the recovery night was significantly low. In this respect, our result differs from theirs.

In our experiment, the fluctuation in the CNV was observed with lapsed time starting from sleep deprivation to the morning after the recovery night in order to obtain more detailed results for the purpose of obtaining information about the fluctuation in attention, arousal, etc. in continuous work through days and nights. The results show that the times when the CNV areas of the five subjects came to a minimum during sleep deprivation were 3:00, 6:00, 9:00, 12:00 and 21:00 of the second day, respectively. The individual differences between the times of occurrence of the miniums are conspicuous.

The coefficient of variation of the CNV area was 1.0 or more after 3:00 of the second day until 21:00, particularly, 1.5 or more from 3:00 to 12:00 of the same day. This indicates that the individual differences in CNV during the period from the early morning after sleep deprivation to the end of work were large. Despite this, however, the CNV areas of all subjects dropped markedly during the same period. This suggests that the strong influence of sleep deprivation on the CNV surpassed individual differences.

The number of subjective symptoms had a close correlation with the CNV amplitude; the SSS had the next closest correlation. Three of the five subjects showed their lowest CNV areas at a time when the number of subjective symptoms was the largest. The times of these three subjects' largest number of subjective symptoms were 3:00, 6:00 and 9:00 of the second day. The fall in physiological functions, which resulted in drowsiness, dullness and difficulty of concentration, are considered to have caused the drop in CNV amplitude.

For this reason, it should be pointed out that the CNV can be used as an objective index for the fall in physiological functions during continuous work at dawn when the number of subjective symptoms is increased.

The CNV amplitude indicated only a slight correlation with the CFF and with the oral temperature. The reason for this is considered to be the fact that the oral temperature and the CFF are unavoidably affected by sleep deprivation although they have a clear circadian rhythm.

Tecce[4] and Nakamura[9] reported that the CNV amplitude is in direct proportion to the intensity of attention but that it has an inverted-U shape correlation with the arousal level, and that the CNV amplitude drops, whether the arousal level is high or low. In our experiment, the drop in the CNV amplitude was caused by reduced attention and also by lowered arousal level, which were indicated by the increase in the number of complaints in Factor I (drowsiness and dullness) on the self-rating questionnaire of subjective symptoms. The state which should be called hyperarousal was not observed.

In our experiment, two subjects showed CPV. Nakamura[9] reported that he sometimes found CPV in the initial stage of schizophrenia and in schizophrenia-like cases of anorexia nervosa. It is very notable that such a phenomenon occurred due to sleep deprivation. In this respect, further study and discussion are necessary.

CONCLUSION

In the day-and-night shift system, some people are often compelled to work continuously in a state of sleep deprivation because of staff shortage or unpredictable circumstances. The CNV in our experiment was proved to indicate clearly the process of drop in arousal level which is likely to cause an unsafe act in such sleep-deprived work. The CNV amplitude was low corresponding to the sleepiness at dawn, was low again during the same day following dawn, and was still low after the recovery night. This indicates a delay in the recovery of the CNV amplitude. This fact is markedly different from the fact that the CFF began to show a process of recovery on the second day (after the sleep deprivation) and after the recovery night. This characteristic of the CFF seems to be a paradoxical phenomenon in the process of fatigue but indicates that the CFF is a function much controlled by the circadian rhythm. In contrast to this, the CNV better reflects the drop in the arousal level.

We concluded that the CNV is a meaningful objective index of the arousal level after sleep deprivation, and that the effects of sleep deprivation on the arousal level remain for a long period of time.

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