THE STUDY OF NATURAL SLEEP AFTER GENERAL ANAESTHESIA IN THE CAT

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SUMMARY

The sleeping patterns of postanaesthetic state and behaviour in unrestrained cats were studied for two weeks. The percentages of wakefulness, slow wave sleep, drowsiness, and paradoxical sleep were not affected by nitrous oxide anaesthesia. Sleeping patterns were changed for several days after halothane anaesthesia; firstly paradoxical sleep decreased and drowsiness increased, then paradoxical sleep increased and drowsiness decreased. The rebound period was different among the 0.5%, 1.0%, and 1.5% halothane. Complete recovery of paradoxical sleep after 1.5% halothane anaesthesia for 5 hours required nine days in this experiment. This finding shows that the recovery of natural sleep from general anaesthesia takes longer than behavioural recovery.

Advances in the physiology of sleep have led to the understanding that sleep consists of two successive functional states (slow wave sleep and paradoxical sleep) which latter is an active mechanism (Aserinsky and Kleitman, 1955a, b; Dement and Kleitman, 1957; Jouvet, 1967, 1969). These two states can be accurately quantified and selectively modified or suppressed by specific manipulations (Dement, 1960; Agnew, Webb and Williams, 1964; Jouvet, Vimont and Delorme, 1965; Jouvet, 1969; Berger and Meier, 1966; Huertas and McMillin, 1968; Friedman, 1968; Wyatt and associates, 1969, 1971). While studying the effects of various concentrations of several anaesthetics on the electroencephalogram in cats, we have noted that there might be some differences between natural sleep and postanaesthetic sleep in the cats. The most striking change was the decrease of paradoxical sleep, not only during anaesthesia but also after anaesthesia (Yanagida, unpublished data). Thus, it can be suggested that the states of sleep after general anaesthesia are modified by the previous anaesthetic episode. Also, it is possible to suggest that this modification differs between anaesthetics. Little information is available on the recovery of natural sleep after general anaesthesia. In order to investigate this problem we have examined how natural sleep is modified after general anaesthesia in cats.

METHODS

Six cats were used in this experiment. Surgical stainless steel electrodes were placed bilaterally on the frontal cranium to obtain a neocortical e.e.g. Bipolar concentric electrodes were implanted in the hippocampus dorsalis. The hippocampal electrodes were made of stainless steel wire coated with enamel. For the neck myogram, stainless steel surgical wire electrodes were placed in the splenius capitis. All procedures were performed under pentobarbitone anaesthesia. Heart rate was also recorded. Several days were allowed for recovery from the surgical procedures before the experiments. Each cat was isolated in an airtight observation box (70 × 80 × 40 cm) for at least 2 weeks before the insufflation of anaesthetic gases, in order to allow time for adaptation to the new environment. The observation box has a window for observation and a gas inlet and outlet. The outlet was mounted with a “pop-off” valve to prevent contamination. The cat was considered to have adapted to its new environment and to be ready for changes in its environment when its sleeping habits had become stereotyped and the restlessness, which characterized its early days, had ceased. As a control, baseline data were taken for a period of 2 weeks after adaptation. The cat was then made to inhale anaesthetic gases for 5 hours. Four different mixtures were used: 80% nitrous oxide in oxygen, 0.5% halothane in oxygen, 1.0% halothane in oxygen, and 1.5% halothane in oxygen. Each anaesthetic was given in turn to all six cats. More than 30 days was allowed between experiments.

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before proceeding to test the next anaesthetic or halothane concentration. After the box was filled with the gas mixture, 10 l/min of this gas was supplied to the box for 5 hours. At the end of this period, the anaesthetic gases were washed out with oxygen, and the animal was allowed to recover. The concentration of oxygen in the box was frequently checked with a paramagnetic analyser (Beckman, E2) to allow accurate maintenance. The concentrations of anaesthetics were checked using gas chromatography (Ohkura). Contamination with nitrogen was less than 4%. Carbon dioxide was removed by soda lime. A 9-channel ink-writing electroencephalograph (Nihon-Koden ME92) was used for polygraphic recording. Polygraphic recordings and behavioural observation were continued for 2 weeks after the termination of anaesthesia. The classification of the phases of consciousness was that used by Jouvet (1967). The wakeful, drowsy, slow wave sleep, and paradoxical sleep phases varied in time, ratio, and order from cat to cat, so that the total time spent in each state within 24 hours was summed and expressed as percentage with standard deviation. The temperature inside the box was maintained at 26±1°C. At the end of the experiment, the animal was sacrificed by injection of pentobarbitone. The brain was perfused with formalin and the position of electrodes in the brain was checked by gross observation and histological examination.

RESULTS

Baseline study.

The control state was divided into four phases: wakefulness, drowsiness, slow wave sleep, and paradoxical sleep. Figure 1 shows the average results for six cats during the baseline period. The percentages of wakefulness, slow wave sleep, drowsiness, and paradoxical sleep during a 24-hour period were 47.0±1.3, 30.1±2.1, 12.8±1.1, and 10.1±2.6 respectively.

Changes of the four phases after anaesthesia and observed behaviour.

80% nitrous oxide in oxygen. Under 80% nitrous oxide in oxygen, the animals showed a state of tranquillity which was characterized by "lying still". Within 20±9 min of the termination of nitrous oxide, the animals showed waking behaviour. The relative distribution of four stages and their courses after nitrous oxide appeared to be almost the same as during the baseline period (fig. 2).

They had good appetites. Nausea, vomiting and diarrhoea were not observed. They were steady in their gait and no abnormal behaviour was observed.

0.5% halothane in oxygen. The phase of waking almost disappeared under 0.5% halothane in oxygen. After termination of the inhalation of halothane, animals showed a state of drowsy behaviour. This situation remained unchanged until 30±18 min after the termination of halothane. On the first day, four of the six cats showed loss of appetite. One vomited three times. Three of the six had not the least interest in the observer. Two of six walked unsteadily. Slow wave sleep increased and paradoxical sleep decreased significantly compared with baseline values. On the second day, drowsiness increased and paradoxical sleep decreased. Their e.e.g.s. were normal. Increase in appetite in five and restless behaviour in four were observed. Two previously tame animals showed a defiant attitude toward the observer. From the second day, the percentages of slow wave sleep were almost the same as those of the baseline period. From the third to the fifth day, paradoxical sleep increased (rebound); at the same time, drowsiness decreased remarkably. Their e.e.g.s. and behaviour were normal. From the seventh day, the percentages of the four arbitrary phases were the same as those of the baseline period (fig. 3).

1.0% halothane in oxygen. Twenty-five±9 min after the inhalation of 1% halothane, the cats lay down. This situation remained unchanged until 45±9.6 min after the termination of halothane. Figure 4 shows the courses of the four stages. On the first day, two stages (slow wave sleep and drowsiness) increased and the other two stages (waking and paradoxical sleep) decreased. Appetite declined in five of the six. Three vomited several times. No abnormal e.e.g.s and behaviour were observed but four of the six had not the least interest in the observer. Two walked unsteadily. From the second day, the percentages of waking and slow wave sleep returned to those of the baseline values. From the second to the third day, drowsiness was increased and paradoxical sleep was decreased without alteration in the values of waking or slow wave sleep. Increase in appetite in five and restless behaviour in six were observed. Three previously tame animals showed a defiant attitude toward the observer on the second and the third day. From the fourth to the eighth day, paradoxical sleep increased (rebound); at the same time, drowsiness decreased below any previously recorded value. From the ninth
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FIG. 1. The courses of four stages during baseline period. The ordinates show the percentages during a 24-hour period. Values were obtained from six cats during the baseline period. The total time spent in each stage within 24 hours was summed and expressed as a percentage with standard deviation. Each stage shows almost the same value for 14 days.

FIG. 2. The courses of four stages after 80% nitrous oxide anaesthesia. Each stage is almost the same as during the baseline period.

FIG. 3. The courses of four stages after 0.5% halothane anaesthesia. The fluctuation of two stages (drowsy and paradoxical sleep) was noteworthy until the sixth day.

FIG. 4. The courses of four stages after 1.0% halothane anaesthesia. On and after the eighth day, four stages show almost the same proportions as in the baseline period.

FIG. 5. The fluctuation of two stages (drowsy and paradoxical sleep) continued for 10 days after 1.5% halothane anaesthesia.
day, the relative distribution of the four arbitrary stages returned to that of the baseline value.

1.5% halothane in oxygen. Eighteen $\pm$ 11 min after the inhalation of 1.5% halothane the cats lay down. This situation remained unchanged for a period of 62 $\pm$ 34 min after the termination of anaesthesia. Figure 5 shows the courses of the four stages during a two-week period after anaesthesia. On the first day, two stages (waking and paradoxical sleep) decreased and the other two stages (slow wave sleep and drowsiness) increased. Appetite declined in five of the six. No abnormal e.e.g.s were observed and five of the six walked unsteadily. From the second day, the percentages of waking and slow wave sleep returned to that of the baseline value. On the second and third days, paradoxical sleep was decreased and drowsiness was increased compared to the baseline. Increase in appetite in five and restless behaviour in five were observed. Four previously tame animals showed a defiant attitude to the observer. On the fourth, fifth, sixth, seventh, and eighth days, paradoxical sleep increased (rebound) and drowsiness decreased compared to the baseline. During this period, no abnormal behaviour was observed. From the ninth day, the percentages of the four arbitrary stages were the same as those of the baseline period.

DISCUSSION

The mammalian sleeping brain successively passes through two states which can be recognized very easily with the polygraphic technique in animals with electrodes chronically implanted in the brain. The first state is called slow wave sleep (Jouvet, 1967). In this state the animal adopts a sleeping posture; its eyes are closed, and the pupils are miotic. A degree of postural tonus always remains in some muscle groups of the body (including those of neck). The electrical activity of the cortex is characterized by spindles and slow waves. This state is then followed by a totally different state. Jouvet (1967) has called it paradoxical sleep because cortical activity similar to that of waking and a total absence of activity in the neck muscle appeared paradoxical. In the present study, the percentages and courses of the four stages following the termination of nitrous oxide were the same as those of the baseline period. These results may suggest that natural sleep is not affected by nitrous oxide anaesthesia. On the first day following halothane anaesthesia, loss of appetite, vomiting, unsteadiness, and indifference to environment were observed. These findings may easily be explained by the continued presence of halothane in the body. From the second day, these signs completely disappeared. Therefore, we excluded data for the first day from analysis of the courses of the four stages. Wyatt and associates (1969, 1971) reported that in the human brain the adrenergic and serotonergic brain systems act in opposite directions in the production of paradoxical sleep, with the catecholamines decreasing, and serotonin augmenting. Jouvet (1969) reported that paradoxical sleep appears to depend upon "priming" serotonergic mechanisms located in the caudal raphe system and upon "triggering" mechanisms located in the nuclei of the locus coerleus. Roussel and associates (1967) reported that destruction of these nuclei leads to the suppression of paradoxical sleep without alteration of slow wave sleep. The relative distribution of the four stages following the termination of halothane anaesthesia was different from that of the baseline for a certain period which was associated with the deprivation of paradoxical sleep and its rebound, without alteration of waking and slow wave sleep. These changes were also observed when halothane anaesthesia was administered for less than 4 hours. However, the difference in responses among the groups anaesthetized with 0.5%, 1.0%, and 1.5% halothane was not apparent except when anaesthesia lasted for more than 5 hours (Yanagida, unpublished data). Our findings, namely that the sleeping patterns are changed after halothane anaesthesia and that paradoxical sleep is suppressed and drowsiness increased without alteration of waking and slow wave sleep for several days except for the first day after halothane anaesthesia, would suggest that the caudal raphe system and the nuclei of the locus coerleus are inhibited by the anaesthetic episode.

There are marked discrepancies between human and other mammalian species in the relationship between serotonin and sleep (Wyatt and associates, 1971). These authors reported that l-dopa, the immediate precursor of dopamine and noradrenaline, decreases paradoxical sleep in humans (an effect opposite to that noted in animal studies). This indicates that there might be differences in the adrenergic system between human and other mammalian species. Therefore, the interpretation of our results should be guarded.

The increase in appetite, restless behaviour, and a defiant attitude were observed during the decreased period of paradoxical sleep. They may be related to the suppression of paradoxical sleep, because it has been reported by many investigators (Dement, 1960;
Khazan and Sawyer, 1963; Agnew, Webb and Williams, 1964; Siegel and Gordon, 1965; Berger and Meier, 1966) that the suppression of paradoxical sleep leads to irritation in both humans and animals.

It should be emphasized that the complete recovery of paradoxical sleep from 1.5% halothane anaesthesia for 5 hours required 9 days in this experiment. The natural sleep in clinical cases may be further modified by surgical stress, postoperative pain or other drugs in addition to general anaesthetics.

REFERENCES


