The Effects of Sleep Deprivation on Memory With the Presence of Artificially Induced Arousal

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The effects of sleep deprivation on memory and arousal and the use of a nootropic drug to reverse those effects were investigated. Three groups of rats were used: a nontreatment group, an ephedrine-injected group, and a saline-injected group. All groups were taught a lever-press task in an operant chamber. The ephedrine and saline groups were deprived of sleep 24 hr prior to the learning task and were administered ephedrine or saline 15 min before the session. Four hr later, all groups were tested in the operant chamber for their memory of the learning task. Although the results of this study revealed significance in learning performance as time increased, no significance was found between group learning performance or between group memory performance. It was concluded the mechanisms of arousal and memory may be similar. It was also determined that the claims made for and against ephedrine as a nootropic drug are inconclusive.

As a result of recent research, a number of theories have been developed related to the functions of sleep. One such theory (Adam, 1980) suggests body repair and restoration are the obligatory functions of sleep. Another theory (Edinger & Erwin, 1992) states energy dissipation, oculomotor control refinement, integration of innate behaviors, and increased regulation of the sensitivity of noradrenergic receptors are the main functions of sleep. According to Cai (1991), culminating memories in the limbic system during the waking state create an unbalanced emotional state during sleep. Non-REM or synchronized sleep (SS) functions in the calibration of those emotions disrupted by mounting memories. However, this adjustment and reorganization of emotions in SS tends to disorganize the acquired memories. REM or paradoxical sleep (PS), which occurs subsequent to SS, functions to reorganize those memories disorganized by SS (Cai, 1991).

The two variables most noticeably affected by sleep and sleep deprivation are arousal and memory. When in an aroused state, the brain is prepared to perform on a conscious level in response to numerous stimuli (Revelle & Loftus, 1990). Input signals must stimulate the ascending reticular activating system (ARAS) in order for arousal to occur. In the event of sleep deprivation, changes in stimulations to the ARAS occur and the cerebral cortex is not completely activated resulting in experienced feelings of fatigue and dysphoria, in short, a decreased state of arousal (Revelle & Loftus, 1990).

In order for experiences to become part of memory, physiological changes in the central nervous system must be produced in such a manner that these changes represent the experiences. Important to the memory process is the locus coeruleus (LC) which helps initiate and maintain PS, aids in the control of memory, and limits the sensitivity period of recently acquired information. Stimulation of the LC leads to substantial enhancement of learning (Dujardin, Guerrien, & Leconte, 1990). Some effects of sleep deprivation include decreased information retention, slower thinking efficiency, greater mood disturbance, longer overall response latencies, slowed decision making, impaired perception, slower motor execution, and amnesia for activities that occur just before sleep (Hart, Buchsbaurm, Wade, Hamer, & Kwentus, 1987; Wyatt & Bootzin, 1994).

Despite continuing disagreements over the obligatory function of sleep, most experts agree sleep is a vital part of the circadian rhythm (e.g., Ashkenazi, Reinberg, Bicakova-Rocher, & Ticher, 1993; Bouskila & Dudek, 1995; Elmore, Betrus, & Burr, 1994). The circadian rhythm is the biological system which regu-

lates such variables as growth, behavior, body temperature, blood pressure, sleep propensity (the tendency to sleep), and the sleep-wake cycle (Elmore et al., 1994). Researchers (Ashkenazi et al., 1993; Bouskila & Dudek, 1995; Dijk & Czeisler, 1995; Elmore et al., 1994) have shown the sleep-wake cycle can be manipulated to cause short-term overriding of the sleep propensity rhythm. When the interference is removed, the sleep-wake cycle returns to its original rhythm. No alterations in the sleep propensity rhythm occur, even in the presence of long-term disruptions of the sleep-wake cycle.

A number of individuals, for various reasons, find it desirable to alter their sleep-wake cycle and shield sleep propensity for a day or so. Based on the concept that certain drugs can combat the effects of sleep deprivation, many of these people attempt these changes by artificial means, mainly through the use of nootropic drugs such as caffeine, amphetamine, and ephedrine (Rogers, Spencer, & Nicholson, 1989; Wolkowitz, Tinklenberg, & Weingartner, 1985; Wyatt & Bootzin, 1994). A nootropic drug is one which theoretically facilitates learning, improves memory, and increases the physiological state of arousal in the absence of negative side effects (Sarter, 1986). Ephedrine, which is highly comparable in chemical structure and composition to amphetamine (Devane, Mulligan, Foynes, & Martin, 1991), is the active ingredient in a number of prescription and over-the-counter bronchodilators and nasal decongestants (Rombaut, Alford, & Hindmarch, 1989). Studies have shown ephedrine can reverse the effects of sleep deprivation on arousal through such side effects as increased alertness, higher blood pressure, faster heart rate, greater energy expenditure, and the presence of insomnia (Astrup & Toubro, 1993; Rombaut et al., 1989). As a result, many over-the-counter ephedrine products are marketed and used as stimulants to combat the effects of sleep deprivation and fatigue on arousal. By increasing their level of arousal while being sleep deprived, many people assume they can also reverse sleep deprivation's effects on their memory (Santrock, 1993).

The current study was designed to show ephedrine, despite its inherent ability to reverse the effects of sleep deprivation on arousal, cannot alter the effects of sleep deprivation on memory by artificially inducing a state of arousal in sleep-deprived participants. Favorable results from this study are also expected to provide evidence for the hypothesis that, in the realm of sleep, memory is influenced by the more stable sleep propensity rhythm, whereas arousal is influenced by the changeable sleep-wake cycle.

Method

Participants

Twelve albino rats, litter mates born within 10 days of each other and weighing between 200 g and 250 g, were purchased at a local pet supply store and served as participants. The rats were individually housed in a 41 × 27 × 15 cm plastic bin with a wire mesh top and with attached water bottles. On a daily basis, each rat was fed four whole grain food pellets weighing an average of 4 g each. All rats were free to feed as they chose. All of the bins were placed in a 10 × 10 ft room and the rats were equally exposed to 12 hr of light and 12 hr of darkness each day.

Apparatus

The sleep deprivation apparatus consisted of two chambers which were adaptations of the one successfully used by Schwartzbaum, Hunt, and Davies (as cited in Cohen & Dement, 1965) to deprive rats of REM sleep. Each sleep deprivation chamber consisted of a 80 cm wide × 45 cm long × 41 cm deep plastic tub with a wire mesh top. Each chamber had 2 plastic tumblers, 10 cm high with a bottom diameter of 6 cm, inverted and attached to the bottoms of the chambers. The tumblers were placed approximately 34 cm from each other, 17 cm from a 40 cm chamber length and 20 cm from an 80 cm chamber width. Pilot studies for this study indicated the diameter of the tumblers and their placement within the chamber were too small for the rats to physically interact. Also during these pilot studies, no social interaction was observed while the rats were being deprived of sleep.

Also used was a lever press, water reinforcement Lafayette Instrument Company operant chamber model 84122SS set on continual reinforcement (CRF), which served as the test chamber. The drop-size regulator for the liquid dispenser was set approximately in the middle for each individual rat.

Procedure

Each rat was randomly assigned to one of three groups equal in size ($n = 4$): the nontreatment group, the ephedrine group which received an ephedrine and saline injection, and the saline group which was injected with saline. The experiment was divided into two trials, using 2 different rats from each group for each trial. During each trial, 4 rats, 2 from the ephedrine group and 2 from the saline group, were deprived of sleep. One rat from the ephedrine group and one from the saline group, both randomly chosen, were placed on the inverted tumbler pedestals in the first sleep deprivation chamber. Another rat from the ephedrine group and one from the saline group were placed in the second chamber. The cham-

TABLE 1

Summary of Group Performance Means on Learning and Memory Tasks

	Cumulative Mean Learning Responses			Mean Memory Responses
Group	10 min	20 min	30 min	
Nontreatment	9.50	30.25	104.50	14.75
Saline	19.30	77.00	110.70	18.25
Ephedrine	7.75	52.50	82.75	6.50
Composite Mean	12.18	53.52	99.32	

bers were filled with enough water to just cover the bottoms of the tumblers. The bottom diameter of the tumblers was large enough for the rats to stand on. When the rats fell asleep and began to enter REM sleep, muscular relaxation would cause the rats to fall into the water and wake up, or they would get their noses wet, thus waking them. The pilot studies indicated the rats would not drink the water in the sleep deprivation chambers, therefore, water was used for reinforcement. After the rats and water were in place, the wire mesh tops were secured. The nontreatment rats also were deprived of water for those periods during which the other groups of rats were deprived. None of the rats, however, were deprived of food.

After an initial 24 hr of sleep deprivation, all 6 rats from the first trial were taught a lever-pressing task in the operant chamber using water reinforcement. Fifteen min before the rats from the ephedrine group were to enter the operant chamber, they were injected with an ephedrine and saline mixture equivalent to 0.25 mg of ephedrine per 1 kg of weight, a dose similar to that used by Pradhan and Dutta (1970) and equivalent to twice the single human dose (Sifton, 1994), to induce arousal or to reverse likeliness of falling asleep. Likewise, 15 min before the rats from the saline group were to enter the operant chamber, they were injected with 0.25 mg of saline. This procedure was implemented to control for possible injection effects. Each rat was individually placed in the operant chamber for a 30-min period. The pilot studies showed that shaping was necessary for only five consecutive reinforcements during the first 5 min of learning. Thus, each rat was shaped in this manner. The cumulative number of lever presses made after every 10-min interval was recorded. The shaping reinforcements were subtracted from the initial 10-min period.

After each rat learned the lever-press task on a CRF schedule, they were allowed to sleep for 4 hr without water. After this 4-hr period, all 6 rats were tested for memory retention of the lever-press task, without water reinforcement. Each rat was placed in the operant chamber and its total presses were recorded after 3 min. The pilot studies indicated after 3 min, relearning of the lever-press task rather than memory was occurring. The experiment was then repeated for the second trial (i.e., the remaining participants) in an identical manner.

Results

Table 1 shows the cumulative group means for learning performance as well as the mean group performances for the 3-min memory task. A 3 × 3 mixed factor ANOVA of the data for the learning session yielded a significant increase in performance for the time factor, $F(2, 18) = 74.78$, $p < .001$. However, no significance was found with between-group learning performance $F(2, 9) = 1.56$, $p > .05$, or with between-group learning performance over time $F(4, 18) = 2.33$, $p > .05$. In addition, a one-way ANOVA of group memory performance after 3 min showed no significant groups effect, $F = 1.45$, $p > .05$.

Discussion

The lack of statistically significant group differences supports the hypothesis that ephedrine does not alter the effects of sleep deprivation on memory. The significant increase in learning performance over time indicates that all groups continued to improve at comparable rates.

Two implications can be inferred from the results. The significant difference in time found for learning performance and the lack of significance in between-group memory performance indicate that learning did occur and memory retention was equally efficient for all groups. In other words, the 24-hr sleep deprivation procedure used in the present experiment did not impair learning and memory of the task

used in this study. Therefore, the validity of the claim that ephedrine can reverse the effects of sleep deprivation on learning and memory function is not conclusive. Furthermore, in the absence of favorable results, the hypothesis that memory is influenced by the sleep propensity rhythm and arousal by the sleep-wake cycle could not be supported.

There are three potential factors which could have affected the outcome of the results. The fact that a relatively small sample size was used means the performance by just one atypical participant could have greatly skewed the data. A second factor could have been the amount of sleep deprivation imposed on the participants. Despite indications by Sarter (1986) and from the pilot studies for this research, other research has eluded to the possibility that 24 hr of sleep deprivation has little effect on learning and memory performance in rats (Deming, Zhenyun, Daosheng, & Shanxun, 1991). Finally, based on the methods and findings of Gauvin, Moore, Youngblood, and Holloway (1992), the ephedrine dose used for this study may have been too small. Because of these factors, important differences between the groups may have been overshadowed. Therefore, the hypotheses presented in this study must not be completely ignored. Further research with more participants, a greater dose of ephedrine, and extended sleep deprivation periods should be conducted.

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