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BRIEF COMMUNICATION

ADH and Related Peptides: Effect of Pre- or Posttraining Treatment on Puromycin Amnesia[1]

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FLEXNER, J. B., L. B. FLEXNER, R. WALTER AND P. L. HOFFMAN. *ADH and related peptides: effect of pre- and posttraining treatment on puromycin amnesia.* PHARMAC. BIOCHEM. BEHAV. 8(1) 93–95, 1978. – The peptide Z–Pro–Leu–Gly–NH_2 attenuated puromycin-induced amnesia in mice when administered 5 days prior to training, while arginine vasopressin, lysine vasopressin and cyclo(Leu-Gly), were effective when given 24 hr before training. The activity of all peptides to inhibit puromycin-induced amnesia decreased as the interval after training and before peptide administration increased, suggesting that the peptides influence memory processes rather than generalized arousal mechanisms.

Vasopressin Pituitary peptides Puromycin amnesia Memory

AMONG the effects on memory of the neurohypophyseal hormones as well as some of their analogs and fragments are inhibition of extinction of active and passive avoidance responses [3] and attenuation of the amnesias induced by CO_2 [15] and puromycin [18]. These effects appear to be due to direct action of the peptides on the CNS [3, 13, 17]. We have previously reported both on the effectiveness of a number of these peptides [18] and on their dose-response relationships [6] in antagonizing puromycin-induced amnesia.

The present experiments had two objectives. The first was to estimate how long before training treatment with selected peptides would be protective against the amnestic effects of puromycin and in this way to approximate the duration of those changes that provide protection. The second objective was to test the effectiveness of treatment as a function of time after training. If the peptides modify processes of memory, and do not owe their activity to extraneous factors such as long-lasting arousal, it would be expected that their effectiveness would be time-dependent, decreasing with increase in the interval between training and treatment [10, 14, 16].

METHOD

[8–Arginine]vasopressin (AVP), [8-lysine]vasopressin, (LVP), cyclo(Leu-Gly), and benzyloxycarbonyl-Pro-Leu-Gly-NH_2 (Z–MIF) were from the same batches used in earlier studies [18]. In all experiments the peptides were used at the minimal concentration which was previously found to be fully protective against puromycin-induced amnesia when injected immediately after training [6]. Thus, each injection of AVP contained 0.07 μmole (80 μg); of LVP, 0.2 μmole (200 μg); of cyclo (Leu-Gly), 1 μmole (170 μg); and of Z–MIF, 0.03 μmole (12 μg). The peptides were dissolved in Krebs' bicarbonate buffer just before use; 0.1 ml of the solution was injected SC. Plastic ware was used throughout. Injections were made at 1 and 3 days

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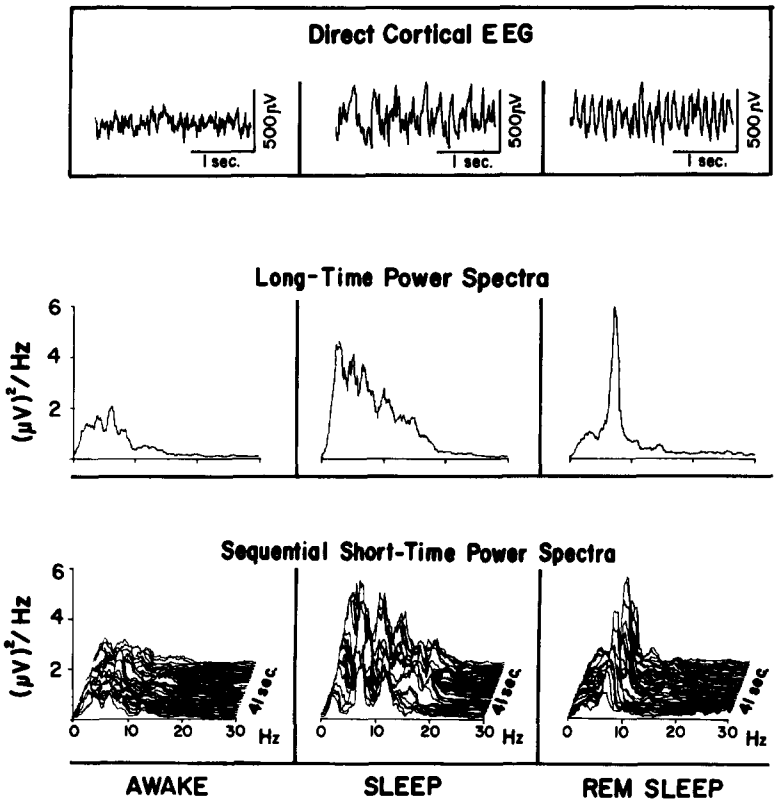

FIG. 1. Direct cortical EEG recordings are shown in the top panel during the awake, sleep, and REM sleep states. Long-time power spectra derived from 41-sec EEG samples during the three behavioral states are shown in the middle panel. Spectral power $[(\mu V)^2/Hz]$ is presented as a function of frequency (Hz). Sequential short-time power spectra derived from the same EEG samples are shown in the bottom panel.

RESULTS

EEG and EMG recordings collected during the behavioral states of sleep, REM sleep and wakefulness in the rat are easily distinguishable from one another [1–5, 7, 8]. Cortical EEG tracings during these three states of behavior and their corresponding power spectra are shown in Fig. 1. As seen at the top of this figure, EEG recordings during wakefulness were associated with relatively low-amplitude high-frequency waves. The sleep EEGs consisted mainly of relativeiy high-amplitude low-frequency waves. REM sleep EEGs exhibited a predominance of 6–9 Hz waves (theta waves). Long-time power spectra derived from the 41-sec EEG samples related to wakefulness, sleep, and REM sleep are also shown in Fig. 1. The awake state was associated with substantially less total spectral power than either sleep or REM sleep. Sleep was associated with a predominance of spectral power in the lower frequency range (zero to 5 Hz) and a gradual diminution of spectral power in the 5–20 Hz range. REM sleep was associated with a predominant peak of spectral power in the 6–9 Hz range. Sequential short-time spectra derived from overlapping specimens of cortical EEG are shown in the bottom of Fig. 1. The awake state was associated with much less total power than that associated with sleep or REM sleep. Sleep was associated with relatively consistent spectral peaks in the zero to 5 Hz range, while spectral peaks in the 5–20 Hz range apparently varied unsystematically in amplitude and location. REM sleep was associated with spectral peaks in the 6–9 Hz range that were confined to a narrow frequency bandwidth, but of flucuating power.

The degree of variability of the power spectra associated with the three behavioral states of the rat is presented in Fig. 2. The top of the figure depicts the degree of variability in power spectra of a single rat. The relative power (% of total power) is shown as a function of frequency at 1 Hz intervals; standard errors of the mean are shown as an indicator of variability between EEG samples. The power spectra at the bottom of the figure indicate the amount of intersubject variability between five rats. Since sleep was associated with the largest amount of total power, the power associated with wakefulness and REM sleep was calculated as being relative to that of sleep, with sleep being 100%.

DISCUSSION

The rat has been used extensively in studies related to experimental psychology and psychopharmacology. Relatively little information is available concerning EEG power spectra during sleep-awake behavior with freely-moving rats prepared with chronic EEG electrodes. This report, therefore, describes the power spectra derived from the rat's cortical EEG during different states of consciousness. In the awake state the EEG spectra consisted mainly of power in the zero to 10 Hz range; there was much less total power than during sleep and REM sleep. In

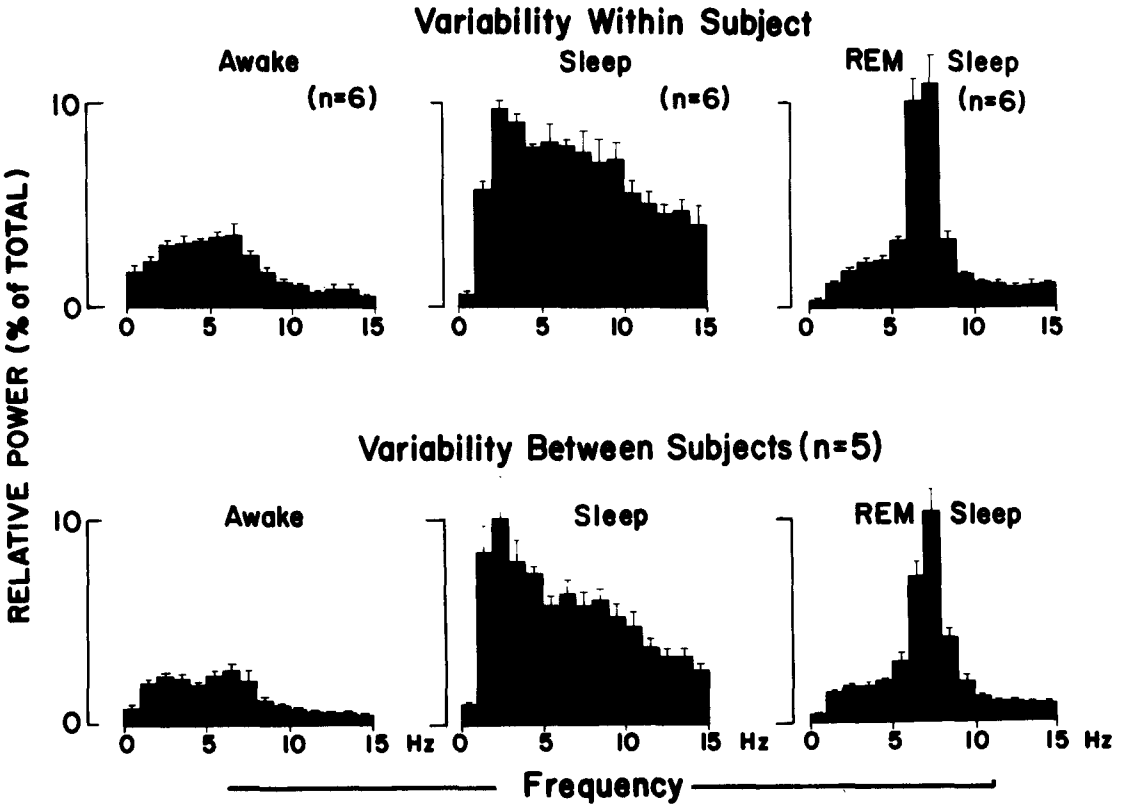

FIG. 2. Power spectra derived from cortical EEG are shown at the top of the figure during the awake, sleep, and REM sleep states. Each spectrum is the average of six, each of which was derived from a 41-sec cortical EEG sample. The relative percent of total spectral power is shown as a function of frequency at 1 Hz intervals. Standard errors of the mean are indicated. Grouped data from five rats is shown at the bottom of the figure. For each rat average power spectra were derived from three 41-sec cortical EEG samples during each of the three behavioral states. These spectra from each of the five rats were then averaged relative to the total power associated with sleep, sleep being 100%. Standard errors of the mean are indicated.

the sleep state there was a predominance of spectral power in the zero to 5 Hz range with a gradual dimunution of power as frequency increased from 5 to 20 Hz. In the REM sleep state there was predominance of power in the 6 to 9 Hz range. Having characterized the EEG power spectra associated with normal sleep-awake behavior in the rat, precise EEG changes which may result from exposure to abnormal behavioral conditions or to effects of psychoactive drugs [6] can be delineated.

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