areas (Table 2) show that all contained significant quantities of serotonin. After treatment with *p*-chlorophenylalanine, average values for serotonin content decreased for all areas except the cerebellum, where there was an increase of 44 percent. The significance of this increase is not understood. Although gross depression of serotonin concentration provides no information on the relative effect of the drug on metabolically stable and labile pools, or on the relation of these pool sizes to site of action, it is clear that a very large depression of serotonin content (greater than 50 percent) in the upper brain stem is not necessary to produce alterations in the sleep pattern of the monkey. It is probable that more pronounced depression of serotonin concentration would produce more profound alterations in sleep pattern, since the animal (9I) in which this alteration was most pronounced showed a great decrease in serotonin content.

These findings support the notion that serotonin-containing neurons of the CNS may play a role in the control of sleep. Our finding of a selective decrease of NREM sleep without a significant change in REM sleep time indicates that the two sleep states can be dissociated and suggests that serotonin may be specifically related to the NREM sleep phase. A study (*3*) of the effect of *p*-chlorophenylalanine on the sleep patterns of cats showed a profound decrease in sleep time. However, in that study both phases of sleep decreased 48 hours after the second of two injections with complete insomnia lasting for 2 days. During the recovery phase, a phasic indicator of REM sleep (pontogeniculo-occipital spikes) returned first, with progressive return of both phases of sleep thereafter. Since regional brain serotonin concentrations were not reported, the differing results cannot be compared. Studies in which lesions destroying the raphe system in the midline of the upper brain stem, a region rich in serotonin neurons (*10*), have shown a linear relation between decrease in sleep and serotonin concentration in several regions of the brain. It is of interest that the greatest decrease in tissue serotonin in the monkey after *p*-chlorophenylalanine occurred in comparable rostral brain stem regions.

The degree of serotonin depletion in our monkeys was not as great as reported for lower mammals, despite a higher dosage of drug (*4*). The NREM sleep pattern of the monkey is much closer to that of man than is that of the cat. This similarity of monkey and man would be consistent with the failure to observe insomnia as a striking symptom when the drug was administered to normal man and to patients (*9*).

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Hippocampal Correlates of Aversive Midbrain Stimulation

Abstract. *Hippocampal synchronization during aversive dorsal midbrain stimulation was observed in rats both in a conditioning procedure and under* d-*tubocurarine paralysis. The results restrict the generality of previous reports which correlated hippocampal synchronization and desynchronization with approach and withdrawal behavior, respectively. Relative to the condition of free movement, curarization reduced the frequency of both "spontaneous" and dorsal midbrain-evoked synchronization, thus suggesting possible direct and indirect effects of* d-*tubocurarine on subcortical structures.*

Since Green and Arduini's (*1*) extensive analysis of theta patterns in rabbit hippocampus, several attempts have been made to determine the behavioral correlates of hippocampal activity. One characteristic of hippocampal activity as examined by electroencephalographic techniques is the occurrence of distinct shifts between synchronization and desynchronization. An important series of investigations by Grastyan and coworkers (*2*, *3*) has suggested that this biphasic activity of the hippocampus is directly related to motivational mechanisms such that "there is a strict correlation between approach behavior and hippocampal theta rhythm on the one hand and withdrawal behavior and desynchronization on the other" (*2*, p. 91). These investigators prefer the terms "pull" and "push" to describe the "two irreducible behavioral patterns during which the animal moves toward (pull) or away from (push) an object or environmental stimulus" (*3*). The behavioral data suggest that "pull" and "push" behaviors occur, in the terminology of American behavioral analysis, during rewarding and aversive situations respectively.

In our laboratory (*4*) rewarding hypothalamic stimulation was recently found to produce concomitant hippocampal synchronization, supporting the hypothesis of Grastyan *et al.* (*2*). However, rebound effects reported by these workers were not found. In addition, other studies of hippocampal activity during eating, drinking, and grooming disclosed desynchronization, not synchronization, during such approach-type behavior (*5*). These latter results suggested the possible need to modify the correlation between synchronization and reward. Since the strict relation of desynchronization and aversion could also be questioned, the present experiment examined the generality of the desynchronization-aversion correlation by observation of hippocampal activity during stimulation of dorsal midbrain, an area shown by Olds (*6*) to have aversive properties.

Five adult albino rats were implanted

with two bipolar Nichrome electrodes with the use of stereotaxic procedures. One electrode was directed toward the dorsal hippocampus, the second toward the dorsal midbrain region. A single bare wire attached to a screw in the frontal bone served as subject ground. The electrode wires and ground lead were attached to the female half of an Amphenol connector which was fastened securely to the skull with stainless steel screws and acrylic. The male half of the connector was attached via low-noise Microdot cable to a five-channel mercury-pool swivel which allowed free movement of the rat without introduction of artifact. Hippocampal recordings were obtained with an Offner type-R Dynograph with filters set to pass activity between 0.6 and 32 hertz. Sine wave stimulation of 60 hertz was applied to the dorsal midbrain electrodes.

The motivational properties of dorsal midbrain stimulation were determined by use of a 24 by 10 by 18 inch (61 by 25 by 46 cm) shuttle box apparatus and testing procedure similar to that described by Valenstein and Meyers (*7*). By moving to alternate ends of the box every minute, the rat could determine whether it would receive an intracranial stimulus of 1.0-second duration presented once every 3 seconds. Since 300 stimuli were presented in each 15-minute trial, random activity would result in receipt of 150 stimuli. By our criteria, if the animal received 100 or fewer stimuli the stimulus was considered aversive; receipt of 200 or more stimuli indicated the stimulation was rewarding. One 15-minute trial was given daily for 6 days, and hippocampal records were obtained during the first and last 3-minute periods of each trial. Stimulus intensity employed for each animal was that which produced an arousal or escape reaction. Behavioral and hippocampal responses to additional levels of stimulation (10 to 60 μa) of 1.0- and 1.5-second duration were determined after completion of the the procedure described above.

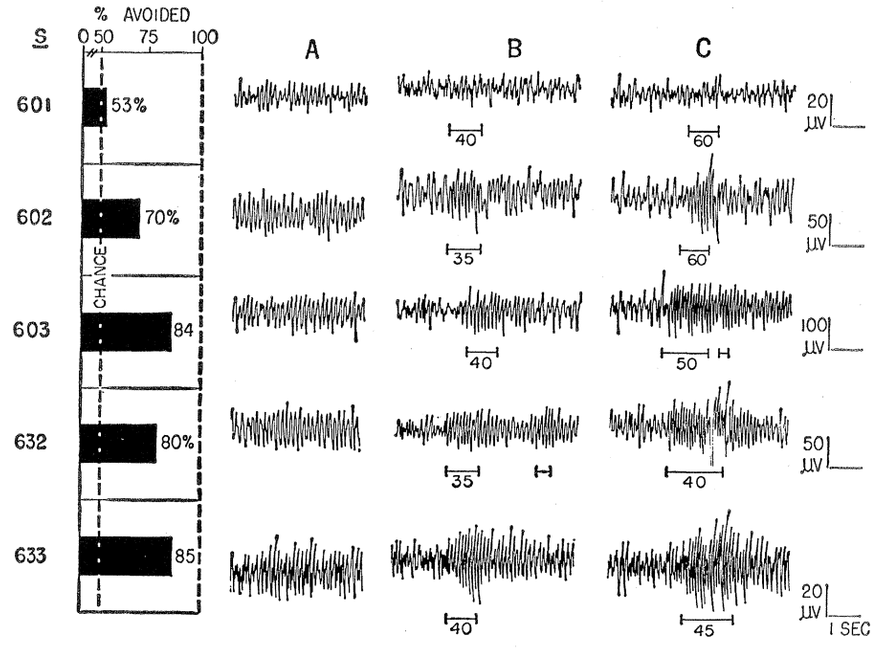

Fig. 1. Behavioral and hippocampal activity of five animals during dorsal midbrain stimulation. Behavioral response is summarized by the bar graphs, which represent the mean percent of stimuli avoided during the last four sessions. Hippocampal response observed in three conditions: (A) Normal exploration, 7 to 9 hertz; (B) low-intensity aversive stimulation employed during shuttle box trials, 8 to 10 hertz; (C), high-intensity aversive stimulation employed in the freely moving animal after completion of shuttle box trials, 10 to 13 hertz. The stimulus duration is indicated by the length of the markers under the records in comparison with the length of the 1-second lines at far right. The numbers under these markers indicate the intensity of the stimuli, in microamperes.

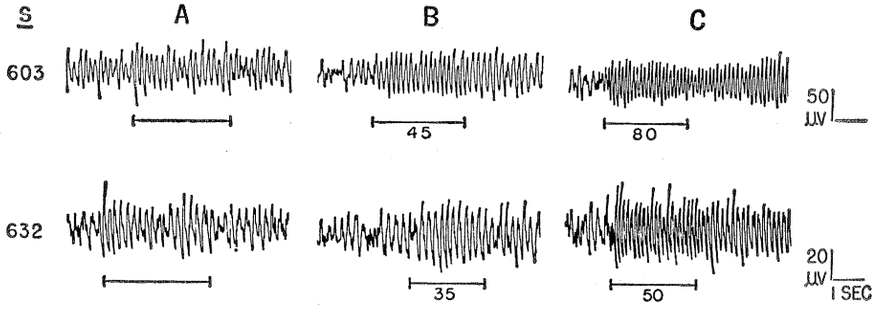

Fig. 2. Hippocampal response to tactile and aversive dorsal midbrain stimuli during *d*-tubocurarine paralysis. Hippocampal response: (A) tactile stimulation, 5 to 6 hertz; (B) low-intensity stimulation, 6 to 7 hertz; (C) high-intensity stimulation, 7 to 8 hertz. Stimulus intensity and duration indicated as in Fig. 1.

Theta of 7 to 9 hertz was obtained from all rats during exploratory activity. Perusal of histology indicated that the recording electrodes were located in the dorsal hippocampus. In Fig. 1, the bar graphs show the percent of total stimuli received by each animal. These graphs indicate that, by our criterion, intracranial stimulation of low intensity was aversive for all animals except No. 601, for which the stimulation was neither aversive nor rewarding. Histological analysis revealed that midbrain electrodes terminated in dorsal tegmentum or ventral tectum, with the placement in No. 601 being most lateral.

During aversive midbrain stimulation, hippocampal synchronization always occurred (see Fig. 1). The frequency of this elicited synchronization varied directly with the intensity of the intracranial stimulus. Behavioral observation suggested, in addition, that synchronization frequency was related to the intensity of the behavioral response and not the stimulus intensity required to produce that response (compare 603 low intensity and 632 high intensity in Fig.

1). Thus, for example, synchronization of 12 to 13 hertz occurred during similarly violent behavioral responses, while 9- to 10-hertz synchronization appeared during well-controlled escape or withdrawal behavior. Perhaps because this behavior was acquired on the first 15-minute trial of testing, we noticed no difference in hippocampal activity in response to dorsal midbrain stimulation between early and late trials. Within a 15-minute trial, however, we observed a waning of the behavioral response which was directly related to a reduction of hippocampal synchronization frequency.

Rebound effects were not apparent either following termination of individual stimuli or following successful movement to escape stimulation. Instead the synchronization occasionally continued with a slight decrease in frequency after stimulus offset (see 603, Fig. 1).

Three animals were not used in this study because one animal was accidentally killed with an overdose of ether, and two developed stimulus artifact in the hippocampal records which made the interpretation of the electroencephalographic records difficult. As in the freely moving condition, aversive midbrain stimulation elicited hippocampal synchronization during paralysis (Fig. 2). The relation between intracranial stimulus intensity and frequency of synchronization seen in the behavioral situation was also maintained under paralysis. It may be concluded, therefore, that the general features of the results obtained in the freely moving animal were present in the paralyzed subject. There was, however, a reduction in synchronization frequency during paralysis. Thus, for the same stimulus intensity applied to the freely moving rat, the frequency of hippocampal synchronization during curarization was reduced by 2 to 4 hertz. Tactile stimuli which normally produced synchronization of 7 to 8 hertz in the freely moving animal now produced synchronization of 5 to 6 hertz. Since *d*-tubocurarine is generally considered to have no direct central effects (*8*), this reduction in hippocampal synchronization frequency was unexpected, and, to our knowledge, has not been previously reported. Possibly the reduction in frequency was related to the joint effects of *d*-tubocurarine on blood pressure (*8*), proprioceptive feedback (*9*), and behavioral variables related more directly to execution of the aversive response itself.

Our results limit the generality of the view of Grastyan *et al.* (*2*) correlating push (aversive) behavior with hippocampal desynchronization. In the present study, hippocampal synchronization, not desynchronization, consistently occurred during aversive stimulation. In contrast to the results of Grastyan *et al.* (*2*), hippocampal desynchronization did not occur in the present study while the animals were withdrawing from the aversive stimulus. It is worth emphasizing, too, that the consistent occurrence of synchronization during aversive stimulation questions the view that synchronization occurs primarily during pull (approach) behavior or rewarding stimulation. Apparently, then, the biphasic character of hippocampal activity may not differentiate between aversive (push) and rewarding (pull) motivational situations. Our present speculation is that hippocampal synchronization correlates with the processing of inputs, rewarding or aversive, and that desynchronization in hippocampus correlates with the processing of outputs (*4*, *5*). Further discussion of this view awaits the collection of data.

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Optomotor Responses to Monocular Stimulation: Relation to Visual System Organization

Abstract. *Results of tests on 4 mammalian, 19 reptilian, and 17 avian species confirmed the prediction that lack of optomotor response to monocular optokinetic stimulation in one of the two horizontal directions would correlate with afoveate retinal organization, whereas consistent optomotor responses to monocular stimulation in either horizontal direction would correlate with foveate organization.*

Optomotor reflexes are mechanisms by which animals hold their eyes in a stable orientation relative to the visual surroundings, regardless of changes in head and body position. This is important for maintenance of perceptual orientation and acuity. Optomotor responses of animals from arthropods (*1*, *2*) through anthropoids (*3–5*) have been studied by placing the animal in a rotating cylindrical screen: As the screen turns, the animal moves in a manner which reduces or eliminates retinal movement of the screen's image (*2*, *6*). If the animal turns only its head and eyes, without substantial body rotation, then turning in the direction of stimulus movement is interrupted at intervals by brief rapid "recovery" movements in the opposite direction, producing an oscillatory ("nystagmoid") pattern of head or eye movement (or both) termed optokinetic nystagmus (OKN). In primates the OKN pattern normally will be the same no matter which eye is stimulated (*5–7*), but this is not the case for all mammals: a "unidirectional" response pattern has been described in rabbits (*5*, *6*) and guinea pigs (*5*, *8*). In these animals, if one eye is occluded, OKN is elicited when movement of the stimulus pattern is directed across the anterior visual field from the uncovered eye toward the covered eye (u→c), but it is minimal or absent when movement is in the reverse direction (c→u). Thus, if only the right eye is stimulated, optomotor response will be elicited when the cylinder turns to the left but not when it turns to the right; if the left eye is stimulated, response will occur only when the cylinder turns to the right. This type of unidirectional response pattern has also been reported for domestic pigeons (*9*) and chickens (*10*).

The unidirectionality observation [as well as those concerning effects of central nervous system damage on OKN in the normally bidirectional primates (*4*, *7*, *9*)] may be placed in correspondence with certain findings concern-