edema is a release phenomenon resulting from the removal of centers which were presumed normally to inhibit activity in a postulated hypothalamic edemagenic center, the present data indicate that this phenomenon, like hyperphagia, may be the result of tissue irritation. The failure of the syndrome to appear after radiofrequency lesions may be attributable to the fact that such lesions are relatively clean, leaving little foreign debris in the tissue and cauterizing blood vessels in the vicinity. Electrolytic lesions, on the other hand, characteristically leave large metallic deposits and frequent small hemorrhages in the tissue surrounding the lesion. These can serve as foci for the chronic irritation of the surrounding tissue. Pulmonary edema, therefore, is quite likely the result of irritation of fibers in sympathetic pathways descending through the hypothalamus rather than the release of an edemagenous center from inhibition. These data in turn lend support to the hypothesis (*3*) that those effects of electrolytic lesions which have been described as "release" phenomena are actually the result of irritation of surrounding tissue by the lesion (*4*).

ROBERT W. REYNOLDS
Department of Psychology, University of California, Santa Barbara, University

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4. This work was sponsored by grants (2-B5032 and BT-961) from the National Institute of Neurological Diseases and Blindness.

27 March 1963

Sleep: Cortical and Subcortical Recordings in the Chimpanzee

Abstract. *Electroencephalographic sleep patterns of chimpanzees reveal greater similarities to human records than those of lower mammals. Flash-evoked responses in the midbrain reticular formation remain during "paradoxical" sleep, which does not appear to necessarily involve deep unconsciousness. Characteristic spindling occurs in the amygdala during a "paradoxical" type sleep while other areas were desynchronized. Telencephalic sleep-control mechanisms in higher primates are considered.*

Although a phase of sleep characterized by rapid electrical records has been recognized for many years (*1*), it has been the formulation of the term "activated sleep" by Dement (*2*) and later "paradoxical" or rhombencephalic sleep by Jouvet (*3*) in studies with cats that has elicited such interest in this phenomenon. Their studies provoked interest not only in the general mechanisms of sleep, but also as to whether this rapid electrical phase related to deep or light sleep. The latter question was a prime motivation for the present study on three chimpanzees. Fifteen all-night records were obtained, and there was good consistency in electroencephalographic (EEG) records and sleep states on different nights in the same animal and some minor differences between animals.

Electrodes were stereotaxically implanted in the following subcortical areas: left and right amygdala, left anterior and right posterior hippocampus, left rostral midbrain reticular formation, and left entorhinal (posterior pyriform) cortex. Screw electrodes were placed over the (left) frontal, parietal, and occipital cortex. Recordings were made with a Grass EEG (eight channels) and also recorded on magnetic tape. Stimuli, signal markers, and timing were controlled with Tektronix wave form, and pulse generators and flashes were delivered by a Grass stroboscope unit.

The animals were placed in a sound-attenuated box (6 by 6 by 8 ft) and were lightly restrained in a comfortable form-fitting chair in a slightly reclining position. A strobe light source was adjusted to flash in the face, regardless of the position of the animal (the restraint prevented a complete turn), and the general position and movement were monitored by television. A dim light was left on (for television monitoring and to reduce fear) and the air-conditioning noise presented a constant background sound. Flashes were presented once every 5 seconds in series of 40 or continuously through the night. Visual evaluation of the EEG was used to determine the consistency of the electrical activity during stimulation. Evoked responses were averaged either by a Mnemotron C.A.T. computer or a Control Data Corporation 160-A general-purpose digital computer.

Sleep patterns, based primarily on surface cortical recordings, showed essentially the same phases as described in man (*1*). With the onset of sleep, cortical leads always showed an initial alpha fragmentation, followed by spindling and K complexes, and then slow waves at 1 to 3 cy/sec. Subcortical leads showed dissociated patterns in the initial descent to the phase of large slow waves. Rostral midbrain reticular activity showed a slight increase in fast components until cortical slow waves predominated, but then followed the pattern of cortical slow activity. It is of considerable interest that in these phases of spindle and slow-wave sleep the hippocampal leads failed to show the reciprocity of rhythm patterns said to characterize relations between the hippocampal system and neocortex in the cat, guinea pig, and rat (*4*). Initially, the hippocampal activity was intermittently rhythmic, with sharp-wave or spike-like configurations, followed by a spindling phase, coincident with the phase of cortical spindles. Records from adjacent entorhinal cortex exhibited close similarities to occipital cortical rhythms.

The "paradoxical" phase of sleep appeared only after 3 to 5 hours of spindle and slow-wave patterns, and was characterized by eyelid and eyeball movements, fleeting jaw movements, and head turning, all clearly visible on the television monitor, but with characteristic EEG patterns, fulfilling the criteria of this sleep phase (Fig. 1). Neocortical, hippocampal, and reticular leads showed fast, essentially irregular activity, but the most dramatic manifestation was consistently in amygdaloid leads, which have not been shown to exhibit such graded characteristics from consciousness to deep sleep in lower mammals. The typical rapid irregular amygdaloid records in the waking state showed a slowing during cortical spindling, with spindle bursts at 4 to 5 cy/sec coincident in frequency and duration with those in cortical records. With the progression to delta waves in cortical records, the amygdala continued to show short irregular spindle bursts.

In the "paradoxical" phase, long trains of rhythmic waves at 6 to 8 cy/sec were noted in the amygdaloid

leads, and were seen only in this phase of sleep. They did not occur in other cortical or subcortical structures in this phase of sleep. Behavioral arousal from "paradoxical" sleep led to immediate disappearance of this 6- to 8-cy/sec activity. It is emphasized that this behavioral arousal could be induced very rapidly with neutral stimuli of sufficient intensity, or by the use of significant stimuli, such as the animal's name. In these circumstances, there was no transient period of disorientation between sleep and wakefulness, and the EEG records showed an abrupt transition.

Figure 1*A* shows typical portions of spindling, slow-wave, and "paradoxical" records. The waking record was secured while an animal was watching an orange cut. The spindle and slow-wave records occurred during quiet sleep, and the "paradoxical" record was accompanied by varying amounts of facial grimacing, and with eye and other movements of the type described above suggestive of dreaming. In each instance the configuration of the amygdaloid lead related characteristically to the state of sleep or wakefulness. A slightly different phase of sleep (not shown) has also been recorded, with peripheral and EEG criteria of "paradoxical" sleep (eye movement, low-voltage EEG, and so forth), but without amygdaloid "spindling." This latter is more closely concordant with patterns of "paradoxical" sleep described by others in scalp records, but at the present time the two stages cannot be adequately separated other than by amygdaloid rhythms. Work is currently underway to differentiate or more adequately define these two stages.

During the "paradoxical" phase of sleep the evoked cortical responses to flash were depressed, as described for man by Williams, Tepas, and Morlock (*5*). With the exception of the reticular formation, which will be discussed separately, it was possible at times to utilize a flash to evoke a lighter stage of sleep or to arouse the animal. That is, during the "paradoxical" phase, slow waves could be brought forth by the first of a series of flashes, then spindles and K complexes. Usually, if the "paradoxical" phase was present at the beginning of a series of flashes, the records would either remain in this state, or revert, only slowly, to a spindling phase near the end of the series. However, in all other states there would be a progression to an actual waking state, with opening of the eyes and general movement.

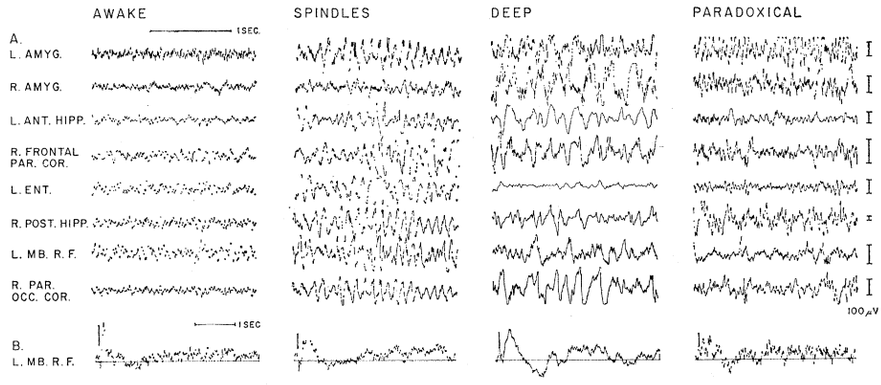

Fig. 1. (*A*) Typical EEG segments during different states of consciousness. (*B*) An average evoked response to 40 flashes, typical for the EEG segment directly above. Amyg. = amygdala, Hipp. = hippocampus, Par. Cor. = parietal cortex, Ent. = entorhinal cortex, MBRF = midbrain reticular formation, Par. Occ. Cor. = parietal occipital cortex.

Evoked responses in the rostral midbrain reticular formation were remarkable for their invariable contradiction of those found in sleep studies in cats (*6*). The evoked response in the rostral midbrain reticular formation never dropped out, regardless of phase of sleep, although it was of lower amplitude during the high-voltage, low-frequency epochs of the EEG records. Typical averaged evoked responses for the various stages are shown in Fig. 1*B*, with the response being typical of the EEG stage shown in Fig. 1*A*. The changes noted in this midbrain response essentially involved only the dissociation or disappearance of secondary or tertiary parts of the response.

The computed average in the waking state showed early primary and secondary responses and a small tertiary response. In the spindling and slow-wave phases, there was a substantial broadening of the secondary response and increased amplitude in the tertiary response. In the "paradoxical" phase, all three phases were discrete, of low amplitude, and more closely resembled the waking configuration than those in spindling or slow-wave sleep.

Although conclusions on preliminary data must be drawn with caution, it appears that the chimpanzee EEG sleep patterns shown certain distinct differences from other animals tested. These findings, together with the similarities of chimpanzee EEG to that of man, suggest that a general theory of sleep mechanisms based exclusively on studies in lower mammals should be viewed with caution, particularly where such great differences are seen in the evoked activity of the reticular formation and in the hippocampus. Simple occlusion in ascending reticular conduction scarcely seems to provide an adequate explanation for sleep phenomena. In the light of the curious activity found in the amygdaloid leads, future investigations may indicate that a primate's important mechanisms in sleep control lie at higher levels than previously thought. Moreover, the findings suggest that the "paradoxical" phase is not necessarily one of deep unconsciousness, but rather may involve an internalization of attention, with decreased sensitivity to peripheral stimuli and with reversion to behavioral wakefulness occurring rapidly if peripheral stimulation reaches an appropriate level. Further, there may be two types of "paradoxical" sleep (*7*).

W. Ross Adey
Raymond T. Kado
John M. Rhodes

Brain Research Institute, University of California Medical Center, Los Angeles 24

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24 June 1963