considerable facility in nonvisual control of both limbs.

After the tests were terminated on day 65, the monkeys were removed from the apparatus and placed singly in cages. Initially they remained prone and clung tenaciously to the diapers covering the cage floor, but they remained alert and ceaselessly looked about their new environment. Within hours they were manually exploring the cage sides and a bottle holder which was suspended a few inches overhead. By the end of the first week both monkeys could walk and climb with near normal ease. By the age of 4 months their locomotor behavior was indistinguishable from that of a monkey of comparable age reared under normal laboratory conditions (*10*).

The results show that an infant primate initially fails to reach accurately for attractive visible objects with a limb that it has never previously viewed. Yet the animal demonstrates both its interest in the objects and its ability to control movements of eyes and head by orienting them to the target. At the same time, it shows the ability to control movements of its limbs and hands with respect to its body. Integration of visuomotor control of head movement and of nonvisual control of limb movement resulting in the ability to perform a visually directed reach appears to require the specific experience of viewing the moving hand. Sight of the moving hand enables the adult to adapt coordination of the eye and hand to the changes produced by optical rearrangement; likewise, sight of the moving hand perfects accurate visual control of reaching in the neonate (*1*).

The act of reaching for a visible target by an adult primate appears to depend upon his capability first to orient his eyes and head to the target and, second, to match the direction of reaching by the hand with the actual or potential orientation of the head to the target. The match is altered when adults adapt to displaced vision of the arm (*11*), and the alteration shows little or no transfer to the contralateral unexposed arm either in man or monkey (*12*). We believe that the earliest experience of watching the moving limb provides the information necessary for the infant to match orientations of head to target and directions of reaching of the arm, and this information integrates the two control systems. If both of these systems are permitted to develop independently, as in the present experiment, hand-watching becomes the prepotent activity when the hand is first seen. Since no more effective means of integrating the systems could be devised, we regard this behavior as a dramatic manifestation of an adaptive mechanism.

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28 November 1966

Brain Stem Structures Responsible for the Electroencephalographic Patterns of Desynchronized Sleep

Abstract. *Contrary to the results of transecting one half of the rostral pons, unilateral partial lesions of the rostral pons, involving either "specific" or "aspecific" structures, do not prevent the appearance of the desynchronized electroencephalographic patterns of deep sleep in the ipsilateral hemisphere in cats. This effect, however, is obtained by lesions of the medial as well as lateral tegmental structures of the midbrain. These findings seem to indicate that (i) there is not a single pontine structure or group of structures of crucial importance for the EEG desynchronization of deep sleep; the whole rostral pons appears to contribute to the EEG-desynchronizing influence; (ii) this influence runs rostrally through the midbrain tegmentum, without following any known fiber pathway.*

Recent experimental researchers have shown that, in the cat, the phase of sleep characterized by desynchronized electroencephalographic (EEG) rhythms, complete muscular relaxation, and rapid eye movements ("desynchronized" or "deep" sleep) is dependent on structures located in the low brain stem (see *1* for references). The pons seems to be the main site of origin of the hypnogenic influence responsible for this sleep phase (*2*, *3*). However, the precise anatomical identification of the pontine structures involved is still controversial. In a previous work (*3*), it was found that unilateral transection of the brain stem prevents or retards the appearance of the typical EEG patterns of this phase of sleep in the ipsilateral cerebral hemisphere; the most caudal brain stem hemisection that was constantly followed by such an effect was located in the rostral pons. It was then assumed that: (i) structures of relevant importance for the EEG patterns of desynchronized sleep are located in the rostral pons, or immediately behind (that is, in the middle pons); (ii) the EEG-desynchronizing influence arising from such structures has a prevalent ipsilateral ascending course. In the present research, an attempt was made to reproduce the EEG effect obtained with brain stem hemisection by making more discrete, localized brain stem unilateral lesions, with the aim of getting

information on (i) the anatomical identification of the structures desynchronizing the EEG during deep sleep, and (ii) the ascending pathways carrying the EEG-desynchronizing influence.

Forty-two adult cats were used. The brain stem lesions (no more than one in each animal) were always made on the right side, under general anesthesia. The lesions were produced electrolytically through a stereotaxically oriented electrode having a diameter of 0.5 mm and isolated except at the tip, with the neutral electrode attached at the free margin of the skin. The active electrode was pushed down in 1.5-mm steps, each point being destroyed with a constant current of 2.5 ma for 10 to 15 seconds. The electrode was then taken out and moved 1.5 mm laterally, and the procedure was repeated until the desired extent of the lesion was reached. This technique is therefore similar to that employed in the earlier experiments of our laboratory (*3*) and of others (*2*). The EEG recording, completed with the recording of the electrical activity of the posterior cervical muscles and of the movements of the eyes, usually started 24 hours after surgery and was repeated for several days, lasting several hours (even 24) each day. The precise extent and location of the lesions were checked anatomo-microscopically, on serial sections of the brain stem.

The first group of experiments constituted a search for the site of origin of the ascending influence desynchronizing the EEG during deep sleep, made by unilateral lesions at the level of the rostral and middle pons. Three types of lesions were made (23 animals): (i) lesions involving one or more "specific" structures (medial lemniscus, lateral lemniscus, trapezoid body, medial longitudinal fasciculus, pyramidal tract, middle and superior cerebellar peduncles, nuclei of the lateral lemniscus, nuclei of the trigeminal nerve, superior olive); (ii) lesions involving one or more "aspecific" structures (nuclei reticularis pontis oralis, reticularis pontis caudalis, reticularis tegmenti pontis, dorsalis tegmenti, right part of the raphe nuclei); (iii) lesions involving both "specific" and "aspecific" structures, in variable combination and extent. In no case was EEG asymmetry of the type produced by pontine hemisections observed; even if the pontine lesions were very large (see Fig. 1), the EEG rhythms of desynchronized sleep were unaffected in both hemispheres (Fig. 2A). These negative results were present even in animals operated under ether anesthesia and recorded only a few hours thereafter. On the other hand, the appearance of the EEG activity of desynchronized sleep in the ipsilateral hemisphere could be prevented or delayed by transforming the partial unilateral pontine lesion into a complete pontine hemisection with additional electrolysis.

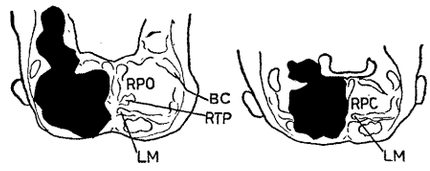

Fig. 1. Pontine unilateral (right) lesions in two different cats. In spite of the extent of the lesion in both cases no alteration of the EEG rhythms of desynchronized sleep was observed. *BC,* brachium conjunctivum; *LM,* lemniscus medialis; *RPC,* nucleus reticularis pontis caudalis; *RPO,* nucleus reticularis pontis oralis; *RTP,* nucleus reticularis tegmenti pontis.

The findings from this group of animals seem to indicate that the ascending influence responsible for EEG desynchronization during deep sleep does not arise from a discrete pontine region or pontine nucleus or fiber tract; no single pontine structure or group of structures appears to be of crucial importance for the EEG patterns of deep sleep. Our results indirectly suggest that all the structures located in the rostral half of the pons appear to contribute to the origin of these EEG patterns. This conclusion is apparently at variance with those of Jouvet and of Carli and Zanchetti (*2*), who report disappearance or marked reduction of desynchronized sleep following bilateral selective destruction respectively of the nucleus reticularis pontis caudalis and of the nucleus reticularis pontis oralis, or of parts of them.

Though it appears from our previous experiments (*3*) that the brain stem structures responsible for the EEG desynchronization of deep sleep control chiefly the ipsilateral hemisphere, it is likely that they have some influence on the contralateral hemisphere as well. This might account for more evident results following bilateral lesions. However, it remains to be explained why the destruction of all structures located in one half of the rostral pons (or their

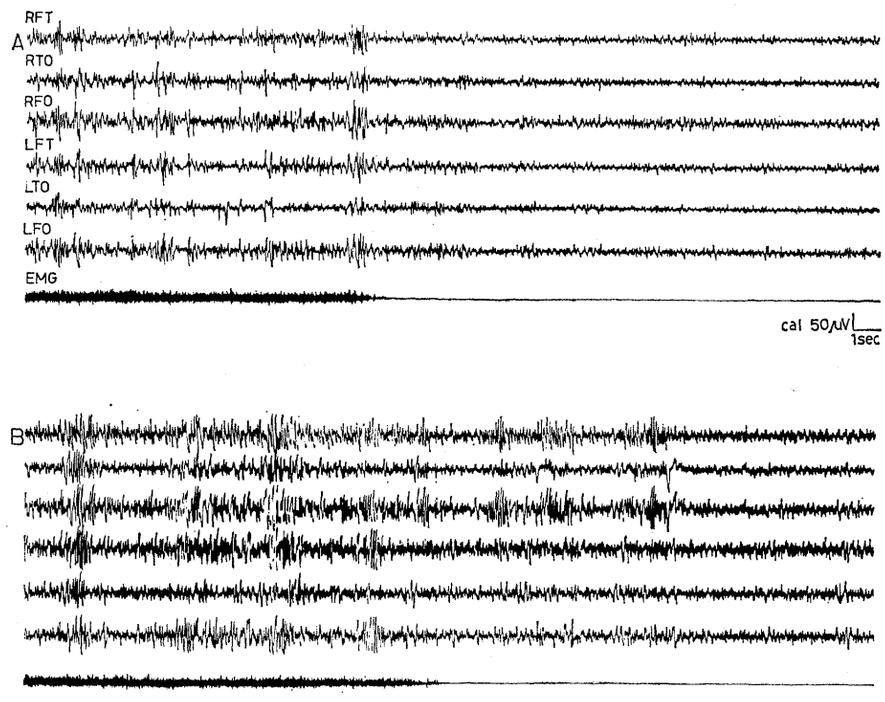

Fig. 2. Electroencephalographic recording 24 hours after pontine (A) and midbrain (B) unilateral (right-side) lesion at the beginning of an episode of desynchronized sleep. No EEG changes are produced by the pontine lesion, while the mesencephalic one is followed by an evident EEG asymmetry due to a delay of the appearance of the typical desynchronization of deep sleep on the ipsilateral hemisphere. *R,* right; *L,* left; *F,* frontal; *T,* temporal; *O,* occipital EEG recording; *EMG,* electrical activity of the posterior cervical muscles.

disconnection from the anterior part of the brain) prevents or retards the appearance of the ipsilateral EEG patterns of desynchronized sleep, while the integrity of even a small part of them, belonging to either "specific" or "aspecific" systems (compare the two anatomical schemata of Fig. 1), permits their normal appearance and development. Unsatisfactory as it is, our hypothesis of a general participation of the rostropontine structures in the EEG desynchronization of the deep sleep phase seems the only one fitting the findings of the present results.

The next experiments constituted a search for the ascending pathways carrying the impulses desynchronizing the EEG during sleep, and was made by unilateral lesions at midbrain level. As with the preceding group of experiments, three types of lesions were made (19 animals): (i) lesions involving mainly "specific" structures; (ii) lesions involving mainly "aspecific" structures (Fig. 3A); (iii) lesions involving both "specific" and "aspecific" structures (Fig. 3, B and C). Electroencephalographic asymmetry during deep sleep, of the type observed following brain stem hemisection (namely, suppression or delayed appearance of the EEG desynchronization in the hemisphere ipsilateral to the lesions) was produced by the lesions of types ii and iii, provided that they were of large size (Fig. 2B).

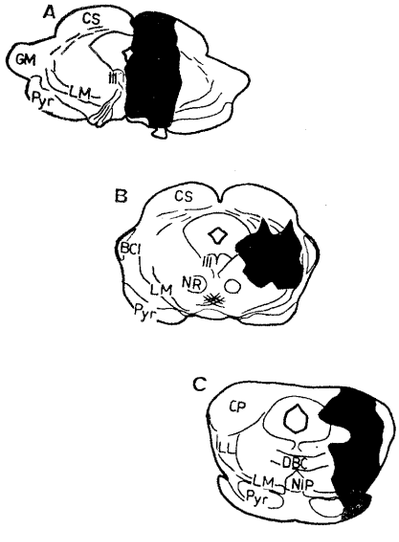

Fig. 3. Mesencephalic unilateral (right) lesions in three different cats. In the three animals the EEG patterns of desynchronized sleep were altered as in Fig. 2B. *BC*, brachium conjunctivum; *CP*, posterior collicullus; *CS*, superior colliculus; *DBC*, decussatio brachium conjunctivum; *GM*, medial geniculate body; *LL*, lateral lemniscus; *LM*, medial lemniscus; *NIP*, nucleus interpeduncularis; *NR*, red nucleus; *PYR*, pyramidal tract; *III*, nucleus of the third cranial nerve.

These findings confirm that the EEG desynchronization of deep sleep is due to or is facilitated by structures located in the low brain stem. If it is accepted, on the basis of previous work (*2*, *3*), that the site of origin of the desynchronizing influence is at pontine level, our findings indicate that this influence is carried rostrally by paths running through the midbrain tegmentum. No evidence for a discrete path has been obtained, EEG changes having been observed following both medial and lateral tegmental lesions (compare A and B in Fig. 3), and no EEG effect having been produced by small lesions (that reproduced in Fig. 3B is one of the smallest effective lesions of our series). As is well known (see *4* for references), so-called "specific" fiber systems pass through the "aspecific" tegmental mesencephalic structures to ascend to the diencephalon. Therefore, our results do not bring crucial evidence of the nature of the pathways mediating the ascending influence desynchronizing the EEG during deep sleep. However, on the basis of analysis of the topographical details of the effective and noneffective lesions in our animals, it is unlikely that the EEG-desynchronizing pathways belong to anatomically known ascending "specific" fiber systems. The hypothesis of their "aspecific" nature indirectly supports the "aspecific" nature of the structures from which the desynchronizing influence would originate (*2*, *3*).

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Genetics of Mitochondria

McDaniel and Sarkissian [*Science* **152**, 1640 (1966)] appear to have demonstrated complementation between two kinds of mitochondria in maize, but they did not ask a perhaps equally interesting question to which their data are also relevant. This is whether the mitochondria from F_1 heterozygotes are superior to a 1 : 1 mixture of mitochondria from the two parental lines. If such a superiority is found, an influence of the F_1 genotype (presumably the chromosomal part) on its own mitochondria would be indicated. The underlining in their Table 1 suggests that two comparisons of this type do not individually give a difference significant at the 5 percent level, but the other relevant comparisons are not made and the matter is not discussed in the text.

This hypothesis cannot be adequately tested by the published results; but of the eight comparisons given, all independent under the null hypothesis, seven are in the expected direction, so $p = .06$. This value should not be taken seriously because the hypothesis was suggested to me by some of the data. The appropriate test, which is of a powerful kind almost never used, is to compare each pair (F_1 and mixed) separately by a two-tailed t test and then to combine the resulting probabilities, most easily by R. A. Fisher's method [*Statistical Methods for Research Workers* (Hafner, New York, 1958)]. Use of one one-tailed test per cross, if randomly allocated, will not affect the assumption of independence and is permitted by the hypothesis. The null hypothesis tested is that all of the differences within pairs are due to chance, or, more broadly, that there is no real difference within pairs in the direction predicted.

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