BEHAVIORAL AROUSAL BY STIMULATION OF THE BRAIN IN THE MONKEY*

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DURING the past five years, many data from animal experimentation have accumulated concerning the physiological mechanisms involved in sleep, arousal, and wakefulness. These observations, made on acute preparations, have indicated that appropriate stimulation of extensive but discrete areas of the central brain stem or cerebral cortex of the monkey may induce a change in the electroencephalogram identical with that observed at the onset of arousal to natural stimuli and called "arousal," "activation," or "desynchronization." Animals capable of so reacting, also exhibit movements of the eyelids and extremities suggesting that such excitation does induce a behavioral shift functionally related to that observed in arousal from normal sleep to awareness.3,13,14

These observations, being short-term and hence complicated by conditions of immobilization, operative trauma, artificial ventilation and other necessary concomitants of acute experimentation, require a reassessment on preparations capable of normal behavior and response. The purpose of the present experiments, therefore, was to test the effect of comparable stimulation applied through chronically implanted electrodes to monkeys examined during states of natural wakefulness and sleep. The results indicate that direct excitation of appropriate regions of the brain may indeed induce behavioral arousal of a naturally sleeping animal.

METHOD AND PROCEDURE

Experiments were made in 19 monkeys (Macaca mulatta) anesthetized with intravenous pentobarbital (Nembutal) and operated upon under aseptic conditions. The electrodes employed for stimulation of deep structures consisted of a pair of stainless steel wires (.005 in. in diameter and 1 mm. apart) insulated except at the tips and fastened to a thicker wire strut. They were introduced through appropriate cranial openings either stereotaxically for deep placements or under direct vision for superficial positioning. These latter placements were in the white matter immediately subjacent to the cerebral cortex.

After proper insertion, the electrodes were secured in place with liquid Kadon.

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Lead wires were brought out through a stab wound in the skin of the suboccipital region and threaded through the links of a leash for subsequent easy accessibility to a stimulator. Wounds were closed with subcuticular sutures. A detailed description of the electrode and methods of implantation for chronic stimulation has been recorded elsewhere.\(^7\)

Eleven electrodes were implanted in deep structures and 27 in the various cortical regions described in Figs. 1 and 2. No animal had more than 4 placements and all stimulation sites were verified anatomically at the termination of the experiment.

After at least 3 days postoperatively, the animal was placed on an illuminated stage in a quiet room from which the examiner could not be seen. It was necessary to perform tests at night when the background noise was of low intensity and the animal could sleep continuously. When no reasonable doubt existed that the animal slept, as indicated by continued immobility, closed eyes and lack of reaction to noises of moderate intensity, stimulation was applied, beginning with subliminal in-

![Fig. 1. "Cortical" electrode placements transferred to the right hemisphere. Black circles=arousal with intensities under 12 V. Thick open circles=arousal with intensities over 20 V. Thin open circles =no arousal. Number indicates the serial number of the animal.](image)

...tensities. The voltage was then gradually increased until the threshold for an overt response (arousal or movements) was attained or until levels of excitation that commonly induced these responses were far exceeded. Stimuli were delivered from a Grass square pulse generator (2–60 V., 1 msec., 10–300 c./sec., 1–15 sec.). Each electrode placement was tested on from 5 to 15 different nights for a period of up to 4 months after implantation. It was possible, therefore, to record typical responses photographically. Similar excitation was applied to the animal when it was awake.

In order to assess, simultaneously, the EEG and behavioral changes associated with arousal, observations were made upon 2 animals (#76, #77) with electrodes placed in cortical and subcortical loci. Sites selected were the reticular formation, the superior temporal gyrus and the cingulate gyrus. All electrode placements in these experiments were paired so that the area of excitation could be monitored electroencephalographically for afterdischarge. Additional EEG recordings were made in these animals from points in the brain stem and cerebral cortex distant from the stimulated site. Needle contacts were inserted into the skull to record activity on both sides of the cranial vault.