Elevation in Brain Temperature during Paradoxical Sleep

Abstract. *During ordinary sleep, the temperature of the rabbit brain tended to drop, but during paradoxical sleep it rose sharply 0.1° to 0.4°C, a greater elevation than was observed during arousal. Changes in body temperature generally did not parallel the alterations in brain temperature. Shifts of direct-current potential in the brain are basically independent of the changes in brain temperature.*

Paradoxical sleep (rapid-eye-movement or activated sleep) is a peculiar state observed in many animals, in which behaviorally the subject shows a most relaxed posture and minimal responsiveness to external or brainstem stimuli, while the electrical activity of the brain, shown by electroencephalogram (EEG), evoked potential, and d-c potential, is generally at its highest level (*1–5*). In human sleep this state is often observed to be accompanied by dreams (*6*).

To clarify further the nature of paradoxical sleep, we chose a study of changes in brain temperature as an indicator of alterations in brain activity other than the more commonly studied electrical changes and investigated relations between these respective activities.

Twenty-one New Zealand white female rabbits were used. Electrodes (stainless steel for EEG and Ag–AgCl for d-c recording) were implanted stereotaxically under pentobarbital anesthesia. The occipital bone was chosen as the reference point of d-c recording. For recording temperature, copper-constantan thermocouples sealed in glass tubing (diameter, 0.7 mm) were implanted (time constant was less than 2 sec). We used a Grass electroencephalograph, model 111D, for recording EEG's, and a two-channel Grass polygraph system and two Varian servo-recorders, model G-10, mounted over the EEG pens, for recording d-c potential and temperature. The unrestrained and unanesthetized rabbit was kept in a sound-attenuated box, and behavior was observed through a mirror window.

Simultaneous recordings of temperature from two regions of the brain revealed that temperature changes in various parts of the brain, including the neopallium, posterior hypothalamus, and pons, roughly paralleled changes of temperature in the preoptic region during sleep–arousal sequences. This region registered temperature changes somewhat earlier (several seconds) than other parts of the brain did.

During slow-wave sleep, the temperature of the brain tended to drop rather abruptly in many cases, but during paradoxical sleep, the brain temperature showed a very marked elevation (up to 0.4°C), and there was a tendency for the longer periods of paradoxical sleep to be correlated with the highest elevations in temperature. Usually the elevation in temperature associated with an arousal reaction was less than that accompanying paradoxical sleep (Fig. 1).

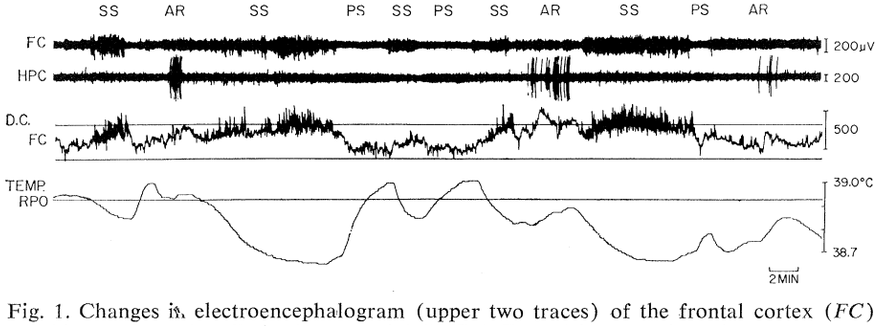

Fig. 1. Changes in electroencephalogram (upper two traces) of the frontal cortex (*FC*) and hippocampus (*HPC*), in d-c potential (*D.C. FC*), and in preoptic-region temperature (*TEMP, RPO*) during slow-wave sleep (*SS*), paradoxical sleep (*PS*), and arousal (*AR*). Upward deflection of d-c recording denotes a positive shift. During slow-wave sleep a marked positive shift of d-c potential and dropping of brain temperature are seen, whereas during paradoxical sleep a negative d-c potential shift and elevation of brain temperature are recorded. During simple arousal, initial negative shifts of d-c and temperature elevation are recorded, but when arousal was related to licking (indicated by high amplitude artifact in the hippocampal channel) a positive shift of d-c potential is seen.

In three rabbits which had thermocouples in the pons, the elevations of temperature during paradoxical sleep occurred later in the pontine reticular formation than in the preoptic region. Delays in elevation of temperature in the pontine reticular formation as compared with the preoptic region were approximately 10 sec. Usually the temperature elevation of the preoptic region occurred within 7 to 15 sec after the onset of paradoxical sleep, as gauged by changes in the EEG.

During paradoxical sleep, temperature changes in other parts of the body were not as marked as those within the brain. For instance, thermocouples implanted under the skin of the neck or in the uterus did not show significant parallel changes with the rise in brain temperature during paradoxical sleep, whereas, after eating, or drinking of cold water, temperature changes in these regions paralleled those observed in the brain.

To what extent certain underlying physiological mechanisms exert similar influences on changes in d-c potentials and in temperature are problems still to be solved. However, d-c potential shifts, which are among the slowest electrical processes of the brain, and temperature changes are not two aspects of the same phenomenon: The elevation in temperature due to an arousal reaction was less than that accompanying paradoxical sleep, even when the two states showed similar degrees of negative d-c shift. A marked elevation in the temperature of the preoptic region was also seen to accompany the positive d-c shift. The results indicate that the changes in d-c potential and in temperature are fundamentally independent phenomena.

The question of whether the elevation in brain temperature during paradoxical sleep (*7*) is due to a regional rise in metabolic activity in the brain or to an increase in cerebral blood flow is currently under investigation.

Elevation of brain temperature during paradoxical sleep is consistent with the concept of high activity in the brain during this peculiar state, and as far as the forebrain is concerned, paradoxical sleep may represent not a restorative deep type but, rather, an active state of sleep.

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7. The present results were reported at the annual meeting of the Association for Psychophysiological Study of Sleep in Washington, D.C., March 1965. At the same session Rechtschaffen, Cornwell, and Zimmerman of the University of Chicago reported quite similar elevations in temperature in the cat brain during paradoxical sleep.
8. Supported by grants from NIH (NB 01162) and the Ford Foundation. We thank J. N. Hayward for advice in making thermocouples and David Whitmoyer for technical assistance.

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Prolonged Excitation in the Visual Cortex of the Cat

Abstract. *Intense light flashes produce maintained increased in cortical activity not dependent on continuous excitation from the retina.*

Cells in the visual cortex of the cat respond to precise stimulation in specific ways, but these responses are transient (*1*). Other workers have shown that the tonic output of the retina is modified by changes in illumination (*2*). In man long-term changes in absolute threshold may be produced by exposure to bright sunlight (*3*) and, following a brief, intense stimulus, a characteristic persistence of vision commonly referred to as an after-image occurs.

We have produced persisting changes in the firing rate of cells in the primary visual cortex of the cat following an intense, diffuse light flash to the contralateral retina (*4*). We now present results which confirm our original findings and in addition show that repeated flashes of equal intensity may produce step-like increases in firing rate. The persistence of these effects is a cortical phenomenon and is not due to a maintained increase in retinal output.

Twenty cats weighing between 3 and 5 kg were anesthetized with ethyl chloride followed by ether. After insertion of tracheal and venous cannulae, a mid-collicular section was made through the brainstem (*5*) and the animals were then maintained by artificial respiration. The skull and dura were removed to expose a large area of the visual cortex of one hemisphere. A well, filled with warm mineral oil, was made by suturing the scalp to a ring above the head (*6*). The eye to be used in the experiment was protected from desiccation with a contact lens. The cat's temperature was maintained within 0.5° of 37°C by a heating pad controlled by a thermistor probe inserted in the rectum. Anesthesia was not maintained, but the preparations were paralyzed with continuous intravenous infusion of 10 mg of gallamine triethiodide (Flaxedil, M&B) per hour. Continuous infusion was employed because it had been found in a previous study that a single injection of 40 mg, as normally used, sometimes stopped spontaneous unit activity and reduced the amplitude and high-frequency components of the electrocorticogram. In some cases the preparation was kept for 2 or 3 days without any apparent deterioration or change in properties of the cortex. To do this it was necessary to supply glucose intravenously and penicillin by intramuscular injection.

Glass micropipette electrodes with internal tip diameters of 1 to 5 μ and resistances between 0.2 and 1 megohm, filled with 90-percent saturated NaCl solution, were used to make extracellular recordings of unit activity; data were stored on magnetic tape for subsequent analysis. The electrodes were suspended from a steel wire tensioned in such a way that they were effectively weightless and hence free to move with the cortex (*7*). Single units could therefore be "held" for several hours without dislodgement of the electrode tip from the recording site by movements caused by heartbeat and respiration.

An intense, diffuse flash was provided by a 1000-joule flash bulb fired 15 cm from one of the cat's eyes, the pupil of which had been dilated with atropine. No attempt was made to correct for refractive errors. The other eye was covered with an opaque shield. In some experiments pressure of 100 g was applied to the contact glass to produce retinal ischemia (*8*). In pilot studies the effectiveness of the ischemia in preventing transmission from the retina was tested by stimulation with a flashing neon bulb (Fig. 1).

Recordings were made from 75 cells. Figure 2 shows the effect of a single flash on the mean firing rate of a single cell in the primary visual cortex. Characteristically, the unit exhibits an immediate sharp discharge

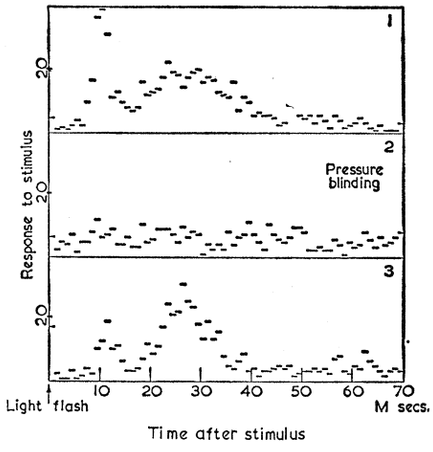

Fig. 1. Post-stimulus histograms showing the effect of "pressure-blinding" on the response of a cortical cell to a flashing light at the retina. Each histogram is the total response of the unit to a flash repeated once a second for 3 minutes: part 1 is before pressure-blinding, part 2 during, and part 3 after. Ordinates are number of impulses recorded from the unit at time after flash on the abscissa.

followed by a "silent" period of up to 30 seconds. From this point, activity increases steadily. Peak activity is normally attained within 10 minutes of the flash. Firing rate may then subside to the control level, the whole sequence taking approximately half an hour. About 70 percent of the cells tested with a single flash responded in this way.

Figure 3 shows the effects of flashes repeated at regular intervals; their effects summate, confirming the finding reported in our previous note (*4*).

While individual flashes invariably provoke an immediate burst of firing, long-term changes are not always present. Flash 2 in Fig. 3, for example, seems to have had no tonic effects on maintained, or tonic activity, though the transient post-stimulus burst was observed. Flashes 3 and 4, however, show marked summation effects, and the remaining flashes hold the mean firing level at a generally constant value. (The time scale of Fig. 3 is too coarse to show transient responses; in any case these responses have little effect on mean firing rate, for they include a brief burst of firing followed by a period of inactivity.) Flash 3 clearly provoked a surge of firing that reached a peak approximately 5 minutes after the flash, the rate subsequently falling to the basic level. This response was consolidated by the flash 4, which produced a large increase in firing rate, reached a peak 9 minutes