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OBSERVATIONS ON THE UNIQUE ELECTRICAL DISCHARGE FOLLOWING STIMULATION IN MONKEY BRAIN*

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This is a further report to one given before this group at the December 1960 meeting.1 We have continued to observe the unique discharge reported in 1960, and have increased our observations to include a further eleven monkeys with 26 placements, totaling 51 ports (paired electrodes). This discharge continued to show a latency of onset accompanied by DC shifts, with a frequency 1½ to 4 cps., occasionally shifting to harmonics of these frequencies. The duration of the discharge continues to be lengthy.

TECHNIQUE: The techniques for electrode design and placement remained unchanged.1 The parameters of stimulation were defined and are set out below using the Grass SB-4 stimulator.

- Frequency: 4 - 400 cps.
- "Voltage": 4 - 16 volts.
- Current: 2.5 - 3.5 M.A.
- Duty Cycle: 70%
- Stimulation: 5 - 10 seconds.

The further areas stimulated included the thalamic structures, cingulate gyrus, hippocampus, septal region, cerebellum, parietal cortex and parietal white matter. Areas previously stimulated were again stimulated using additional animals. The particular areas in the above group are set out in Table I.

In addition to monkey brain, similar stimuli were applied to cat brain (cortex and white matter of parietal lobe), human and monkey blood (whole blood, serum and clot) and finally human cerebral spinal fluid.

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Areas of stimulation in monkey brain.

Observations

Behavioral Changes

The behavioral changes observed in the limbic system, mesencephalic reticular formation and hypothalamus merely confirmed those observations reported in 1961 at the III World Congress of Psychiatry as follows:

"In the limbic system, using 2 - 8 volts, the following responses were observed: (1) alerting or impairment to perform a learned task, (2) smacking, licking and chewing, (3) gritting of teeth and trismus, (4) serpent-like darting of tongue, (5) guttural cries, (6) yawning (7) pupillary changes, (8) eye blinking, (9) blunted emotional tone, post stimulus, (10) lethargy, post stimulus and (11) sexual responses.

On stimulating in the mesencephalic reticular formation, using 2 - 6 volts, the following responses were observed: (1) alerting or impairment to perform a learned task, (2) spastic chewing movements and inability to swallow food, (3) gritting of teeth, (4) restlessness, (5) acute agitation or rage and (6) varying stages of impaired consciousness, even to the point of trance-like states.

On stimulating in the hypothalamus, using 2 - 6 volts, the following responses were observed: (1) pupillary changes, (2) restlessness, anxiety and acute panic, (3)
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guttural cries, arrest phenomena, (4) somnolence, (5) ejaculation and urination, (6) gritting of teeth and (7) head turning."

The behavioral changes noted on stimulating other than the above areas are set out below:

Monkey #37 with depth electrodes in the midline interpeduncular area screamed on stimulating this area with low voltage (1.5 V).

Monkey #39 with depth electrodes in the left dorso-medial nucleus of the thalamus (inferior electrode pair) showed grimacing and slight deviation of the head to the left, both arms flexed and fingers extended. On stimulating the superior pair of electrodes, the only response was turning of the head to the left.

Monkey #33 with depth electrodes in the cerebellum, stimulation using 10 V gave no observable response.

Monkey #33 with depth electrodes in the right nucleus ventralis lateralis of the thalamus showed, on stimulation at voltages below 15 V, forced grasping of the chair arms, frequent scratching of both soles of the feet, and the animal would not perform a learned task during stimulation. At 15V (highest voltage used), the animal extended the left arm and leg, and sat rigidly during the stimulation. During approximately 2 weeks when the animal was stimulated 4 to 5 times per day, foot scratching became more frequent without stimulation, particularly when head holder was placed on the animal, probably due to conditioning.

Monkey #35 with depth electrodes in the right nucleus centralis lateralis of the thalamus on stimulation with 10 V showed tonic seizures involving the entire musculature of face and limbs with vocalization and pupillary dilatation without deviation of the eyes. With lowered voltage so as not to produce these tonic seizures, the animal could perform a learned task at pre-stimulus efficiency.

Cat #1 with depth electrodes in the parietal white matter stimulating up to 10 V produced no significant change in behavior.

OBSERVATIONS

Post Stimulus Discharge

Further to the unique discharge we have described previously,\textsuperscript{1,2} (following stimulation and the "usual" after discharge), the appearance of this discharge in other than the electrodes being stimulated remains variable from monkey to monkey and from day to day in the same animal. On rare occasion the discharge remained confined to the electrode pair (port) stimulated. More often it spread to the adjacent port (2½ mm. distant in the vertical plane). Usually the discharge was transmitted to distant structures, both ipsilateral and/or contralateral, (sometimes accompanied by spread to adjacent port, but on several occasions completely bypassed the adjacent port, yet was conducted to distant structures).
ELECTRODE PLACEMENT (MAGGIE)

*Note: Discharge by-passed the cortex

Figure 1
Location of epidural and deep electrodes in "Maggie".

Figure 2
"After discharge" following stimulation of epidural electrode in "Maggie".
An interesting observation concerning the relationship of the cerebral cortex in this phenomenon was gained from the stimulation of the monkey brain through a pair of epidural electrodes adjacent to the left parietal cortex (Figure 1). The delayed discharge appeared in a port located in the white matter of the parietal lobe more than 10 mms. away from the stimulating port, but did not appear at the port in the adjacent parietal cortex immediately above the "responding" port in the parietal white matter, (Figures 2, 3, 4, and 5). In this present series of monkeys this unique discharge (oscillation) was never observed in the cerebral cortex, although in the

**Figure 3**

"Delayed oscillation" at site of epidural stimulation in "Maggie".

**Figure 4**

Transfer of "delayed oscillation" to parietal white matter.

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group of monkeys reported December 1960 there was one occasion on which the cerebral cortex was definitely activated following the appearance of the discharge in the amygdaloid nucleus.

The following figures are examples of the unique discharge:

Figure 6. Sample of discharge from the right nucleus centralis lateralis of the thalamus. This particular sample shows the harmonics of the discharge (oscillation) which were most often seen during the latter part of this oscillation.

Figure 7. Shows phase shift in this discharge.

Figure 8. Shows a spontaneous unique discharge (not following stimulation) from the right cingulate gyrus.

Figure 9. Shows the unique discharge from the parietal white matter in the brain of a cat.

Figure 10. Is a diagram of the recording system used to study this oscillatory phenomenon as it appears in the blood and spinal fluid (humans and monkeys). This followed the suggestion that we were dealing with a molecular rather than a cellular phenomenon.

Figure 5
“Slowing” of the oscillation with a prolonged appearance.
Figure 6
An example of harmonics present in a "delayed oscillation".

Figure 7
An example of a phase reversal of the delayed electrical discharge.
Figure 8

A spontaneous “oscillation” in cingulate gyrus without any stimulation.

Figure 11. Shows the appearance of this discharge following stimulation of monkey serum. In this experiment whole blood, serum and clot were separately stimulated at various voltages, 80 per cent duty cycle and 400 cps. The discharge (oscillation) appeared in the serum with the least voltage (10 V). An increase to 12 V produced it in whole blood. In both instances the current flow was 3.5 MA. In the case of the clot the discharge never appeared on even raising the voltage to 60 V, and at 60 V no current flow could be detected within the sensitivity range of our equipment (250 M U A). Human C.S.F. was studied similarly and our results are shown in figure 12 and 13, the discharge lasting 15 minutes. During this discharge another recording electrode was inserted into this system approximately 2 mms. from the original electrode. This second electrode picked up the discharge, but with the identical recording gain showed only half the amplitude.

Figure 14. Shows radiologically the depth electrodes in the anterior left hippocampus, the posterior left hippocampus and in the right dorso medial nucleus of the thalamus.
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STIMULATION OF BLOOD OR SPINAL FLUID

A diagram of the technique used in studying blood and spinal fluid.

Figure 10

The "oscillation" in monkey blood.

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Initial appearance of the "oscillation" following stimulation of human spinal fluid.

The persistence of the "oscillation" in human spinal fluid.
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Figure 14
Radiograph of typical electrode implantation.

DISCUSSION

It is no small task to attempt to bring experimental observations into relationship with the more accepted views of the electrical and physiological activity of the nervous system. We have proved, at least to our own satisfaction, that this phenomenon of a continuous electrical oscillation within the brain substance is indeed a real episode of organic activity and cannot be dismissed as some "accident of technique".

At first thought it seems somewhat suspect that these observations have been confined to our own laboratory, but this is not the case. It seems that a similar electrical discharge has been seen before; for example, the experiments of Sem-Jacobsen with egg albumin, or the slow discharge from the human amygdala reported by Heath.
Choh-luh Li has seen oscillation of the resting membrane potential of muscle fibers, and monorhythmic discharges in the clinical EEG are most familiar.

Our introduction to this phenomenon was most serendipitous. The failure to change the delay setting of the square wave stimulator as the frequency was increased produced a pulse with a duty cycle approaching d.c. current. This type of stimulus has long been considered taboo because of an alleged tendency to produce electronic lesions. Careful pathologic examination of our post mortem specimens has yet to give evidence of any significant electrolytic lesions. In view of this we are not concerned about relating the uniqueness of this discharge to our laboratory.

As was stated initially, the purpose of the discussion is to picture the results of the experiment in relationship with a more total picture of electrical and physiological activity of the nervous system.

In this case the first step in describing such a relationship is to resolve the appearance of this discharge in brain, blood and spinal fluid. Two assumptions may be made: (a) either the underlying mechanism is the same for all three or (b) it is different. It seems to us that the first assumption may be the easier to defend. If the first assumption is true, then the mechanism of this phenomenon must lie in a factor common to all, one of which would be protein molecules capable of accepting and rejecting electrical charge. In such a case the appearance of this activity in the central nervous system could be due not just to the membrane of the neuron, but to membranes of all cellular elements plus substances in the intra and extracellular fluid. The tabulating of our results suggests that, indeed, the neuronal membrane may not be involved in this phenomenon. During and after stimulation of the brain the electrical recording shows considerable activity that is generally referred to as “after discharge”, and is usually related to changes in the animal behavior, and in some of our monkeys their behavior was altered as manifested by seizures ranging from focal minor seizures to generalized convulsions. The “oscillation phenomenon”, however, was always delayed until the after discharge had disappeared and the behavioral pattern had returned to “normal”. This oscillation continued sometimes for hours with no definite signs of behavioral changes.

The quality of this discharge seemed in inverse relationship to the neuronal population. No quantitative studies were carried out, but certainly the best examples of this disturbance were from areas that were predominantly white matter, the cerebral cortex being the most resistant. An excellent example of this is evidenced by observations on a monkey where the disturbance “jumped over” the cortex from an origin on the dura to the subcortical white matter of the parietal lobe.

Many questions concerning these phenomena can be raised, even on the basis of the information that has just been presented. For example, the transmission of this disturbance to distant structures. This suggests that communication pathways are involved and poses the question of whether this discharge serves as a signal or a block to these pathways.
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The apparent lack of behavioral changes related to this oscillation unfortunately provided no clues to this aspect of the problem. If we assume this oscillation does not significantly affect neuronal communication then the question is posed as to the validity of this activity as a representation of cerebral electrical activity as presently understood. If this is the case, then we must question all EEG cerebral electrical activity on the same basis for the parameters of measuring these are essentially the same.

Such a discussion is beyond the scope of this paper and we only would like to suggest this question.

SUMMARY

Further observations of behavior and electrical discharges (oscillations) are reported on stimulation of areas in the brain of the Macaca mulatta. The results of similarly stimulating monkey whole blood, serum, clot and human spinal fluid are reported. The parietal lobe of one cat was stimulated and behavioral and electrical results noted.

CONCLUSIONS

Previous observations on behavioral changes through stimulation in various areas of the brain of the Macaca mulatta, predominantly areas involving the reticular and limbic formations, have been confirmed.

Observations of the unique discharge previously reported following stimulation in the limbic and reticular formation structures have shown this discharge (oscillation) producible in other than the above structures of the brain with the exception of the cortex. It is apparently not limited to monkey brain since it occurred also in the cat brain.

A similar, if not identical phenomenon has been produced on appropriate stimulation of monkey blood and human cerebral spinal fluid.

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