THE LOCALIZATION OF THE CENTER DEALING WITH THE TONIC EXTENSOR SEIZURE OF ELECTROSHOCK

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Toman, Swinyard and Goodman (1) found that the extensor component of tonic convulsion produced by supramaximal electroshock stimulation disappeared after the administration of several anticonvulsant drugs. According to this fact they presented a new method to evaluate antiepileptic drugs in experimental animals. Using the similar method in rabbits, we confirmed (2) that phenobarbital, diphenylhydantoin, cyclohexenylmethylbarbituric acid and phenylacetylene in non-depressant doses protect against the tonic extensor seizure of electroshock.

The present study is an attempt to find what part of brain is responsible for the manifestation of the tonic extensor seizure. Solution of this problem may contribute in deciding the site of action of antiepileptics.

METHODS

Seizures were produced in adult rabbits, weighing 2–3 kg, by a simple electroshock apparatus. The ordinary 100 volt electricity of 60 cycle alternating current with stimulus duration of 0.2–0.5 sec. was applied to the animal through the needle electrodes thrust into hypoderma at posterior corners of both eyes. This stimulating method is quite simple and convenient, and the intensity of the current is always supramaximal, as Kan (3) in our laboratory investigated it in detail.

The seizure pattern in the normal animal consists of the following phases:— (1) tonic flexor convulsion (lasting average 4 sec.), (2) tonic extensor convulsion (lasting average 14 sec.), (3) clonic convulsion, (4) running movement, (5) post-convulsive depression.

Anticonvulsant drugs abolish the tonic extensor component in a small dose, all tonic convulsions in a moderate dose and both tonic and clonic phases in a large dose.

Operations to cut the brain were performed under temporary ether anesthesia, occasionally without anesthesia. Artificial respiration was adopted if necessary, but neither the carotid nor the vertebral artery was ligated, while the bleeding was stopped with tampons and gelatine sponges.

The levels of cutting were as follows:— (1) bilateral excision of cerebral
hemisphere, (2) transection between thalamus and midbrain, (3) intercollicular transection, (4) excision of cerebellum, (5) transection between midbrain and pons, (6) transection at several levels of pons and medulla oblongata.

After the operation, electroshock was applied to the animal to observe whether the tonic extensor component was maintained or not. When the experiment was over, the whole brain was drawn out and the section was ascertained.

RESULTS

a) Sections not modifying the tonic extensor component

All transections and excisions of brain higher than the upper border of pons (the levels of (1)—(5) described above) did not alter the tonic extensor component of electrically induced convulsion, though the clonic phase disappeared generally after the removal of higher brain.

The most caudal section we gained without abolishing the tonic extensor component, was the plane of which the dorsal side corresponded to the upper line of tuberculum acusticum and the ventral side to the upper border of trapezoid body (Fig. 1).

b) The section eliminating the tonic extensor component

Every total transection below the medulla oblongata abolished the tonic extensor component. The most rostral section we succeeded in eliminating the tonic extensor phase, was the plane of which the dorsal side was just under tuberculum acusticum and the ventral side was the lower border of trapezoid body (Fig. 2).

The part between this section and that of Fig. 1 must be responsible for the presentation of tonic extensor convulsion.
c) Bilateral incision of lower pons

At the level of Fig. 2, bilateral horizontal incision with the depth of one third of the diameter was performed in other intact animals, but this procedure failed to eliminate the tonic extensor phase (Fig. 3).

It is presumed, therefore, that the medial part of pons may be responsible for that.

d) Efficacy of antiepileptics after the removal of higher brain

The intravenous injection of a small dose of phenobarbital sodium could abolish the tonic extensor phase of the animal, whose brain had been transected between midbrain and pons.

DISCUSSION

Two experimental data are presented by us;—(I) the tonic extensor component of electroshock convulsion is abolished by several antiepileptic drugs in relatively small doses, (2) the rostral brain higher than midbrain is unnecessary for the presentation of tonic extensor convulsion. To admit these data simultaneously, two possible mechanisms are conceivable:—(1) Antiepileptics act on the lower part of the brain where the center dealing with the tonic extensor seizure exists, (2) they act on the higher center at first, from where a depressing impulse develops to the lower brain to modify the tonic extensor seizure. From our result that phenobarbital is effective after removing the higher brain, we can dispense with the latter conception.

The part of the brain affected first by barbiturates is accepted usually as hypothalamus. The results of the present investigation suggest, however, that anticonvulsants involving barbiturates have a greater influence on the lower part of the brain such as pons, because they can modify the tonic extensor seizure of which the center lies in pons, in such a small dose that they cannot display any hypnotic action.

According to our other experiments (2), the intracarotid injection of phenobarbital in a small dose can manifest a hypnotic action without modifying the tonic convulsion of electroshock, while the intravertebral administration of the same drug can abolish the tonic extensor phase without provoking hypnosis. These data make us believe that hypnotic and anticonvulsant actions do not belong to the equal mechanism issued from the same part of the brain. The
similar conception has been suggested by Stille (4), who observed that the anticonvulsant action of diphenylhydantoin was potentiated by phenylisopropylamine, though the former sedative action was replaced by the latter exciting action.

CONCLUSION

The center dealing with the tonic extensor seizure induced by electroshock lies in the lower part of pons in the rabbit. Transection or excision of the brain higher than pons does not modify the tonic extensor seizure, which can be abolished by antiepileptics. It is assumable, therefore, that antiepileptic drugs affect the lower part of the brain more than is usually accepted.

REFERENCES

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