Production of Anxiety Behavior and Avoidance Conditioning by Stimulation of Bulbar Reticular Formation. (23908)

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Avoidance behavior and conditioning during electrical stimulation of various cortical and subcortical areas have often been reported (1-4). This report presents some observations on behavior of conscious and unrestrained cats during stimulation of the bulbar reticular formation. These observations were made while we were attempting to produce bulbar inhibition of motor activity in intact and unanesthetized cats(5,6).

Procedures. Bipolar electrodes were aseptically and stereotaxically implanted in the bulbar inhibitory areas previously described by Magoun and Rhines(7), following modification of technics used by Segundo *et al.*(8). Stimulus parameters and criteria of placement have previously been described(5,6). Five animals were studied 72-322 hours postoperatively and observations were made on behavioral activity and learned avoidance responses during stimulation of ventro-medial bulbar regions. Learned avoidance responses were induced and measured by 2 different instrumental conditioning technics. The first procedure involved random escape from a round platform in response to bulbar stimulation which was paired with a buzzer sounding 8 seconds previously. The second type of experiment involved a buzzer and light combination stimulus which was followed in 8 seconds by bulbar stimulation. The bulbar stimulation could be avoided when the animal learned to respond by jumping a 6-inch fence barrier. Measures were made of response latencies and percentages of correct responses. Histological confirmation of electrode placements was made following sacrifice.

Results. The usual behavioral response during bulbar stimulation can be described as a series of gradual and consecutive changes from an initially increased but non-directed awareness to apparent uneasiness, apprehension, or anxiety to an ultimate stage of obvious fright. In the last stage, animals which had been extremely friendly prior to stimulation, exhibited such reactions as crouching, scratching at the floor, running behind chairs, hissing and yowling in a highly agitated fashion. Frequently pupillodilatation and piloerection were also noted. Although each animal reacted individually to electrical stimulation, these responses were almost identical with their particular individual reactions to such stressful stimuli as startle noises, squirts of water, etc. However, reactions during bulbar stimulation were not stimulus directed. Similar responses have been described for the monkey by Segundo *et al.*(8) during electrical stimulation of certain cortical and subcortical areas.

Masserman(9) has emphasized the necessity of using conditioning experiments to distinguish between an apparent emotional response and an induced motor response (non-conditionable hypothalamic "rage" reaction of Masserman). To determine whether the responses reported here reflected some negative effect or were complex motor reactions directly induced by stimulation, the animals were conditioned to avoid bulbar stimulation. The block diagram of Fig. 1 indicates the proportion of correct responses in a typical "fence-jumping" experiment. Median response times are indicated by the curve shown in Fig. 1 and appear to approach asymptote at 40 seconds. This long latency corresponds closely to observed time interval required for the gradual succession of behavioral changes described above, in which animals demonstrate a progression from increased awareness to an obviously unpleasant effect after onset of stimulation. In random escape response procedures, cats learned to escape the unconditioned stimulus but did not demonstrate any directional tendencies. This fact suggests that classical sensory components are probably not directly involved in this phenomenon. One control animal stimulated in the dorsolateral medulla manifested jerking and limited turning movements of the head

without exhibiting any of the behavioral phenomena described above.

A photomicrograph of the placement of a typical stimulation electrode is shown in Fig. 2. All electrode placements were similarly limited to ventromedial bulbar reticular areas except for the control preparation described above. Electrode placements generally varied from 5 mm to 12 mm ventral to the floor of the fourth ventricle and in an area bounded 4 mm bilateral to the midline. Antero-posterior dimensions were limited by the cochlear nucleus and the most caudal limits of the medulla. At no time were the classical sensory or motor tracts or cranial nerve nuclei impinged upon.

Conclusions. Behavioral responses, characterized by signs of anxiety, do not solely originate from suprabulbar sites, but also may be produced from ventromedial reticular areas of the medulla. The close correspondence between median response latencies in avoidance conditioning produced during stimulation in this region of the medulla and time intervals elapsing between initial increased arousal and appearance of overt signs of apprehension resulting from the same stimulation, suggests development of a negative "effect" resulting in avoidance behavior rather than direct induction of complex motor responses. Absence of directional tendencies in random escape experiments implies that classical ascending sensory pathways are not directly involved in these effects. Apparently the medullary reticular formation not only participates in respiratory, vasomotor and spinal reflex events but is also involved in certain aspects of conscious behavior associated with emotional signs.

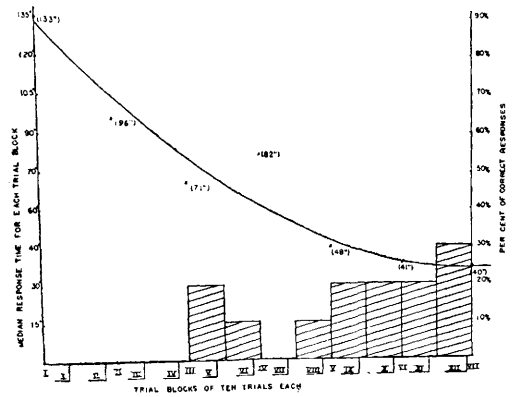

FIG. 1. Correct responses rate and median latency times in a typical "fence-jumping" avoidance conditioning experiment during bulbar stimulation. Each bar represents % correct responses in 10 trials for one animal; 12 hr separated each block of 10 trials. The curve represents change in median *latency* times (in sec.) during the 7 groups of 10-trial blocks for one animal; these are taken as criteria of median *response* times.

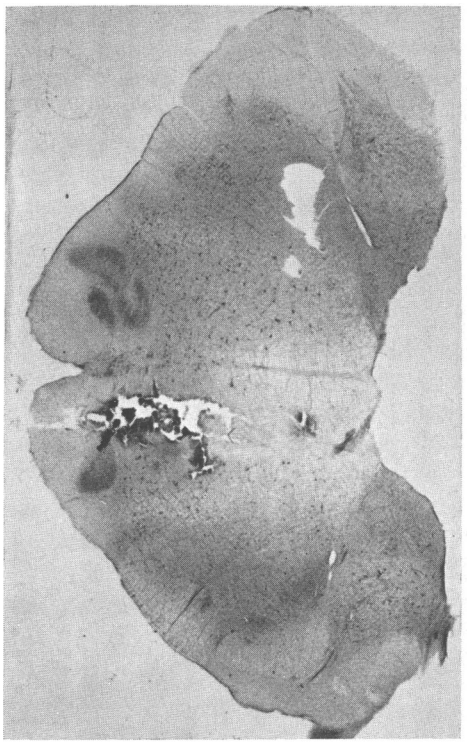

FIG. 2. An implanted stimulating electrode site in ventromedial bulbar reticular formation typical of experiments described in text.

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