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Simple Technique for Study of Cortical Arousal Response

Abstract. A new method is described for eliciting a stable spindle burst response after the production of unilateral lesions in the reticular formation of the cat. This permits quantifying the effects of stimulation of the reticular activating system, either electrically or by injection of epinephrine, on the cortical arousal response.

The cortical arousal response, produced by either direct or indirect stimulation of the reticular activating system, has been used extensively as a test for drug action since its first description in 1949 (*1*). Unfortunately, unless facilities for elaborate electronic analyses are available, the evaluation of the magnitude and duration of this response is quite subjective. We herein describe a method for quantification of this response in cats by the use of unilateral brain stem lesions which produce a stable ipsilateral cortical spindle burst response. This is abolished during electrical or pharmacological stimulation of the reticular activating system.

Bremer in 1935 (*2*) discovered that transection of the anterior portion of the midbrain (*cerveau isolé*) led to spindle bursts which recurred during several hours. Lindsley *et al.* (*3*) reported on lesions in different areas of the brain stem and demonstrated stable spindle burst activity after mesencephalic and basal diencephalic bilateral lesions.

As an extension of their work we placed complete unilateral electrolytic lesions stereotaxically, using the coordinates described in the atlas of Jasper and Ajmone-Marsan (frontal, 3; horizontal, −2; vertical, 0 to 4) (*4*). The exact frontal placements were not critical for the production of the spindle bursts. There was an indication, however, that the response decayed somewhat more rapidly as the lesion was moved caudad or cephalad.

Surgery was performed under ether anesthesia; the animal was subsequently immobilized with gallamine triethiodide and maintained on artificial respiration and local anesthesia with 1 percent procaine hydrochloride. The animals were in a sound proof room and were kept as comfortable as possible during the recording sessions.

Some experiments were carried out using the *encephale isolé* preparation and, although the burst characteristics and background activity were slower, the response remained as stable as that seen with the immobilized animal. After a 1 hour recovery period, spontaneous electrical activity recorded from the cortex ipsilateral to the lesion showed the spindle burst phenomenon. The rate of bursting varied from 8 to 15 bursts per minute from animal to animal, but was relatively constant for a given animal. A stable response could be maintained for 3 to 4 hours if the animal remained in good condition. The spindle bursts could always be recorded from the suprasylvian and posterior sigmoid gyri and sometimes from the anterior sigmoid gyrus.

Since the contralateral side of the brain stem was intact, electrical or drug stimulation of the reticular activating system could still produce a cortical arousal response. This response was manifested by a disappearance of the spindle burst activity and, in some cases, by an increase in the frequency of the background activity of both sides of the cortex. The duration of the abolishment of the spindle bursts was directly correlated with the strength of the electrical stimulus or the dose of epinephrine, within normal physiological ranges. Figure 1 illustrates the effects of sciatic nerve stimulation and of intravenous epinephrine on the cortical spindle bursts in a cat with a unilateral brain stem lesion.

The disappearance of the spindle bursts lasted throughout the duration of the sciatic stimulation and about 10 to 15 seconds after the end of the stimulation. The rate and frequency of the electrocorticogram on the contralateral cortex seemed to return to prestimulus activity about 4 or 5 seconds after the return of the bursts on the ipsilateral side. Intravenous epinephrine caused the burst response to vanish about 10 seconds after the beginning of the injection (see *5*). The bursts began to reappear about 30 seconds later and sometimes showed a secondary effect of an increased rate for about 10 to 20 seconds before returning to the preinjection rate (*6*).

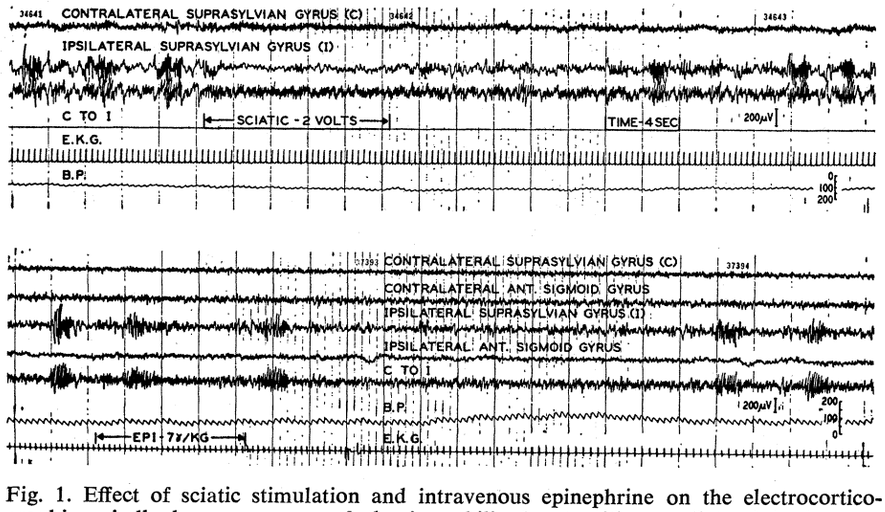

Fig. 1. Effect of sciatic stimulation and intravenous epinephrine on the electrocorticographic spindle burst response of the immobilized cat with a unilateral brain stem lesion. Upper section: Sciatic nerve stimulation (10 pulse/sec) of a 3.0 kg male cat. Lower section: Epinephrine injection into femoral vein of a 2.8 kg male cat.

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6. A description of the use of this technique for the study of drug actions on the reticular activating system is in preparation. The authors wish to thank Peter L. Carlton and Bradford N. Craver for the many helpful suggestions which aided the preparation of this technique and report.

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