Electrical self stimulation of the brain and sensory inhibition¹

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The areas which elicit electrical self stimulation of the brain in the rat also produce inhibition of evoked potentials at the level of the trigeminal nucleus. The data support the hypothesis that ESB inhibits sensory input which may be followed by negative aftereffects.

Electrical self stimulation of the brain (ESB) is commonly regarded as evidence of some type of primary reward mechanism. However, the original investigators also offer the alternate possibility that ESB inhibits residual drive states or reduces noxious aftereffects of the previous ESB (Olds & Milner, 1954). Data from several sources support the alternate interpretation. For instance, a centrifugal inhibitory system which inhibits transmission in all the main sense modalities shows considerable overlap with the areas producing ESB (Hernandez-Peón, 1955). Further, the perception of pain was inhibited in a human during septal stimulation (Heath, 1954), and monkeys (Lilly, 1960), and rats (Cox & Valenstein, 1965) failed to discriminate between an ESB situation accompanied by painful stimuli and one not so accompanied. Other studies suggest some type of aftereffect which gradually decays out (Deutsch et al, 1964). Also, if intervals between ESB trains are sufficiently spaced, animals avoid the ESB situation (Ball & Adams, 1965).

Method

In order to test more directly whether ESB is linked to the inhibition of stimuli, the effect of ESB on the transmission of evoked potentials through the main sensory nucleus of the trigeminal nerve in the rat was studied.

Eleven adult male rats were implanted and tested for ESB behavior in a Skinner box. A 0.3 sec train of 1.0 msec dc pulses was delivered at a rate of 100 pps. A stable current threshold for responding was obtained for each animal. Six animals showed ESB behavior. The remaining five showed only aversive reactions with increasing current.

Following the behavioral procedure, each animal was anesthetized with ether. The infraorbital branch of the trigeminal nerve, ipsilateral to the ESB electrode, was exposed and stimulated once every few seconds. A monopolar recording electrode was introduced into the main sensory nucleus of the trigeminal nerve. Wounds and pressure points were treated with Xylocaine. The animal was injected with Flaxedil, put under artificial respiration, and the anesthesia dis-

continued. ESB was delivered to the animal by the experimenter, who varied the current around the threshold established in the behavioral test. Nerve stimulation was introduced at various times before, during, and after the ESB stimulation. Evoked potentials in the nucleus were monitored on an oscilloscope and recorded on film. At the end of the procedure, the animal was anesthetized and the brain removed.

Results

In all the ESB animals, the postsynaptic potential showed marked inhibition when preceded by an ESB current equal to or above the behavioral threshold. The presynaptic response, when visible, showed no inhibition. The first few ESB pulses were sufficient to elicit inhibition. Also, some degree of inhibition persisted for at least 0.3 sec beyond the end of the train. Figure 1 shows an example of the ESB effect. The amount of current is expressed as a percent of the threshold value. The postsynaptic response is unaffected by ESB equal to 90% of the behavioral threshold, but shows marked inhibition once the threshold is reached. Figure 2 is based on the six ESB animals, showing the mean height of the highest peak of the postsynaptic evoked potential when the nerve stimulation occurred 25 msec after the last ESB pulse. The amount of current is expressed as in Fig. 1. The distribution line around each mean encloses all the

Fig. 1. The effect of ESB on a postsynaptic evoked potential as recorded in the main sensory nucleus of trigeminal nerve.

Fig. 2. Mean amplitude from six ESB animals of the largest postsynaptic evoked potential expressed as a function of the amount of ESB current delivered.

observed scores. A large increase in the amount of inhibition can be seen as the ESB current approaches the behavioral threshold.

In Animals 2 and 4, it was possible to record from units triggered by the trigeminal stimulation. Inhibition of the units also occurred at and above the behavioral threshold, the inhibition showing a similar time course to that seen with the evoked potentials. These units were not activated by the ESB stimulus, indicating that the inhibition was not an antidromic effect.

Periodic stimulation of the nerve without further pairing with ESB produced a type of prolonged rebound in three of the ESB animals. Within 7 sec from the last ESB, a potential with an exaggerated amplitude could be evoked by the trigeminal stimulation in Animals 3 and 4. Further stimulation of the nerve over the next 4 min produced further exaggerated potentials of lesser magnitudes. In Animal 2, which showed unit activity, rebound occurred in the form of increased spontaneous firing which persisted for several minutes. Both the exaggerated potentials and the spontaneous firing could be blocked by further ESB. The other three ESB animals showed no comparable increased response.

Recordings of evoked potentials in two extra animals were made in the ventromedial thalamus as well as the trigeminal nucleus. Inhibition of the sensory evoked potential at the thalamic level was evident, showing similar properties to the inhibition at the trigeminal nucleus.

In the nonESB animals, Nos. 7 and 10 showed slight inhibition when current strengths of twice the aversive thresholds were given. No inhibition was obtained in the remaining three animals at even higher levels.

None of the animals showed any measurable rebound effect.

In the ESB animals, the electrodes of Nos. 2, 4, and 6 were located in the median forebrain bundle, of No. 1 in the ventromedial portion of the caudate nucleus, of No. 3 in the diagonal band of Broca, and of No. 6 in the lateral hypothalamus. In the nonESB animals, the electrodes of Nos. 7 and 8 were located in the hippocampus, of No. 9 in the optic tract, and of Nos. 10 and 11 in the ventromedial nucleus of the hypothalamus.

Discussion

The high degree of correlation between the current required to produce ESB behavior and that required to produce inhibition of postsynaptic responses in the main sensory nucleus of the trigeminal nerve suggests that the same mechanism is involved in both effects. If the ESB areas form part of a more general centrifugal inhibitory system, the other main sense modalities may be inhibited also. This is suggested in the lack of perception of painful stimuli during ESB as exhibited in humans, monkeys, and rats. The rebound effect in some of the ESB animals may be related to the hypersensitivity often seen in animals after ESB.

This experiment suggests that ESB can reduce sensory input, and that any aftereffects, such as hypersensitivity, could be continually delayed, or reduced, by further ESB trains. Viewed in this light, these data better fit the alternate interpretation that ESB is inhibiting stimuli which may take the form of noxious aftereffects of the previous stimulation.

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Note

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