Temporal discrimination in rats during continuous brain stimulation[1]

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Abstract

Rats with electrodes in either the septal region or anterior cingulate cortex received mild continuous electrical stimulation after having previously mastered a DRL-15 reinforcement contingency. Septal stimulation produced a pronounced disruption in DRL performance. Anterior cingulate stimulation had no deleterious effect, but resulted in a shift to longer interresponse times.

Problem

From the time Kaada (1951) reported differential somato-motor and autonomic effects from stimulating either anterior subcallosal or anterior cingulate areas, investigators have looked for behavioral correlates of these effects. In experiments with lesioned cats, McCleary (1961) found behavioral differences between these two areas in passive and active avoidance tasks, and on the basis of his results he postulated the involvement of the subcallosal cortex (septal area) in a circuit mediating response inhibition. If response inhibition is a general phenomenon in which the septal area plays an integral role, results obtained by using aversive techniques, such as those employed by McCleary, should also hold up for situations involving positive reinforcement. The operant schedule of reinforcement labelled DRL (differential reinforcement of low rates) appears to be an ideal situation for measuring response inhibition, while at the same time eliminating the noxious element. On this reinforcement schedule, S receives a reward only if he has refrained from responding for a predetermined delay period. If he responds during the delay, the timers reset and he will not receive a reward again until he has delayed for the correct length of time.

The present experiment, using this operant technique, was designed to further clarify the roles of the septal area and the anterior cingulate cortex in response suppression.

Subjects

Ss were 14 experimentally naive male hooded rats: eight with electrodes implanted in the septal area, and six with electrodes implanted in the anterior cingulate cortex.

Procedure

On the sixth day following surgery, Ss were put on a food deprivation schedule. They were given enough food in the form of dry lab blocks, once per day on three consecutive days, for their weights to stabilize to about 85-90% of their free feeding weights. After testing began, each S received three blocks of lab chow following each experimental session. Water was present in the individual home cages at all times, as well as in the testing apparatus during food reinforcement.

On the tenth postoperative day, Ss were trained to press a lever in order to obtain a 45 mg pellet of food, and on the following day each S remained on this continuous schedule for 100 lever presses. DRL training commenced on the twelfth postoperative day, and Ss were trained by progressively increasing the delay intervals. Under this procedure S was started at a 5 sec. delay (DRL-5), and was stepped up by 2 sec. increments when he had successfully attained 50% rewarded responses on the previous delay for two out of three days. This procedure was continued until S was able to delay his responses for 15 sec. After S performed satisfactorily on DRL-15, he was tested for three more days at this delay setting while receiving continuous brain stimulation. Stimulation was provided by an E&M MK V stimulator, and consisted of a biphasic square wave, 100 cps, 0.5 msec. pulse duration, which was monitored at 20 μa.

Upon completion of testing all Ss were first sacrificed, then perfused with physiological saline followed by 10% formalin. Brains were removed, frozen, sectioned, and stained with luxol fast blue and neutral red. A diagramatic representation of a typical section revealing the locations of the electrode tips is presented in Fig. 1.

Results

By means of analyses of variance, comparisons were made between cingulate and septal groups on measures of percentage of reinforcements and number of leverpresses, three days prior to and three days during continuous brain stimulation.

Data on percentage of reinforcements (see Fig. 2) revealed that although the groups did not differ in performance prior to stimulation, there was a pronounced difference between them during stimulation. Whereas cingulate Ss showed no observable change during stimulation, septal stimulated Ss displayed a noticeable drop in performance. An analysis of variance

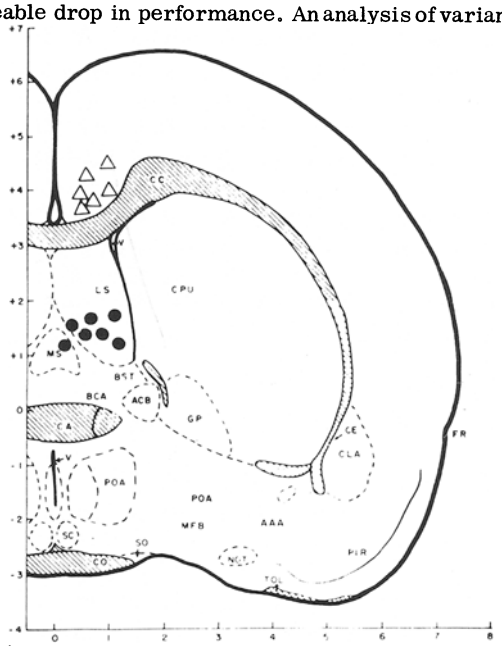

Fig. 1. Schematic representation of histological data. Triangles indicate cingulate placements, and dots indicate septal placements. Abbreviations: ACB, lateral parolfactory area; CC, corpus callosum; CPU, caudate nucleus/putamen; GP, globus pallidus; LS, lateral septal nucleus; MS, medial septal nucleus.

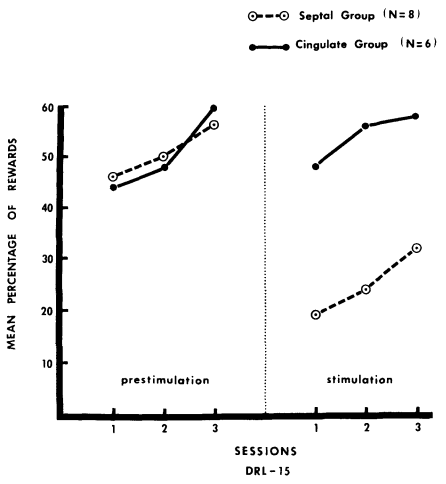

Fig. 2. Mean percentage of rewards obtained by cingulate and septal groups three days prior to and three days during stimulation.

revealed a group (G) effect, a pre-during stimulation (P) effect, and a PxG interaction, all being significant at $p < .001$ level.

Similar results were obtained from data on number of lever-presses. Although the groups did not differ before stimulation, there was a significant G effect ($p < .05$), a significant P effect ($p < .01$), and a significant PxG interaction ($p < .001$) when prestimulation days were compared with days with stimulation.

It is obvious that continuous septal stimulation had a deleterious effect on acquired DRL performance. Stimulation to the anterior cingulate region, on the other hand, did not have any such deleterious effect. Wilcoxin matched-pairs signed-ranks tests, comparing days before and during stimulation, revealed no significant differences between cingulate Ss on either of the two measures that were significant in the case of the septally stimulated Ss. Cingulate stimulation did appear to have some effect, however. Inspection of interresponse time distributions suggested that cingulate stimulation had the effect of producing a "flattening" of the distribution curve, with more responses occurring at longer delays. In contrast with this, septal Ss displayed a noticeable shortening of their interresponse times.

Discussion

The data obtained in the present experiment are consistent with the notion of the septal area's importance in tasks requiring response inhibition. This line of explanation has already been offered to account for impaired passive avoidance in septal lesioned animals (Kaada et al, 1962; McCleary, 1961) as well as in septal stimulated animals (Kasper, 1964). The increased number of lever-presses along with the decreased percentage of reinforcements, found with septal stimulation in the present experiment, could reflect a similar disturbance of response inhibition. Furthermore, the present findings, using septal stimulation, are consistent with previous communications with septal lesioned Ss, which have reported impaired acquisition of DRL (Ellen et al, 1964), and increased responding during non-reinforced components of a discrimination task (Schwartzbaum et al, 1964).

Results from the present experiment with cingulate stimulation might be closely related to the fact that cingulectomized Ss are capable of delaying their responses for much longer periods of time than normal Ss, (Stamm, 1964), or to those studies which find deficient active avoidance behavior with cingulate lesions (McCleary, 1961; Peretz, 1960; Thomas & Otis, 1958).

Evidence from other investigations using noncontingent continuous stimulation (Goddard, 1964; Kasper, 1964; Pellegrino, 1965) indicates that the low-level stimulation produces effects similar to those obtained from lesions. Together, those studies involving either septal lesions or mild septal stimulation, in situations requiring suppression of a dominant response, implicate this area in the mediation of behavioral inhibition.

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Note

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