The Kamin effect in hippocampal-lesioned animals

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Ventral hippocampal and sham-operated rats were given one-way active-avoidance training followed by relearning either 5 min, 1 h, or 24 h later. Both ventral hippocampal and sham-operated rats showed deficits in active-avoidance relearning performance 1 h after original avoidance acquisition. The failure of ventral hippocampal lesions to influence avoidance performance 1 h following original avoidance acquisition may indicate that neither the adrenal-pituitary nor the adrenergic-cholinergic systems are essential for the occurrence of the Kamin effect.

The functioning of the limbic system of the brain and the endocrine system have been found to be integrally related. Lesions in the ventral hippocampus result in increased resting levels of ACTH and a decreased amount of change in ACTH produced by a stressful event (Knigge, 1961). With respect to behavioral measures, it has been demonstrated that administration of pituitary-adrenal hormones may have effects quite similar to those observed following lesions in the limbic system. Both hippocampal lesions and treatment with ACTH produce increased resistance to extinction of an avoidance response (Ackil, Mellgren, Halgren, & Frommer, 1969; Miller & Ogawa, 1962) and increased intertrial avoidance responding on a shuttlebox avoidance task (Ackil et al, 1969; Bohus & Lissak, 1968). On the basis of such parallel effects, Antelman and Brown (1972) have hypothesized that much of the "abnormal" fear-motivated behavior of hippocampectomized rats can be attributed to increased levels of ACTH brought on by such lesions.

With respect to this apparent relationship between ACTH, the hippocampus, and behavior, certain predictions about behavior can be made. Of special interest to the present authors were predictions concerning the Kamin effect. Kamin (1957) observed that rats were unable to perform a previously acquired two-way active avoidance on an intermediate retention test, while avoidance performance was excellent both immediately and 24 h after the initial aversive experience. The absence of ACTH induced by corticoid inhibition has been suggested as a possible cause of the Kamin effect; treatments which produce the presence of ACTH during intermediate interval following avoidance training eliminates the retention deficit seen in the Kamin effect (Brush & Levine, 1966; Klein, 1972; Levine & Brush, 1967). Since rats with lesions in the ventral hippocampus have been shown to have chronically elevated levels of ACTH and exhibit less change following stress, the Kamin effect might not be expected to occur in animals with this type of lesion. The purpose of this experiment was to determine if the Kamin effect occurs in animals with ventral hippocampal lesions.

METHOD

Subjects

The subjects were 40 experimentally naive male rats purchased from Sprague-Dawley Laboratories (Madison, Wisconsin). All rats were 75 to 90 days old at the time of original training.

Apparatus

The apparatus was a two-chamber black and white avoidance apparatus (previously described in Klein & Spear, 1969). A 1.6-mA footshock was employed for both active-avoidance acquisition and relearning.

Surgery

All surgery was performed under sodium pentobarbital anesthesia (50 mg Nembutal/kg body weight). Twenty animals received a bilateral lesion of the ventral hippocampus. With the incisor bar set 5 mm above the interaural plane, using bregma as the zero point, the following coordinates were employed: posterior-3.4 mm, lateral $\pm$ 5.0 mm, and ventral-7.5 mm. Lesions were produced electrolytically by passing a 2-mA anodal current through the uninsulated .5-mm tip of a stainless steel electrode for 30 sec. The remaining 20 animals received a sham operation in which they were anesthetized, placed in the stereotaxic instrument, and had an incision made in their scalps. All animals were allowed approximately 1 week to recover from the effects of surgery prior to initial avoidance training.

Aversive Conditioning and Testing

Forty rats were given one-way active-avoidance training to a criterion of five successive avoidance (as described in Klein & Spear, 1969). In order to avoid shock, the rat had to cross from the white chamber into the black chamber before the 5-sec CS-UCS interval elapsed. The rat remained in the black chamber approximately 5 sec after trial termination. The subject spent the 30-sec intertrial interval in a holding cage.

After the fifth successive avoidance, rats in two experimental conditions were given active-avoidance relearning training after 5 min, 1 h, or 24 h. Active-avoidance reacquisition was given to a criterion of five successive active-avoidance responses.

Histology

At the end of the experiment, all hippocampal rats were given an overdose of Nembutal and perfused with physiological saline followed by 10% Formalin. All brains were placed in 10% Formalin until the histological analyses were performed. The brains were frozen with CO₂ and sliced into sections 60 microns thick. Brain sections were mounted on slides and viewed microscopically to identify area of lesion.

Fig. 1. Representative lesion of ventral hippocampus on a plate from Pellegrino and Cushman (1967) Atlas.

RESULTS

Morphological

Histological examination of the brain sections showed that all lesions were in the approximate vicinity of the desired location in the ventral hippocampus (see Fig. 1). Damage to the entorhinal cortex was incurred in some animals. However, no relationship was observed between extrahippocampal damage and behavior. One subject was discarded because its lesion was located totally outside of the hippocampus.

Behavioral

Active-Avoidance Acquisition. No significant trials-to-criterion differences were found between groups for active-avoidance acquisition, indicating that all groups equivalent at the beginning of training ($F < 1$, $df = 2/34$, $p > .05$). In addition, the results demonstrated that the ventral hippocampal lesion did not affect the acquisition of the active-avoidance response ($F = 3.0385$; $df = 1,34$; $p > .05$).

Retention Test. Figure 2 presents the median number of avoidances on Trials 1-5 of relearning for each group. Statistical analysis of avoidance performance on Trials 1-5 of relearning indicated a significant effect of retention interval ($F = 6.30$; $df = 2,34$; $p < .01$), and a nonsignificant effect of surgical treatment ($F < 1$; $df = 1,34$; $p > .05$). Individual group differences were evaluated, using a Duncan's range test. The avoidance performance of both hippocampal and sham-operated rats was superior both 5 min and 24 h after training, compared to their performance after 1 h ($p < .05$). Thus, the Kamin effect did not differ for ventral hippocampal and sham-operated rats.

The performance of subjects in terms of a trials-to-criterion measure yielded results identical to that over Trials 1-5 (see Fig. 2). Statistical analysis showed a significant effect of retention interval ($F = 15.74$; $df = 2,34$; $p > .05$). Again, multiple range comparisons showed that rats tested 1 h after original avoidance acquisition required significantly longer to

relearn the active-avoidance response than subjects tested either 5 min or 24 h after initial acquisition. Thus, in terms of trials to criterion as well as number of avoidances of first five trials, both ventral hippocampal and sham-operated rats demonstrated a U-shaped retention function during the first 24 h following active-avoidance training.

DISCUSSION

The results of this experiment demonstrated that the Kamin effect occurred in animals with ventral hippocampal lesions. Both ventral hippocampal and sham rats showed deficits in active-avoidance performance 1 h after original avoidance acquisition. The magnitude of the performance deficit on an intermediate interval test was equivalent for both ventral hippocampal and sham subjects. In addition, relearning performance in both hippocampal and sham rats was significantly more rapid both 5 min and 24 h after initial active-avoidance training than after 1 h. The hippocampal and sham rats learned the active-avoidance response at the same rate on both the 5-min and the 24-h retention test.

To the extent that the hippocampus is important in the adrenal-pituitary functioning, the appearance of the Kamin effect in ventral-hippocampal lesioned rats suggests that nonnormal adrenal-pituitary function has no appreciable effect on retention differences following

Fig. 2. Median trials to relearn active avoidance response as a function of retention interval after one-way active-avoidance training for ventral hippocampal and sham-operated rats.

avoidance training. These results are in agreement with those showing that neither adrenalectomy (e.g., Barrett, Leith, & Ray, 1972; Klein¹; Klein & Kopish²; Snider, Marquis, Black, & Suboski, 1971; Marquis, Black, & Platenius, 1970) nor hypophysectomy (Klein, 1974; Klein & Kopish, 1974; Marquis & Suboski, 1969) influenced avoidance deficits noted during intermediate intervals following initial aversive conditioning. These results suggest that an intact adrenal-pituitary system will not prevent performance deficits after intermediate retention intervals.

The failure of ventral hippocampal lesions to influence avoidance performance 1 h following original avoidance acquisition also suggests that parasympathetic inhibition is not essential for the occurrence of the Kamin effect. Ventral hippocampal lesions appear to reduce inhibitory tendencies in avoidance situations (see McCleary, 1966) while this ability of the hippocampus to inhibit behavior has been attributed to cholinergic systems (Carlton, 1969). Anisman (1973) suggested that cholinergic inhibition was responsible for retention deficits on intermediate interval tests. The poor relearning performance on a 1-h test in ventral-hippocampal lesioned rats observed in this experiment may indicate that the Kamin effect will occur in the absence of cholinergic inhibition.

Other experimental evidence exists indicating that parasympathetic rebound alone is not responsible for the Kamin effect. First, inescapable shock alone does not produce a U-shaped retention function. Fear conditioning appears to be a necessary prerequisite for obtaining the Kamin effect (see Brush, 1971 for a review of the literature). If inhibition alone was responsible for poor avoidance performance, inescapable shock should produce the Kamin effect, which of course it does not (e.g., Spear, Klein, & Riley, 1971). Second, ACTH reactivated appropriate avoidance behavior when presented prior to an intermediate interval test presumably during the period of parasympathetic inhibition (Klein, 1972) while Anisman (1973) was unable to demonstrate retention deficits on a 24-h test following physostigmine administration. If cholinergic inhibition is sufficient to produce the Kamin effect, physostigmine should induce retention deficits on 24-h tests. Finally, Bintz, Braud, and Brown (1970) observed that approach tendencies on a conflict situation were greatest 3 h following shock in the goalbox. A cholinergic inhibition hypothesis would predict freezing on an intermediate interval test.

Reactivation by either ACTH (Klein, 1973; Klein, 1974) or adrenalin (Hablitz & Braud, 1972) on an intermediate interval test indicates that the adrenal-pituitary and adrenergic-cholinergic hormonal systems play a role in the retrieval of aversive experiences. Yet the Kamin effect can occur in the absence of intact adrenal-pituitary and adrenergic-cholinergic systems. Future research should

attempt to determine other systems controlling the Kamin effect and the precise role of the adrenal-pituitary and adrenergic systems in memory.

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NOTES

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