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THE UNIVERSITY OF ALBERTA

THE EFFECT OF METHYLPHENIDATE AND AMYGDALECTOMY ON ACTIVE AVOIDANCE PERFORMANCE IN THE RAT

by

© LORNE T. YEUDALL

A THESIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "The Effect of Methylphenidate and Amygdalectomy on Active Avoidance Performance in the Rat", submitted by Lorne T. Yeudall, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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Abstract

The present study was designed to test the hypothesis that the amygdaloid complex is not essential in the learning of an active avoidance response. A latent learning paradigm was employed in which amygdalectomized Ss were trained for eight days under non-drug conditions followed by eight days of drug acquisition under four dosage levels (0, 4, 8 and 16 mg/kg). The administration of methylphenidate on day nine produced a significant shift in performance for the 4, 8 and 16 mg/kg amygdaloid Ss. A significant decrease in the amygdaloid S's latencies paralleled the increase in correct avoidance responding whereas their intertrial activity did not differ from their respective controls. Post-drug retraining one month after drug acquisition demonstrated a significant retention effect for the three amygdaloid drug groups as compared to the non-drug amygdaloid Ss.

The findings of the present study were congruent with the hypothesis that the amygdala is not essential for the acquisition of an active avoidance response in a two-way shuttle box learning situation. It was hypothesized that components of the amygdaloid complex are primarily involved in the facilitation of other neural structures (e.g. hypothalamus and thalamus) involved the acquisition of an active avoidance response.

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In Memory of Helen Yeudall

and

to Hugh and Joan Yeudall

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Introduction

The history of experimental investigations of amygdaloid function begins with the early studies of Brown and Schaffer (1888), and Klüver and Bucy (1937). The classical Klüver-Bucy syndrome consisting of tameness, hypersexuality, hyperoralism, hypermetamorphosis and psychic blindness was produced by the removal of the temporal lobe which contains the amygdaloid complex. Later studies demonstrated that the phenomena of psychic blindness was due to the destruction of infero-lateral temporal cortex. (Ades and Rabb, 1949; Chow, 1951; and Mishkin and Pribram, 1954).

Since the pioneering work of Klüver and Bucy, many studies have shown that lesions to the amygdaloid complex affect a diverse range of behaviours including arousal, fear, aggression, rage, food intake, mating, appetive and avoidance learning, reward and punishment, attention, incentive motivation, habituation, autonomic responses as well as motor inhibition and facilitation (Gloor, 1960; Goddard, 1964a; McCleary, 1961; and Thomas et al., 1968).

Anatomical Considerations

The amygdala consists of a number of subcortical and cortical nuclei which are relatively densely packed deep within the temporal lobe of the brain. Even though there has been conflicting opinions, these nuclei have generally been subdivided into two main groups in terms of anatomical (ontogentic and phylogenetic) and functional criteria (Goddard, 1964a; Gloor, 1960; and Ursin and Kaada, 1960).

The more primitive corticomedial complex consists of the central, medial and cortical nuclei, nucleus of the lateral olfactory tract and the cortico-amygdaloid transition area. The phylogenetically more recent basolateral complex consists of the lateral nucleus, accessory basal nuclei, and the basal nuclei. Phylogenetically the corticomedial group has been decreasing in size whereas the basolateral complex has reached its greatest development in man.

The amygdala is richly connected with most parts of the brain via a primary and secondary projection system of efferents as well as receiving afferents from all of the sensory modalities (most of them have only been demonstrated electro-physiologically, Gloor, 1960).

The primary efferents of the amygdala consist of the stria terminalis which receives input from all of the amygdaloid nuclei and the ventral amygdalofugal pathway which was traditionally thought to originate only in the basolateral nuclei of the amygdala. Recent evidence (Cowan et al., 1965) indicates that the ventral amygdalofugal system originates in the pyriform cortex and they suggest that the resultant ventral amygdalofugal projection system is a lateral extension of the medial forebrain system. The monosynaptic connections of the stria terminalis fibres project primarily to the medial and anterior regions of the hypothalamus, preoptic area, and piriform cortex, whereas the ventral amygdalofugal fibers are thought to project to the rostral part of the hypothalamus and midbrain tegmentun as well as having an overlapping projection field with much of the stria terminalis projection field (Gloor, 1960). Direct connections to the thalamus, septal region, lateral hypothalamus, and preoptic region from the

corticomedial nuclei (via the central nuclei) have also been demonstrated (cowan, Reisman & Powell, 1965).

These projection fields of the amygdala are of interest as it has been shown that they are intrinsically involved in development and expression of motivation and emotion (Grossman, 1967; Olds, 1962; Vanderwolf, 1969).

It has also been demonstrated electrophysiologically that direct amygdalomesencephalic connection exist which bypass the hypothalamus (Gloor, 1960). The complex interconnections within the amygdala, the convergence of sensory and nonsensory afferent information on single cells within the amygdala suggests that the amygdala might be intimately involved in many tasks involving the intergration of external information and ongoing motivational or emotional states of the organism.

Behavioural Considerations

Several studies using various species (monkeys, cats, dogs, rats and mice) sustaining lesions in the amygdaloid complex have demonstrated significant impairment in active and passive avoidance learning. Although there is some contradictory evidence as to the effect of amygdaloid lesions in regard to active avoidance learning, the majority of the studies have demonstrated that amygdaloid lesions can significantly disrupt acquisition and/or retention of an active avoidance response (AAR).

The following literature review includes both positive and negative findings as a result of permanent (electroytic) or temporary induced lesions

(electrical or biochemical) and is organized in terms of what appear to be the major theoretical positions concerning amygdaloid functioning.

Fear

The emotional aspects of the Klüver-Bucy syndrome suggested the involvement of the amygdala in fear and arousal (Klüver & Bucy, 1938; Rosvold, Fuller & Pribram, 1951; and Schreiner & Kling, 1953). These observations led Brady et al. (1954) to conduct the first systematic and quantitative study of the effects of amygdalectomy on the acquisition and retention of an AAR. They trained cats to a 90% criterion in a double-grill active avoidance shuttlebox using a 30 sec CS-US interval, a variable intertrial interval ($\overline{X}$ = 90 sec) and a shock level of 3.5 ma. The amygdaloid lesions were found to significantly impair the acquisition of the AAR. Also, the amygdaloid Ss did not show any decrement in the retention of the AAR on the postoperative trials. No significant differences were found between the amygdaloid animals and their operative and non-operative controls in the retention of a preoperative AAR.

As did previous studies (Anand & Brobeck, 1952; and Schreiner & Kling, 1953) they found the experimental Ss with amygdaloid lesions to be relatively docile. The amygdaloid Ss were also observed to rarely manifest any emotional behaviour (anxiety or fear) to the onset of the CS during avoidance training as did the control animals. Their acquisition results are consistent with the hypothesis that fear or anxiety reduction plays an important role in avoidance acquisition (Mowrer & Lamoreaux,1946). On

the other hand their finding that amygdalectomy had no effect on the retention of a preoperatively trained response does not support the hypothesis that fear reduction plays an important role in maintaining avoidance behaviour (Mowrer & Lamoreaux, 1946).

King (1958) trained male adult rats to a 90% criterion in a double grill conditioning box using a 10 sec. CS-UCS interval, a variable intertrial interval (60-180 secs.) and a shock level between 0.10 ma to 0.25 ma. He also rated the animals for emotionality on a six-point scale adapted from Brady and Nauta (1955). The amygdaloid rats did not differ significantly from the operated and non-operated controls in the rate of acquisition of the AAR. They did, however, manifest significantly longer response latencies during the acquisition of the AAR. The amygdaloid lesion did not significantly alter the emotionality of the rats postoperatively. These contrasting findings with that of Brady et el. (1954) may be due to a difference in species and/or in task difficulty, in that Brady et al. punished intertrial responses.

Kemble and Tapp (1968) using a one-way active avoidance task did not find rats with basal amygdaloid lesions to be different in the number of errors to reach criterion. Similar to King (1958), however, they found that the amygdaloid animals had significantly longer latencies for the last five acquisition trials. They interpreted this finding as being a possible apparatus effect, i.e., the one-way active avoidance is not complex enough to demonstrate the effect of basolateral lesion on performance.

Robinson (1963) found that amygdaloid rats were significantly impaired in the acquisition of an AAR in a modified Miller shuttle box. After the Ss reached criterion performance they were given an additional 30 trials of overlearning. On the following day the amygdaloid Ss were tested for acquisition of a wheel turning response without shock reinforcement. Only one amygdalectomized S learned the wheel turning response.

She also found that the amygdaloid animals froze (crouching behavior) significantly more than the control animals during the training session. Contrary to previous interpretations (that amygdalectomy reduces fear in animals) she concluded that amygdalectomy in rats produces more fearful animals as indicated by the significant increase in the couching response and latency to respond in the training sessions. Although she entertained(Bovard's and Gloor's, 1961) the over-arousal hypothesis of plasma corticosterone response to stress and McCleary's (1961) response inhibition theory she found the impairment of the amygdaloid animals in the AAR and wheel turning task best explained in terms of an interpretation based on increased fear motivation.

On the other hand, Goldstein (1965) found that amygdalectomized rats failed to transfer a previous conditioned emotional response to a new situation which demanded a hurdle response, i.e. they failed to demonstrate retention of a previously learned fear response. He also noted that the amygdaloid animals had higher shock thresholds and suggested that the acquisition and retention differences of amygdaloid

animals in noxious learning situations may be due to the changes in pain sensitivity mechanisms.

Support for this interpretation comes from several related studies (Bagshaw and Pribram, 1968; Goldstein, 1968; Kemble and Beckman, 1969). Bagshaw and Pribram (1968) demonstrated that amygdalectomized monkeys did not respond differentially to different shock levels and that animals' GSR levels were significantly depressed. Similarly Goldstein (1968), and Kemble and Beckman (1969) found that rats were insensitive to different intensity levels of shock.

Horvath (1963) found that amygdaloid cats manifested a significant impairment in post-operative acquisition and retention of a pre-operatively learned AAR in a two-way shuttlebox whereas training in a one-way apparatus produced only a minimal impairment of the AAR. The difference between the animals' performance in the simple one-way and more complex two-way AAR tasks led Horvath to conclude that the avoidance deficit of the amygdaloid animals was not due to a reduction of fear motivation.

The findings of various studies (Bagshaw & Pribram, 1968; Brady et al., 1954; Goldstein, 1968; King, 1958; and Kemble & Tapp, 1968) provide evidence for a reduction in the normal fear response to the CS or an increased threshold to electric shock. Robinson (1963) on the other hand has suggested that rats with amygdaloid lesions are more emotional than normal rats which results in an avoidance deficit whereas Brady et al.

(1954) and Horvath (1963) concluded that the avoidance deficit in cats could not be attributed to changes in fear or anxiety of their animals. As these various studies differ in regard to species, procedures, size and location of lesions and types of apparatus it is difficult to conclude the nature of the relationship between the effect of amygdaloid lesions and fear or anxiety as pertaining to the acquisition of an AAR.

Attention and Orienting Behaviour

The early observations of Klüver and Bucy (1937) of amygdalectomized animals (in terms of curiosity responses, lack of habituation and lack of reduction of fear of objects) in combination with stimulation studies of the amygdala (producing arousal, alertness, attentional responses, orienting responses, etc.) strongly suggest that the amygdala is intimately involved in attention.

Recently a series of studies by Bagshaw (Bagshaw and Benzies, 1968; Bagshaw and Coppock, 1968; Bagshaw and Pribram, 1968; Bagshaw, Kimble & Pribram, 1965) and Pribram (1969) have shown that amygdalectomies in monkeys result in a significant depression of GSR to novelty and loss of respiratory and cardiac components of the orienting response while EEG desynchrony and ear movements were within the normal range. Pribram (1967) has suggested that the orienting is made up of two components--one an alerting reaction indicated by the ear flick, the other a focusing function which allowed registration of the event which produced the alerting. It is this second stage which involved the amygdala and is signalled by the appearance of a GSR.

Schwartzbaum and Pribram (1960) using monkeys with bilateral lesions and Barrett (1969) using monkeys with bilateral and split-brain unilateral amygdaloid lesions found that the Ss were significantly impaired in learning a visual transposition problem and discrimination-reversal learning set, respectively. They interpreted their findings as suggesting that the amygdala is involved with the processing of sensory input. Barrett (1969) concluded that the deficit of his split-brain preparations were definitely not due to a motor deficit per se but due to the inability in placing the stimulus in proper context, i.e. in making the present relevant to past experience.

More recently Kemble and Beckman (1969a) found that rats with amygdaloid lesions were impaired in the acquisition and reversal of a position discrimination. They found that the amygdaloid Ss made significantly more vicarious trial and error responses after both rewarded and non-rewarded trials than the control animals. The amygdaloid Ss were found to have difficulty in inhibiting orienting responses to irrelevant stimuli which interferred with their acquisition and reversal performance. They concluded that the amygdala plays an integral role in "attention-directing" behaviour.

The studies interpreting the behavioural deficits of amygdaloid Ss in terms of attention have primarily involved monkeys as experimental subjects. Other studies (Brady et al., 1954; Kemble & Tapp, 1968; King

1958; and Kling, 1960) using different species have demonstrated that the lesioned animals were impaired in their responses to the CS. The findings of Kemble and Beckman (1969) suggest that the behavioural deficit produced by amygdaloid lesions in rats can be interpreted within an attention or orienting framework.

Although there may be species differences in the function of the amygdala, the above data suggests that the avoidance deficits found in studies using rats may be due to interference with normal orienting to the CS.

Long-Term Memory and Consolidation

Brady et al. (1954) demonstrated that cats with amygdaloid lesion were impaired in postoperative acquisition of an AAR whereas retention of a preoperatively learned response was not impaired by the lesions. As their postoperative cats did eventually learn the task, they concluded that the amygdala was not crucial in the acquisition or rentention of avoidance behaviour.

Horvath (1963) trained cats with lesions in both the corticomedial and basolateral divisions of the amygdala in simple and complex avoidance learning situations. The amygdaloid animals tested in a two-way shuttlebox (complex task) were significantly impaired in the postoperative acquisition and retention of the preoperative trained AAR. The lesioned animals trained in a one-way avoidance task (simple) manifested only slight impairement on the acquisition of the AAR. Horvath concluded that the basolateral complex of the amygdala was primarily involved in the acquisition process and the deficit of the lesioned

animals could be described as an inability to integrate their motivational state and the experimental cues with the anticipatory response which was most efficient for solving the problem of avoiding the painful shock.

Horvath (1963) suggested that the retention deficit found in his study as contrasted to the lack of a retention deficit in Brady et al. (1953) study could have been due to differences in training procedures. More specifically he noted that Brady et al. (1953) gave their animals additional learning trials after they had reached criterion, i.e. overlearning. Horvath's data suggested that if the retention deficit could be eliminated by overtraining it would imply that the amygdala's primary influence would be in the acquisition of an AAR and not in the long-term storage of the AAR.

To clarify the nature of this hypothesis, Thatcher and Kimble (1966) overtrained one group of amygdalectomized rats preoperatively to determine the effect of overlearning during acquisition on later retention of the AAR. They found no differences between the overtrained amygdalectomized rats and their respective controls. The general interpretation of their findings tended to support Horvath's position and more specifically, they suggested that the amygdala is primarily involved in acquisition processes and not long-term memory storage .

Goddard (1964b) trained implanted hooded rats with continuous electrical stimulation of the amygdala during sessions in a double-grill avoidance task. He found that 80% of the control animals learned the task within

the 200 trials, while none of the animals receiving amygdaloid stimulation learned the AAR criterion of 10 consecutive correct responses. On the other hand, the same animals showing the marked deficit on day one, showed a significant increase in correct responses on day two during a block of non-stimulation trials. Goddard concluded that the low intensity electrical stimulation disrupted amygdaloid functioning by scrambling the normal input and output of electrical activity of the amygdala. In the same study he demonstrated that stimulation of the amygdala did not disrupt the acquisition of a one-way avoidance response however, the Ss were found to extinguish significantly faster than the controls. Goddard ran a further series of experiments to determine the nature of the deficit in terms of the time sequences during which the amygdaloid animals were stimulated during training. In a series of independent experiments involving a CER paradigm he stimulated the amygdala during the entire training session, only during the CS period or for five minutes immediately after shock termination. He found that the critical period of stimulation was immediately after shock termination. This finding suggested to Goddard that the amygdaloid stimulation disrupted the consolidation process, i.e., the consolidation of the association between the conditioned stimulus and the negative reinforcement.

More recently Goddard (1969) found that bilateral carbachol injection into the amygdala resulted in a significant deficit in a passive avoidance response (PAR) under distributed training whereas it did not impair acquisition under massed training. On the other hand, he did not find any impair-

ment in the acquisition or retention of an active avoidance response under massed and distributed training conditions. He concluded that his previous hypothesis of consolidation was not compatible with the passive avoidance findings and suggested that the data could be explained in terms of the utilization of memory for response inhibition.

The above studies provide fairly clear evidence that the amygdala plays an important role in the expression of learned behaviour during the acquisition of the response. Once the animal is consistently performing the correct response, amygdaloid lesions do not seem to interfere with performance. The amygdala does not appear to be intrinsically involved in long-term memory storage per se, but does seem to be primarily involved in the expression of behaviour during the acquisition of a learned response.

Facilitation

The studies so far reviewed have conceptualized the amygdala's role in the acquisition of an AAR as being involved in (1) the process of fear as related to noxious situations, (2) attention or orienting to the CS and (3) the consolidation of memory or long-term storage of memory.

Another interpretation suggested by several researchers (Caruthers, 1968; Kling et al., 1960; Stokman & Glusman, 1970; Ursin, 1965; and Ursin, & Kaada, 1960) is that the amygdala has a triggering or facilitatory role rather than playing an intrinsic role in learning per se. (the term "facilitation" in this instance is descriptive in that it refers to the be-

havioural manifestation of the response to be learned and does not refer to the underlying neurophysiological mechanism). Ursin and Kaada (1960) demonstrated that stimulation of the basolateral nucleus of the amygdala in cats yielded flight reactions whereas stimulation of the medial amygdala produced defensive reactions. In a later study (1965) he showed that lesion in the flight zone significantly blocked flight behaviour without influencing defensive behaviour and vice versa. Stimulation of the pyriform cortex did not produce flight, defensive or attentional responses (Ursin and Kaada, 1960).

Ursin (1965), in contrast to Horvath's (1963) findings, found that amygdaloid animals with lesions in the flight zone (basolateral nuclei) were significantly impaired in the acquisition of an AAR in a one-way avoidance apparatus. McNew and Thompson (1966) also found that rats with damage to the basolateral nuclei were significantly slower than the controls in reaching criterion during the acquisition of a one-way avoidance task. Ursin suggested that the contrast with Horvath's finding was due to the differences in procedure as Horvath's handling of the animal during its removal after a correct response probably acted as a reinforcing event. Ursin found that the amygdaloid Ss manifested strong emotional and autonomic responses to the CS and UCS as well as being impaired in their escape responses. He concluded that "the flight zone of the amygdala is crucial for the development and maintenance of an AAR."

Kling et al. (1960) found that AAR acquisition and retraining of cats with amygdaloid lesions were within the range of control animals. They did, however, find that the amygdaloid animals made significantly more errors before learning the significance of the CS. The amygdaloid animals could not be differentiated from their respective controls in terms of observed emotional responses to the CS. The amygdaloid Ss were also found to extinguish significantly faster than the control groups. They concluded from their data "that the amygdala (probably in combination with the hippocampus) plays a facilitative role in the acquisition of the conditioned avoidance response but does not constitute a necessary condition for the acquisition or retention of the habit."

Stokman and Glusman (1970) found that amygdaloid stimulation of the basolateral nuclei in cats significantly facilitated flight responses elicited by hypothalamic stimulation. Lesions of the amygdaloid stimulation sites resulted in a loss of the facilitation effect. Although they could not train the animals to avoid hypothalamic or combined hypothalamic and amygdaloid stimulation, their data are compatible with the position that the amygdala acts to facilitate hypothalamic activity.

Caruthers (1968) utilizing a circuit-breaking approach, lesioned the ventral amygdalofugal pathways (which project to the anterior hypothalamus and thalamus) in the region of the ansa lenticularis. He found that the rats trained preoperatively to a flicker CS were significantly impaired in AAR training whereas postoperatively trained animals (as well as animals trained using a tone CS) were very similar

in performance to the normal animals. The lesioned animals did not seem to have any apparent motor disfunction. He concluded that his "results are consistent with the opinion that the amygdala (and pari passu its connections) functions as a modulator or trigger rather than as an integral component of response organization."

Although Stokman and Glusman (1970) and Ursin and Kaada (1960) suggest that the flight zone is independent of the pyriform cortex and Ursin (1965) concluded that the ventral amygdalofugal pathway is critical for the flight response, the findings of Cowan, Reisman and Powell (1965) demonstrated that the amygdalofugal pathway is a projection system of fibres from the pyriform cortex. Their findings indicated that "the ventral pathway of the amygdala is a lateral extension into the telencephalon of the medial forebrain bundle with the anterior amygdaloid area serving as a bed nucleus."

Ursin (1965) found that lesions on the edge of the lateral nucleus of the amygdala produced significant impairment in AAR performance thus implicating the involvement of temporal-lobe structures in the acquisition of an AAR. Similarly Caruthers (1969) found that destruction of the amygdaloid projection system to the hippocampus via the pyriform cortex resulted in a significant impairment in the acquisition and retention of an AAR for both flicker and tone conditioned stimuli. In contrast to his earlier findings with lesion in the region of the ansa lenticularis which impaired only acquisition performance,his later findings suggest "a segregation of mechanisms for learning and retention in the temporal lobe."

Brady et al. (1954) found that cats with amygdaloid lesions were impaired in the acquisition of an AAR but could eventually learn the task, whereas they were not impaired in the retention of a preoperatively trained AAR. Their results suggest that the amygdala probably plays some facilitatory role in the acquisition of an AAR. The findings of King (1958) and Kemble & Tapp (1968) that rats with amygdaloid lesions had significantly longer avoidance latencies could be interpreted as an impairement in the amygdala's possible facilitatory role in the AAR acquisition. The data of Stokman and Glusman (1970) suggest that this possible facilitatory role in acquisition may be the result of amygdaloid influences on hypothalamic flight systems.

In summary, it appears that the amygdala plays a crucial role in the acquisition of an active avoidance response. The evidence suggests that the amygdala is in some way involved in orienting and attention and is not in long-term memory storage per se. The evidence is not clear as to the relationship between amygdalectomy and fear in regard to acquisition of an AAR. The findings of the studies reviewed suggest that an intact amygdala is necessary during the acquisition of an AAR and that the amygdala plays a facilitatory role in the behavioural manifestation of the response in active avoidance learning.

Several studies have shown that psychomotor stimulants can enhance the performance of normal and lesioned animals. (Hearst & Whalen, 1963; Krieckhaus, 1965; and Krieckhaus, Miller, & Zimmerman, 1965). It is not

entirely clear whether an intact amygdala is crucial for learning of an active avoidance response. It was thought that the administration of methylphenidate, a psychomotor stimulant, to impaired animals with amygdaloid lesions may elucidate the role of the amygdala in the acquisition of an active avoidance response.

Methylphenidate

Methylphenidate (Ritalin) is a derivative of 2-benzylpiperidine and is generally classified as a central or psychomotor stimulant. The effect of methylphenidate differs from the amphetamines in that it enhances central nervous activity without adversely influencing the cardiovascular system or appetite. Several studies (Jouvet and Courjon, 1959; and Timo-Iara and Werner, 1957) suggest that methylphenidate has its stimulating effect on the reticular formation. Other studies (Cole and Glees, 1956; and Monnier and Krupp, 1960) have found methylphenidate to affect hypothalamic activity either by direct excitation or by inhibition of inhibitory neurons in sympathetic areas of the hypothalamus.

Methylphenidate used clinically has been described as having mind alterning or awakening properties, and producing a greater awareness of reality in patients. Knight and Hinton (1968) studying the effect of methylphenidate on motor skill performance of children with learning disorders concluded that the ability to pay attention, rather than motor speed or motor control was influenced by methylphenidate .

A pilot study (Yeudall, 1967) indicated that the AAR deficit of amygdaloid rats in a two-way avoidance situation could be eliminated by the administration of 8 mg/kg of methylphenidate. The finding that the elimination of the deficit (i.e., a dramatic shift in performance under drug) persisted in retraining three weeks later suggested that the effect was not state dependent. It was concluded that the dramatic shift in performance of the amygdaloid drug animals was due to latent learning during the predrug training trials during which the Ss had not manifested any evidence of learning.

To the authors knowledge, no other studies have used methylphenidate to enhance performance in two-way and shuttlebox avoidance learning. However, Bindra and Anchell (1963) used methylphenidate in an active avoidance situation where the response to be learned was one of immobility rather than the usual escape response to the CS. They found that normal rats could learn an active response of immobility whereas the performance of rats that had been administered methylphenidate was significantly impaired. The drug was not found to enhance the immobility response as the drug resulted in a general increase in activity which was incompatible with the AAR.

Stretch and Skinner (1967) using a bar-press avoidance with a discriminative stimulus trained two rats over a six month period to avoid shock. The rats before drug administration characteristically responded just before shock rather than immediately after the presentation of the CS.

The administration of methylphenidate increased the response rates with the largest proportion of responses occurring soon after the onset of the CS. The Ss also made more pre-CS responses under the drug. The increase in response rates and the prompter responding to the CS resulted in the S's receiving fewer shocks during the drug sessions.

Several studies (Bindra, 1961; Garberg & Sandberg, 1960; and Greenblatt & Osterberg, 1961) have shown that methylphenidate results in an increase in spontaneous activity with the maximum effect occurring within the first two hours of testing. Although there seems to be consistent evidence that methylphenidate facilitates performance in bar-press avoidance paradigms (Bernstein & Latimer, 1968; Dews, 1958; and Stretch & Skinner, 1967) and increases spontaneous motor activity, this facilitating effect cannot be generalized to all learning situations. Mendelson & Bindra (1962) and Bindra & Mendelson (1963) demonstrated that bar pressing for water reinforcement under low, medium and high deprivation conditions was not facilitated by the administration of methylphenidate. Whereas methylphenidate had no effect under high drive conditions, it produced a significant decrement in performance under the two low drive conditions. In this task the administration of the drug resulted in an increase in sniffing, grooming, and irrelevant behaviour which was incompatible with the learned response.

The effect of methylphenidate on performance appears to depend upon the nature of the task such that performance will be facilitated if the

increase in spontaneous activity is compatible with the response to be learned.

Purpose

Several studies (Horvath, 1963; Kemble & Tapp, 1968; and Ursin 1965) have suggested that one-way avoidance tasks are not complex enough to reveal an avoidance deficit in animals with amygdaloid lesions. In the present study task complexity was increased by requiring the Ss to run from one end of the apparatus to the other in order to terminate the US or CS. The findings of the pilot study (Yeudall, 1967) suggested that the present apparatus and design was effective in producing a near zero response baseline in rats with amygdaloid lesions.

The purpose of the present study was to replicate the findings of the pilot study (Yeudall, 1967) and to determine the effect of 3 dosage levels of methylphenidate on drug acquisition performance and post-drug retention performance.

Method

Design

The variables manipulated were amygdaloid lesions or absence of lesions, drug dosages (4, 8 and 16 mg/kg of methylphenidate) and days. These three variables were combined in a completely balanced 2 X 4 X 16 factorial design. The design consisted of the following groups: normals, no methylphenidate (N-0); amygdaloid lesion, no methylphenidate (AMY-0); amygdaloid lesions, 4 mg/kg (AMY-4); normals, 4 mg/kg (N-4); amygdaloid lesions, 8 mg/kg (AMY-8); normals, 8 mg/kg (N-8); amygdaloid lesions, 16 mg/kg (AMY-16); and normals 16 mg/kg (N-16). The subjects were trained postoperatively for 400 trials and were tested one month later under retraining conditions.

Subjects

The Ss were 64 male albino rats of the Sprague-Dawley strain. Their weight at the beginning of training ranged between 200 and 250 grams. All animals were housed individually during the experiment.

Apparatus

The avoidance apparatus consisted of an automated two-way shuttle box constructed from plexiglass (19 in. long X 4 in. wide and 12 in. high). The CS (1000 cycle tone at 65 db.) was presented through a 2 in. speaker located in the center of the apparatus. Avoidance, escape, and intertrial responses were detected by photo cells placed 3 in. from either end of the apparatus. The avoidance apparatus was housed in an insulated chamber to attenuate extraneous stimuli. The Ss could be observed through one-way glass located in the lid of the test chamber.

The shock source consisted of a 800 v. transformer, Lehigh-Valley 1311SS shock scrambler circuit with a 200 KΩ resistor in series with the animals. (Campbell & Teghtsoonian, 1958). The programming equipment consisted of a Tally 625 tape reader, Hunter Clock counters, Mercury reset counters and Hunter photo-cell amplifiers. The 1000 cycle CS was produced by a Dumont tone generator. The programming equipment was located in an adjacent room. Total correct responses, intertrial responses and response latencies (up to the nearest .01 sec.) were recorded for each conditioning session.

Surgery

All operations were performed under nembutal (60 mg/kg ip) anesthesia. Lesions were produced electrolytically using stainless steel electrodes bared one mm at the tip. Two lesions were made bilaterally with anterior lesions one mm anterior to the bregma and 4.0 lateral to the midline. The posterior lesions were located 1.5 mm posterior to the bregma and 4.5 mm lateral to the mid-line. The anterior and posterior electrodes were inserted to 7.5 and 8.0 mm, respectively, below the dura. The amygdaloid lesions were produced by passing a 2 ma anodal current for 20 sec. through the lesioning electrodes. The holes in the calvarium were packed with gelfoam, the incision then was sutured, the animal was injected with sulfadimethoxine (S-71) and placed in a heated recovery box for 4 hrs. before being returned to its home cage.

Post-operative Recovery

All subjects were given free access to a 40% sucrose solution, sugar cubes, wet mash, food pellets and water. As soon as Ss were

mobile, liquid sucrose solution was injected into their mouths to facilitate eating. The condition of all subjects was monitored very carefully for the week following surgery.

Histological Procedures

At the end of testing, all operated Ss were sacrificed and perfused with normal saline and 10% formalin solution. The brains were removed and sectioned every 50μ. Representative sections indicating the anterior and posterior boundaries of the lesions as well as sections from the maximally damaged areas were stained with Luxol fast blue and Cresy Echt violet.

Procedure

Animals were housed in individual cages and maintained on an ad libitum diet throughout the entire experiment. The Ss were handled for a week before being randomly assigned to the experimental groups. The animals in the lesion groups underwent surgery at this time and were given a post-operative recovery period of approximately 30 days.

Post-operative Training

On approximately the 38th day the Ss were given a 15 min. exposure to the apparatus and returned to their home cage. On the following days the Ss were given 16 days of avoidance training, 25 trials per day. A delayed-conditioning procedure was employed with a 5 sec. CS-US interval, a variable intertrial interval of 1 min. and US of 75 V. (≃ 1.5 ma) which remained on until the subject made an escape response.

The Ss intertrial responses were not punished during the training session.

The three Normal-drug Groups (N-4, N-8 and N-16) were trained under drug throughout the 400 acquisition trials. The Amygdaloid Ss (AMY-4, AMY-8 and AMY-16) were injected with saline for the first 200 training trials and with methylphenidate on the last 200 trials. All Ss were injected 30 min. prior to their daily training session. The N-0 and AMY-0 groups were injected with saline throughout the experiment. None of the groups were injected during retraining.

Post-drug Retraining

A post-drug period of one month was allowed for residual effects of the drug to dissipate before retraining was resumed. The Ss were run using the same stimulus parameters as in post-operative training and were given 6 days of avoidance training, 25 trials per day.

Results

Analysis of the data was carried out in three stages (predrug, drug and retention) for correct avoidances, latencies and intertrial responses (ITR). Analysis of variance and Duncan's Multiple Range Test (DMRT) were performed on all of the data for the three stages of training. Independent t's were performed on selected days.

The means for intertrial responses, correct responses and latencies for all sessions are presented in Appendix A and the analysis of variance tables are presented in Appendix B.

Postoperative Training: (1st 200 trials)

Correct responses. The performance of the eight experimental groups in AAR training during the first 200 trials is shown in Figure 1. No significant differences were found between any of the four amygdaloid-lesioned groups. On the last day of training N-16 made significantly more correct responses than all other groups (DMRT, $p < .01$). Both N-4 and N-8 drug control groups were significantly different from the four amygdaloid groups on the last day of training (DMRT: N-4, $p < .01$; N-8, $p < .01$). The normal group (N-0) differed significantly from all four amygdaloid groups (DMRT, $p < .01$) as well as N-16 ($p < .05$). The N-16 group differed significantly from the N-4 and N-8 groups on the last two days of training ($p < .05$) whereas the N-4 and N-8 groups did not differ from each other throughout the first eight days of training.

Latencies. As in the number of correct responses no significant differences were found in the latency scores (Figure 2) between the four amygdaloid groups. On the last day of training N-8 and N-16 latencies were significantly shorter than any of the other experimental groups

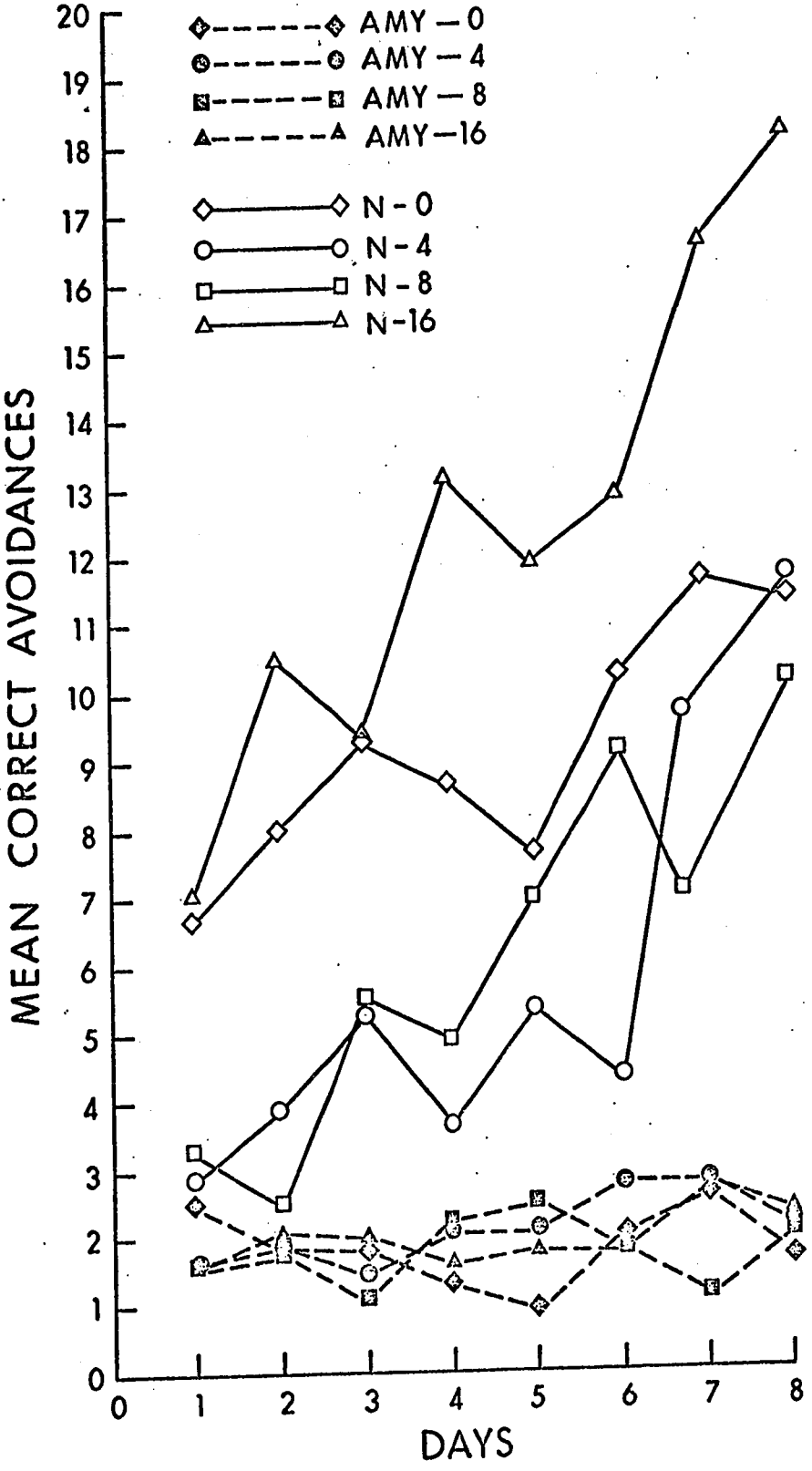

Figure 1 Mean avoidances for all groups for the first 8 days of AAR acquisition

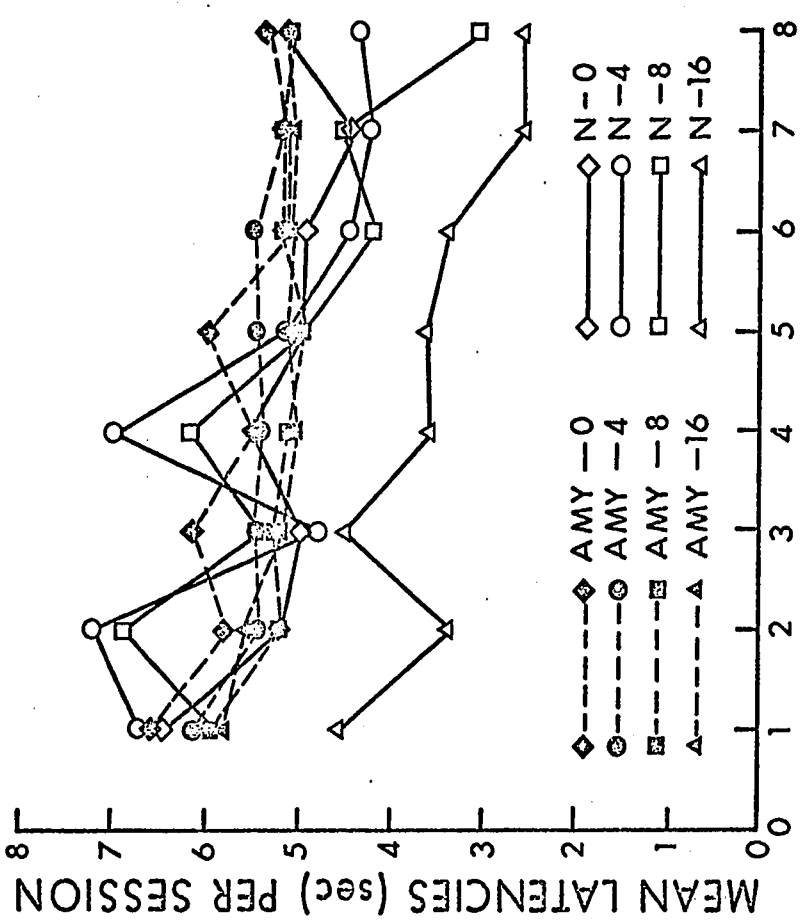

Figure 2 Mean response latencies for all groups for the first 8 days of a AAR acquisition

(DMRT, $p < .05$). None of the other groups differed significantly from one another over the eight days of training.

Intertrial responses. As was the case for correct responses and latencies the four amygdaloid groups did not differ significantly over the eight days of training. On days 2, 7, and 8, N-16 made significantly more intertrial responses than any of the other experimental groups (DMRT, $p < .05$). No significant differences were found between the remaining groups over the eight days of training except for AMY-4 which made significantly more intertrial responses than N-4 on day 1 of training (DMRT, $p < .05$).

Drug Acquisition

Avoidances. The mean number of correct avoidances for the amygdaloid groups (AMY-0, AMY-4, AMY-8, and AMY-16) during the 200 trials of drug training is shown in Figure 3. Day 8, which was the last predrug day for the amygdaloid groups is included for comparison purposes. It is clear that the amygdaloid Ss receiving methylphenidate manifested an abrupt shift in performance on day 9, which was the first drug session. The difference from AMY-0 in correct avoidances was significant for AMY-4 and AMY-16 on day 9 (DMRT, $p < .05$), and for AMY-8 on day 10 (DMRT, $p < .05$). The nature of this shift in performance was dramatic in the case of two subjects in that $AMY\text{-}4_4$ and $AMY\text{-}16_1$ made 19 and 21 correct successive avoidances in the first drug session before receiving any shock.

Two separate analyses of variance were performed comparing the amygdaloid groups to their normal controls. To examine the nature of the

facilitation effect of methylphenidate on the rate of acquisition, the amygdaloid Ss on the first 200 trials of drug training (Figure 3, days 9 to 16) were compared to the first 200 trials of drug acquisition (Figure 1, days 1 to 8) of their respective normal controls. The Lesion X trials interaction was significant ($F = 2.96$, $df = 7$, $p < .055$), indicating a significant difference in the rate of acquisition between the amygdaloid and normal drug groups (Table 1).

Table 1

Means for the Avoidance Lesion X Trials interaction of the Analysis of Variance of days 1 to 8 (Controls) vs.days 9 to 16 (AMYs)

Groups	Days							
	1	2	3	4	5	6	7	8
Normal Controls	6.62	8.29	9.79	10.08	10.58	12.21	14.92	17.12
Amygdaloids	12.54	13.42	14.58	16.08	16.67	17.47	17.42	17.67

The other analyses of variance compared the amygdaloid and normal control groups over days 9 to 16 (Fig. 3). The Dosage main effect was significant ($F = 5.85$, $df = 3$, $p < .01$) as well as the Lesion X Dosage interaction ($F = 4.83$, $df = 3$, $p < .005$). In order to clarify the nature of this interaction a DMRT was performed on the differences between the amygdaloid and normal control groups (Table 2).

Table 2

Mean differences for the Avoidance Lesion X Dosage interaction of the Analysis of Variance of Days 9 to 16 for Amygdaloid and Normal Controls

Groups	Dosage Levels			
	0	4	8	16
Normal Controls	13.94	10.41	10.97	17.19
Amygdaloid	3.55	13.62	14.23	17.59
Differences	10.39	-3.21	-3.26	-.40

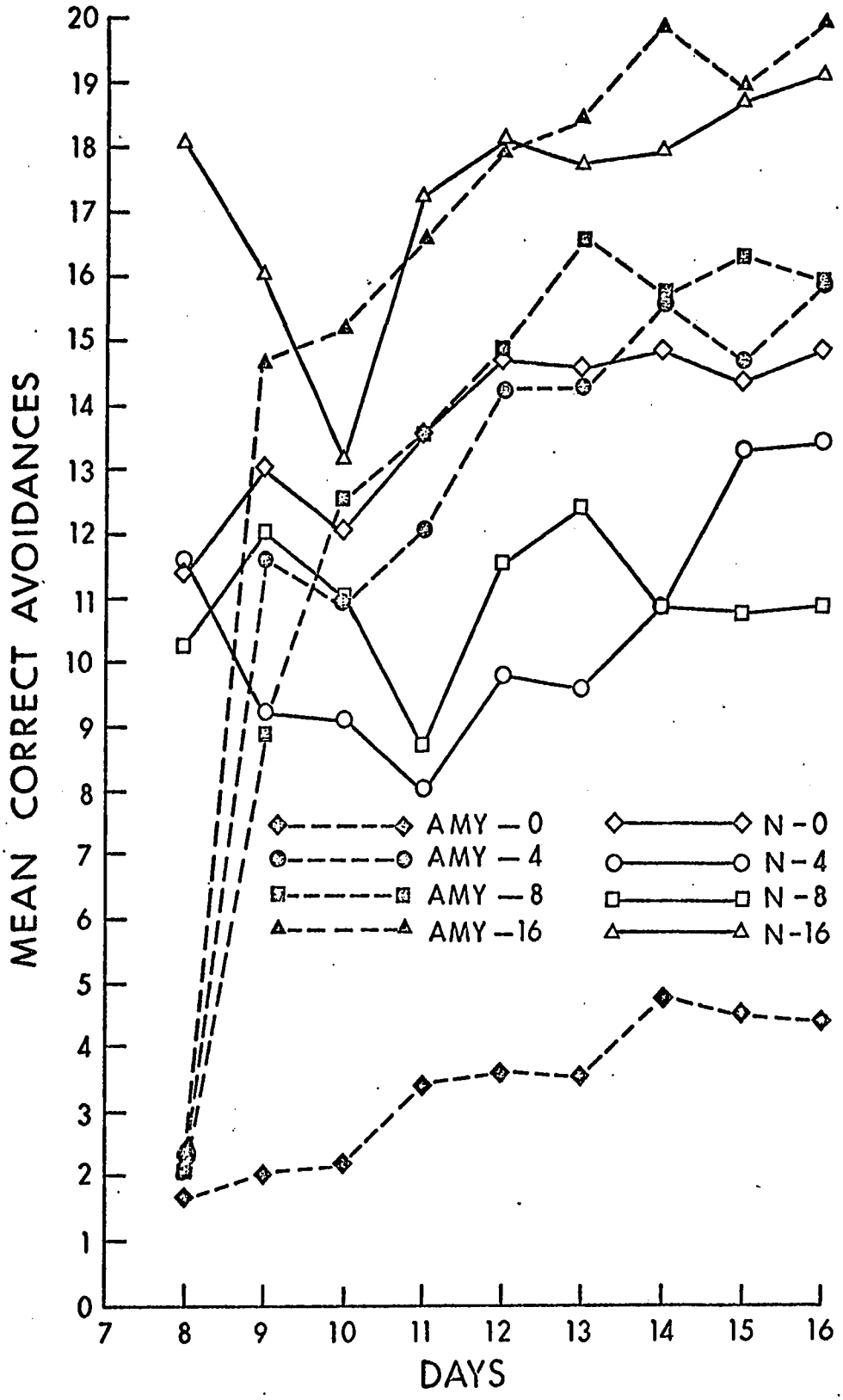

Figure 3 Mean avoidances for all groups for the last 8 days of acquisition

The AMY-0 vs. N-0 difference mean was significantly different from the other three drug group mean differences. (DMRT, $p < .05$). None of the other mean differences differed significantly from each other thus indicating a significant shift in performance for the three amygdaloid lesion-drug groups.

Latencies

The analysis of variance of days 9 to 16 (Amygdaloids) and days 1 to 8 (Normal Controls) yielded a significant Lesion main effect ($\bar{X}$'s =4.20 and 4.84, respectively; $F = 7.55$, $df = 1$, $p < .01$). The Dosage main effect was also significant ($F = 16.00$, $df = 3$, $p < .001$). The corresponding means were 5.46, 4.70, 4.70, and 3.24 for 0, 4, 8 and 16 mg/kg dosage levels. As in the avoidance data, the Lesion X Trials interaction was significant ($F = 5.39$, $df = 7$, $p < .01$), indicating a significant difference in the rate of decreasing latency scores over training sessions (Table 3).

Table 3

Means for the Latency Lesion X Trials interaction of the ANOVA of Days 1 to 8 (Controls) vs. Days 9 to 16 (Amygdaloids)

Groups	Days							
	1	2	3	4	5	6	7	8
Normal Controls	5.88	5.64	4.91	5.83	4.72	4.24	3.94	3.82
Amygdaloids	4.76	4.50	4.41	4.10	4.12	3.81	3.88	3.95

The Lesion X Dosage interaction of days 9 to 16 was significant

(F = 3.03, df = 3, p < .05), indicating a significant decrease in latencies in the amygdaloid groups during drug training (Table 4).

Table 4

Means for the Latency Lesion X Dosage interaction of the ANOVA of Days 1 to 8 (Controls) vs. Days 9 to 16 (Amygdaloids)

Groups	Dosage Levels			
	0	4	8	16
Normal Controls	3.83	4.43	4.00	3.39
Amygdaloids	5.17	3.90	3.54	3.28

Examination of the data for individual days revealed a significant decrease in latencies (Figure 4) on day nine for AMY-4, AMY-8 and AMY-16 as compared to AMY-0 (DMRT, p < .05). The three amygdaloid drug groups did not differ significantly from each other over the eight days of drug acquisition. No significant differences were found between N-4 and N-8 over the eight days whereas N-16 had significantly shorter latencies than N-4 and N-8 on days 2, 4, and 7 (DMRT, p < .05, Figure 5)

Intertrial Responses

The analysis of variance for days 9 to 16 (Amygdaloid-drug) and days 1 to 8 (Normal controls) resulted in a significant Lesion main effect ($\bar{X}$'s = 2.33 and 1.55, respectively; F = 7.16, df = 1, p < .01). Also the Dosage main effect was significant (F = 6.78, df = 3, p < .001). The corresponding means were .27, .44, .52, .66 and 1.89 for 0, 4, 8, and 16 mg/kg dosage levels. In order to rule out the possibility that the

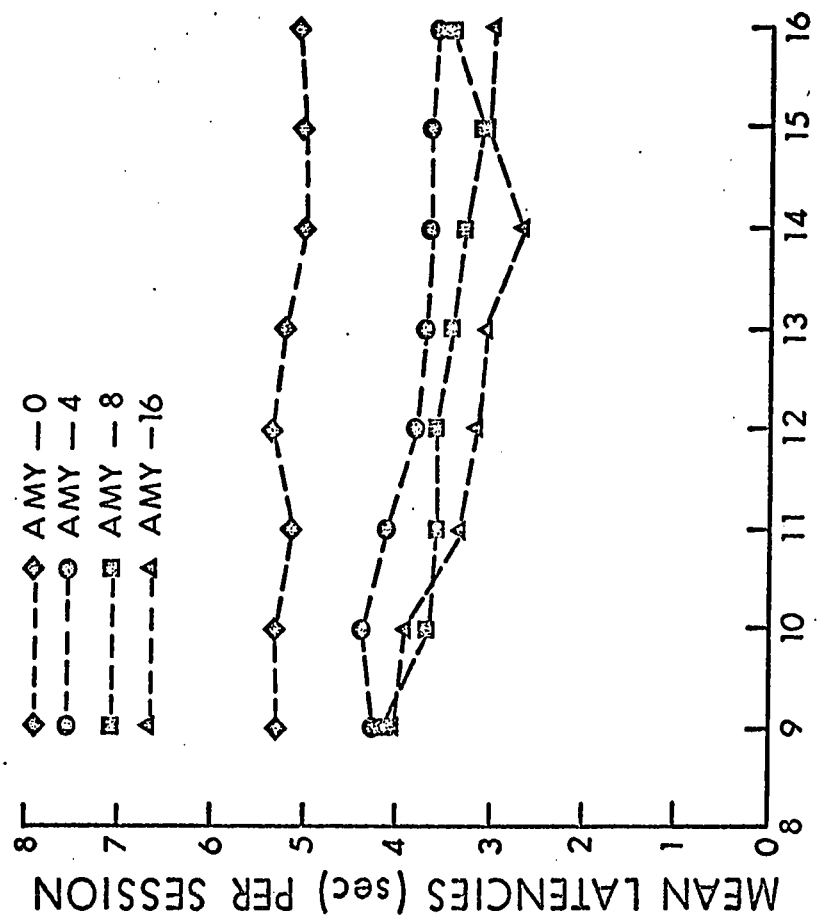

Figure 4 Mean latencies for the Amygdaloid drug S's for the first 8 days (9 to 16) of drug acquisition

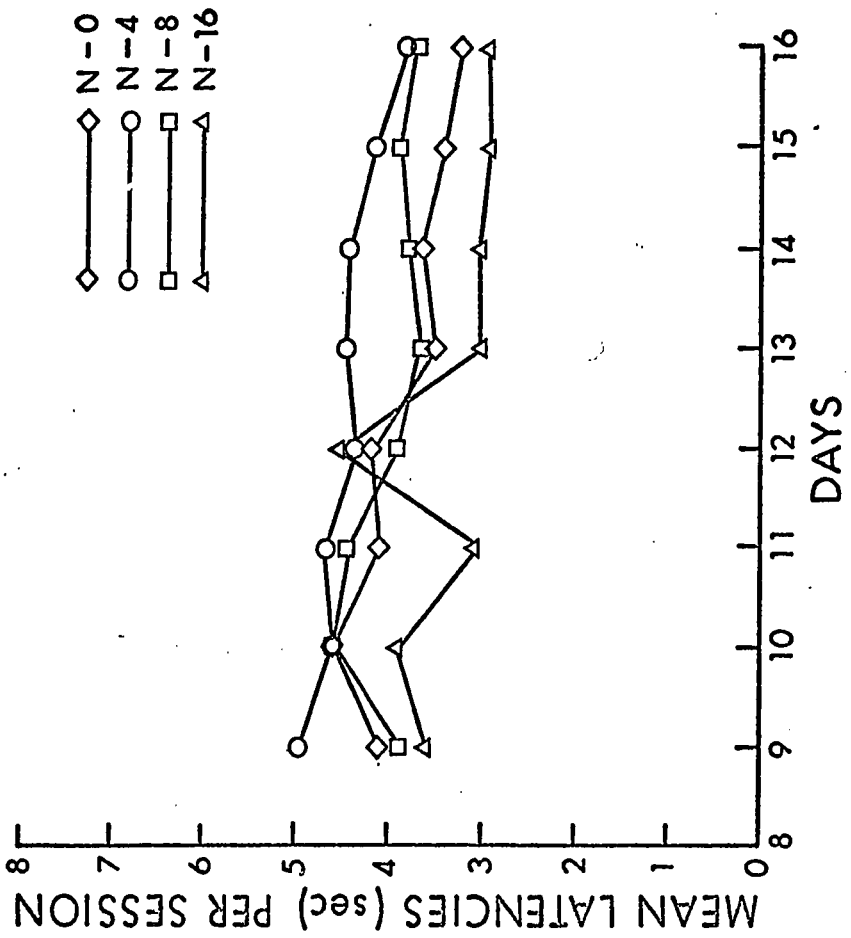

Figure 5 Mean latencies for the Normal Controls, for the last 8 days (9 to 16) of drug acquisition

significant increase in correct responses was a function of the increase in intertrial activity, the probability of making a correct response on the basis of intertrial activity was calculated for the amygdaloid-drug groups. Assuming that intertrial activity was randomly distributed, the probabilities were obtained by dividing the intertrial activity per trial by 13 (which is the number of possible 5 sec. blocks in a trial). The probability of making a response in any 5 sec. block during the intertrial interval and each S's percentage correct on the first and last day of drug acquisition is presented in Table 13, Appendix A. The mean probability of making a response during any 5 sec. period for AMY-4, 8, & 16 was .16, .22, and .22, respectively on Day 9 and .19, .17, and .18, respectively on Day 16 of drug acquisition.

Correlations were performed on the raw data (for the 3 amygdaloid drug groups) in order to determine the relationship between intertrial responses and avoidance performance. The correlations for days 9 through 16 of drug acquisition were .30, .51, .32, .29, .28, .44 and .59, respectively. They were significantly different from zero only on days 2, 7 and 8. The proportion of variance accounted for by the correlation of intertrial responses with AAR performance for day 9 through 16 is 9, 26, 10, 8, 8, 8, 19 and 35%, respectively, which demonstrates that intertrial responding alone cannot account for the increase in performance during acquisition under methylphenidate.

Retraining: Post drug recovery of one month

Avoidances. Analysis of variance of the amygdaloid drug groups and

their respective controls did not demonstrate any significant main effects. A significant increase in correct avoidances occurred over the six days of post-drug retraining. ($F = 6.84$, $df = 5$, $p < .001$). Comparison of the amygdaloid groups with their respective controls using the DMRT did not reveal any significant differences between the groups over the six days. Groups N-0 and N-16 were the only two groups that differed significantly from AMY-0 on the last two days of retraining (DMRT, $p < .05$).

Examination of the retraining data and the near significant mean differences of the DMRT prompted a series of "t" tests on the last 6 days between the amygdaloid groups. As shown in Table 5 the 3 amygdaloid drug groups were all significantly different from the AMY-0 animals on each of the six days of training.

Table 5

"t's" between AMY-0 and AMY-4, AMY-8 and AMY-16 for retraining avoidances (Days 1 to 6)

Groups	Days					
	1	2	3	4	5	6
AMY-4	2.84**	2.11*	1.85*	2.75*	3.04**	2.54*
AMY-8	1.72*	1.81*	1.95*	2.46*	3.17**	2.58*
AMY-16	2.13*	2.42*	2.14*	4.84**	3.67**	3.10**

* $p < .05$
** $p < .01$

A series of correlated "t's" were performed between day 8 (last day of predrug training) and the first and last days of non-drug retraining in order to determine whether post-drug performance differed from pre-drug performance. The "t" values for AMY-4, 8 and 16 for day 1 were 4.30, $p < .005$; 4,18, $p < .005$ and 4.00, $p < .005$, respectively, and for day 6 of retraining were 3.69, $p < .01$; 3.65, $p < .01$ and 3.69, $p < .01$, respectively thus demonstrating a significant retention effect under non-drug conditions.

Latencies. The analysis of variance of the amygdaloid and control groups did not reveal any significant differences for the main effects. Also inspection of Table 8 (Appendix A) reveals that there is no compelling general trend of the latency scores over the six days of retraining as indicated by the nonsignificant trials effect. A DMRT of the eight groups revealed only one significant difference which was between N-0 and N-16 on day 1 (DMRT, $p < .05$).

A series of "t" tests were performed between the AMY-0 animals and the AMY-drug groups. No significant differences were found for the AMY-4 group; the AMY-8 animals differed significantly only on the fourth day ($t = 2.23$, $p < .05$) whereas AMY-16 animals differed on days 3, 4, and 5. ($t = 2.15$, $p < .05$; $t = 2.77$, $p < .05$; and $t = 1.91$, $p < .05$, respectively)

Intertrial Responses. No significant differences were found between

the amygdaloid and controls groups in regard to main effects or interaction components of the analysis of variance. Similarly the DMRT revealed no differences on any of the days between the groups.

The "t" tests between AMY-0 and the AMY-drug groups revealed that the AMY-4 and AMY-8 made significantly more intertrial responses only on day 1 and 3, respectively, ($t = 1.89$, $p < .05$ and $t = 2.47$, $p < .05$) whereas AMY-16 animals made significantly more responses on days 1, 2, 3, 4 and 6.

Behavioural Reaction of Amygdaloid Ss.

Predrug Phase. All Ss were very placid and easy to handle and engaged in a good deal of exploration of the apparatus on the first day of habituation. On the second day after the first 25 trials of conditioning the amygdaloid animals were still very calm in contrast to the normal animals who resisted transportation to the apparatus as well as manifesting various autonomic reactions. However, by the fourth day of training the amygdaloid Ss began to resist transportation to the apparatus and by the 6 th day were manifesting strong avoidance responses of the apparatus (i.e., clinging to the walls, attempts at jumping out of the apparatus while being placed in it, as well as defecating and urinating). The animals generally did not manifest any responses to the CS. If an amygdaloid S was grooming, sniffing or rearing when the CS came on it whould generally continue its ongoing behaviour until shock occurred. The normal animals, on the other hand, characteristically manifested head and body movements towards the source of CS and occasionally

manifested crouching and freezing behaviour. Freezing responses to the CS were not observed in the amygdaloid animals.

Drug Phase. The amygdaloid-drug Ss were more active under methylphenidate and tended to explore their home cages as well as the avoidance apparatus much more than the AMY-O Ss. In general,most of the amygdaloid Ss manifested orienting responses (head rising and body movements towards the CS source) to the CS.

Post Drug Phase. The animals one month after the last drug injection were very placid when handled. On the average by the second day they did show strong resistance to being placed in the test chamber.

Histology

The estimated damage to the amygdaloid nuclei and adjacent structures for the lesioned groups are presented in Table 6. The majority of the lesions included nuclei from both the basolateral and corticomedial division of the amygdala. The nuclei most often damaged were amygdaloideus centralis; amygdaloideus lateralis, pars posterior; amygdaloideus basalis, pars lateralis; and amygdaloideus basalis, pars medialis, whereas the most spared nuclei were amygdaloideus corticalis and medialis.

Damage to the pyriform cortex and the claustrum was fairly extensive whereas damage to the caudate, ventral hippocampus, internal capsule, and optic tract was minimal. An analysis of variance was performed on the predrug avoidance data in which the animals were sorted into four groups with regard to the degree of damage to the claustrum and pyriform

cortex in addition to the amygdala.

The criterion for assigning animals to these groups was whether there was any bilateral damage to the corresponding structures. The four groups consisted of Ss with damage to the clastrum + pyriform cortex + amygdala, claustrum + amygdala, pyriform cortex + amygdala and only the amygdala. The corresponding avoidance means for the four lesion groups were 1.95, 1.44, 2.75 and 1.56, respectively. The F ratio was not statistically significant, thus indicating that the additional damage to the claustrum and pyriform cortex did not significantly influence the avoidance deficit in predrug acquisition.

Table 6. Histological analysis of Amygdaloid Ss: Scores are mean percentage of damage to nuclei of the amygdala as well as to structure adjacent to the amygdala.

Groups	Amygdala							Extra-amygdala					
	basalis, pars lateralis	basalis, pars medalis	lateralis	centralis	medialis	corticalis	Anterior Area	Pyriform cortex	Ventral hippocampus	Caudate	Optic tract	Capsula interna	Claustrum
AMY-0	91.42	63.6	100.0	92.9	33.6	46.4	51.4	27.1	6.0	14.3	3.0	2.9	32.1
AMY-4	96.9	63.8	100.0	77.5	20.0	45.6	51.5	34.9	5.3	6.6	3.4	3.0	52.9
AMY-8	91.2	73.1	100.0	93.8	30.0	40.6	65.0	43.1	6.0	8.3	2.5	3.5	58.1
AMY-16	90.7	60.7	100.0	85.0	33.1	42.9	52.9	33.6	5.1	9.7	1.4	3.1	51.4

Discussion

The general conclusions to be drawn from the results of this study are that amygdalectomy in the rat significantly impairs the learning of a complex active avoidance task, that the deficit can be eliminated, and that learning of an active avoidance response can occur without an intact amygdala. As other neural structures were damaged, the question of whether the predrug avoidance deficit was due to amygdala damage or damage to other structures warrants discussion. In the pretest study damage to the ventral hippocampus, caudate, putamen, optic tract and external capsule was minimal and most likely did not contribute significantly to the predrug deficit. Damage to the claustrum, external capsule, caudate; putamen and pyriform cortex in control animals reported by Goddard, (1969a) and Kemble & Beckman (1969a) was found not to have any significant effects on performance. Several other studies (Campenot, 1969; Brady et al., 1954; Goddard, 1964; Horvath, 1963; Kemble & Beckman, 1969b; Pelligrino, 1968; Robinson, 1963; and Thatcher & Kimble, 1966) did not find any significant differences between the sham operate and normal control animals. These findings are consistent with the results of the present study as the analysis of variance of the anatomical location of extra-amygdala damage in regard to the predrug deficit was not significant. The evidence from the present study in addition to the results of other studies discussed makes it highly unlikely that the predrug deficit was due to anything other than the destruction of the amygdala.

The major finding of this study was that the deficit in AAR performance of rats with amygdaloid lesions can be eliminated by the adminis-

tration of methylphenidate (Fig. 3). The mean performance of the amygdaloid-drug groups on the day previous to drug injection was 8% correct. On the first day of drug training the mean performance of AMY-4, AMY-8, and AMY-16 was 47.0, 35,0, and 58,5% respectively, and by the eighth day of drug training was 63.52, 63.0, and 79.0% respectively. Although not statistically significant, all three amygdaloid drug groups performed better than their respective control groups on day 16 of acquisition.

The dramatic shift in performance on day nine was best demonstrated by AMY-4_4 and AMY-16_1, in that they made 19 and 21 out of 25 successive correct responses before they received their first shock. The behaviour of these two Ss as well as others strongly suggests that the consequences of the CS had been learned, i.e., that shock was forthcoming, but the mechanism for the behavioural expression of this learning was not functioning properly in the amygdaloid animals. The shift in performance on day 1 of drug acquisition and the significant post-drug retention data suggests that learning of the CS-US association had occurred during pre-drug acquisition. Before considering this interpretation, two alternative hypotheses must be considered.

One alternative explanation is that the increase in avoidance responding could be attributed to the increase in intertrial responding during drug aquisition. More specifically, can the avoidance performance be attributed to chance responses that may have occurred during the CS. Incidental observation of the Ss intertrial activity indicated that the greatest frequency of responses occurred after the Ss made an avoidance or escape res-

ponse. Black and Carlson (1959) monitored intertrial shuttlebox responding during a 2 min intertrial interval which was divided into 4 equal periods. They found that on day 1 the responding for the 1st, 2nd, 3rd and 4th periods was 53.1, 23.1, 16.2 and 7.6, respectively. On the criterion day of acquisition the intertrial activity was more evenly distributed within the intertrial interval (23.3, 17.7, 34.4 and 21.6, respectively). The probability of making an intertrial response during the CS in the present study was very low and is not consistent with the hypothesis that the avoidance performance of the amygdaloid drug groups was due to chance responding.

In addition to this evidence, the correlations of the total intertrial activity, irrespective of its distribution within the interval, with CAR performance was not significant on day 1 of drug acquisition and only accounted for 9% of the variance in regard to avoidance performance. As in this study, several other researchers (Bindra & Anchell, 1963; Garberg & Sandberg, 1960; Greenblatt & Osterberg, 1961; and Kamano Powell & Martin, 1967) have demonstrated that an increase in motor activity does not always result in the facilitation of the response to be learned.

The other alternative hypothesis is the possibility of the drug having a sensitization effect upon the animals. The non-lesioned drug groups provided a control for sensitization per se. Comparison of the learning curves of the normal and amygdala-drug groups for the first 8 days of drug acquisition suggests that drug induced sensitization alone cannot account for the marked improvement on day 9. Examination of the learning curves

of the normal-drug groups clearly shows that methylphenidate at 4 and 8 mg/kg impairs acquisition of the AAR such that if the drug produces sensitization at these two dosage levels, it appears to interfer with performance. The issue is then, does the drug interact with the lesion in such a way as to produce sensitization. Such an interaction seems paradoxical in light of the consistent evidence that amygdalectomy alone results in a less responsive Ss. Several studies (Bagshaw & Benzies, 1968, Bagshaw & Coppock, 1968; and Bagshaw & Pribram, 1968) demonstrated that amygdalectomized monkeys do not respond differentially to different shock levels and the Ss GSR levels were significantly depressed in regard to external stimulation. Similarly Goldstein (1968) and Kemble & Beckman (1969) found that rats with amygdaloid lesions were insensitive to different levels of shock intensity.

The results of Swartzbaum and Gay (1966) that amygdaloid lesions in rats can completely reverse the "septal syndrome" (hyperactivity to stimulation, hyperemotionality, and wildness) or rats with septal lesions suggests that rats with amygdaloid lesions would be less susceptible to sensitization effects due to drug treatment. In addition, the finding that the lesioned animals performance under non drug retraining was significantly better than their pre-drug performance and that of the lesioned control group is not consistent with a sensitization hypothesis. In summary, the evidence discussed does not support that spurious intertrial responding and/or a Lesion x Drug

sensitization effect played a significant role in the findings of the present study.

The finding that the amygdaloid-drug groups had significantly better retraining scores than AMY-0 suggests that the amygdala plays a minor role in the expression of an AAR once the response has been correctly performed. This is consistent with the conclusions of several other studies (Horvath, 1963; John & Killam, 1960; and Thatcher & Kimble, 1966). Support for the hypothesis that the consequences of the CS had been learned by the amygdaloid-groups during predrug acquisition is evident from the examination of the final asymptotic performance of the eight experimental groups. It can be seen that the amygdaloid drug groups are performing as well as their respective drug controls who had received twice as many drug training trials. This effect suggests that an intact amygdala is not essential for the learning of the association between the CS and US in an active avoidance task.

In order to examine the implications of the present findings they will be discussed in relation to several theoretical positions (e.g., consolidation, fear-reduction or over-arousal, attention or orienting, and modulatory or facilitatory mechanism).

Consolidation of Memory

Goddard (1964b) found that low level unilateral stimulation of the amygdala resulted in the disruption of CER only when the stimulation occurred for 5 min. after the US period. He concluded that the amygdala is primarily involved in the consolidation of fear motivated

learning. The results of the present study do not support a hypothesis which assumes that the amygdala is involved in the consolidation of the association between the CS and US.

In a more recent study Goddard (1969) injected carbachol bilaterally into the amygdala of rats trained in CER, PAR and AAR (one-way) test situations. He found that carbachol injections resulted in a deficit in passive avoidance acquisition under distributed training but failed to impair acquisition under massed training. Goddard suggests that response suppression during passive avoidance may depend on different memory mechanisms depending upon whether the trials are massed (short term memory) or distributed (long term memory). Carbachol treatment of amygdaloid Ss under both massed and distributed training did not impair acquisition or retention of a one-way active avoidance task.

Goddard concluded that the deficit due to carbachol injection was not compatible with a consolidation hypothesis and suggested that the results be viewed "in terms of the utilization of memory for response inhibition." He further stated that "this concept implies that learning and long-term storage was not affected in either the CER or passive avoidance situation..." This conclusion is compatible with the findings of the present study in that the dramatic shift in performance supports the hypothesis that learning and long-term storage was not affected during the predrug training trials.

Fear Reduction

The fear-reduction interpretation of AAR impairment after amygda-

lectomy upon first analysis would be compatible with the present findings in that methylphenidate would presumably activate or arouse hypothalamic activity and consequently provide the necessary fear for learning to take place. This interpretation is not found to be supported in terms of predrug latency scores, behavioural reactions of the amygdaloid Ss and performance of individual Ss.

In the present study the latency measure was a composite of the excape and avoidance latency. The latencies for the amygdaloid Ss during predrug acquisition consisted primarily of escape latencies, whereas the latencies of the drug controls contained both escape and avoidance components. Examination of the data (fig. 2) shows that the amygdaloid latencies tend to be shorter on the first two days than the normals controls (except for N-16). By the fourth day all of the amygdaloid groups were excaping within 1/2 second ($\overline{X}$ = 5.26) after onset even though their mean performance was only 1.82 correct out of 25 trials. Although these data are not a direct measure of fear, they strongly suggest that the Ss excape responses were not impaired as the mean N-O latencies (which consisted of both avoidance and escape latencies) was 5.48 seconds. Since it is likely that short latency escape responses require some degree of anticipation or preparedness, these data suggest that the amygdaloid S's were somewhat fearful, even though they made few avoidance responses. The amygdaloid Ss by the fourth day of training manifested what appeared to be normal fear responses, during their transportation to the test apparatus. This behaviour in conjunction with the extremely short latencie of the Ss

tend to suggest that the deficit was not primarily due to the lack of fear.

The fear reduction interpretation of Mowrer and Lamoreaux, (1946) would suggest that learning could not occur as the drive reduction component of fear would be absent in terms of their two-factor theory of avoidance learning. If the lack of differences in the response latencies and behavioural observations of the amygdaloid and normal Ss were not considered as sufficient evidence against the fear reduction hypothesis, then the two factor position could be seriously considered. However, the session did not support this position. Two Ss in particular, AMY-4_4 and AMY-16_1 made 19 and 21 consecutive correct responses, respectively, before they received their first shock of that session. Thus, if one assumes that shock produces fear, which in turn provides the drive component of Mowrer's two-factor model, the Ss would have had to receive at least one trial with shock before learning could occur.

The behavioural observations of the amygdaloid Ss and lack of differences in their latency scores on the first day of acquisition in conjunction with the dramatic shift in performance of the amygdaloid Ss without their experiencing shock does not support a fear reduction hypothesis.

The over-arousal hypothesis of Robinson (1963) does not seem to fit the data on logical grounds. If the amygdaloid Ss are freezing because of over-arousal, then the administration of methylphenidate should produce additional arousal which in turn should result in an increase in freezing responses and poorer performance.

Attention and Orienting Behaviour

The hypothesis that amygdaloid lesions interferred with the autonomic components of the orienting mechanism (Bagshaw & Benzies, 1968; and Bagshaw & Coppock, 1968) was not directly tested in the present study. The systematic monitoring of orienting resonses, EEG, and GSR as done by Bagshaw and associates was not done in the present study. Periodic observation of the Ss did reveal however, that amygdaloid Ss appeared to be more alert under drug acquisition in that they manifested ear flicks as well as orienting their head and body in the direction of the CS.

If Barrett (1969) and Pribram (1969) are correct in assuming that the deficit arising from amygdalectomies are due to dysfunction of the sensory input system, then the above observations provide support for their findings with monkeys although it does not preclude the possibility that amygdaloid lesions might also result in motor dysfunctioning in the rat.

Modulation or Facilitatory Mechanism

A facilitating or modulating effect of the amygdala on the hypothalamus has been proposed by several researchers (Caruthers, 1968; Gloor, 1956; 1960; Grossman, 1964; Stokman & Glusman, 1970; and Ursin & Kaada, 1960) based on lesion, electrophysiological, electrical and chemical stimulation studies of the amygdala.

Ursin and Kaada (1960) suggested that the amygdala can be topographically discriminated in terms of flight and defensive reactions.

They found that stimulation of the rostral area of the amygdaloid complex resulted in flight responses whereas stimulation of the ventromedial and caudal parts of the amygdala produced defensive responses. In a later study Ursin(1965) demonstrated that lesions in the flight zone resulted in an acquisition deficit in an AAR. Although there seems to be some doubt as to discrete localization of functions within the amygdala (Gloor, 1964), there does seem to be reasonable evidence that the amygdala does have facilitatory influences on hypothalamic elicited motor behaviour (Gloor, 1960; and Stokman & Glusman, 1970).

The finding by several studies (Cole & Glees, 1965 and Monnies & Krupp, 1069) that methylphenidate's central site of action is the hypothalamus is consistent with the author's hypothesis that the amygdala has an effect on hypothalamic activity. It is assumed that the basic flight sequences intrinsic to the hypothalamus (Glickman & Schiff, 1966; and Roberts, 1970) may have to be primed or activated by some other center in the brain. It is further assumed this extra-hypothalamic center integrates external information with the ongoing activity of the hypothalamus. The role of the amygdala may be to provide the necessary priming of hypothalamic neurons such that external stimuli (conditioned or innate releasers) will trigger hypothalamic flights systems (active avoidance) or will trigger hypothalamic defense systems (passive avoidance). The findings of Kaada (1960) Stokman & Glusman (1970); Ursin and Kaada (1960); and Ursin (1965) suggest that at the level of the amygdala and hypothalamus there is evidence for such

a dual mechanism operating differentially for passive and active avoidance conditioning.

The findings of Vanderwolf (1969) that the thalamus is involved in the initiation of movement and that the amygdala has direct connections with the thalamus (Cowan, Reisman & Powell,1965) suggests yet another possible interpretation of the data. Vanderwolf (1969) found that "medial thalamus-damaged rats give evidence of an ability to learn what to do in an aversive situation even though they fail to perform active avoidance responses". Vanderwolf (1969b) also found that medial thalamic Ss froze less than normals during exploration and tended to defecate less than normal animals in novel situations (1962). Vanderwolf concluded from his findings on medial thalamic lesions that "higher level motor control can be disrupted by a lesion which leaves perceptual mnenonic processes relatively intact".

The parallel results in the present study in conjunction with the evidence that the amygdala has some direct connections with the thalamus suggests that the amygdala may have an effect on the thalamic trigger system as outlined by Vanderwolf (1969).

In summary, the implications of the present study were discussed in terms of several hypotheses of amygdaloid functioning. The results were not consistent with the hypothesis that the amygdala is essential for the learning of an active avoidance response. Although the data were not compatible with Goddard's (1963) earlier consolidation hypothesis it does appear to be congruent with his later hypothesis that the amygdala plays a role in the utilization of long term memory (Goddard, 1969). The demonstration of latent learning in the amygdaloid Ss under the influence of methylphenidate was interpreted as support for the hypothesis

that the amygdala acts primarily as a facilitatory mechanism on other neural structures involved in the acquisition of an active avoidance response.

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APPENDIX A

Means for Avoidances, Latencies and Intertrial Responses for Acquisition and Retraining

Table 1. Mean Avoidance for first 8 days of Acquisition

	Days							
Groups	1	2	3	4	5	6	7	8
AMY-0	2.50	1.75	1.75	1.38	.88	2.00	2.62	1.62
AMY-4	1.62	1.88	1.50	2.00	2.12	2.75	2.75	2.12
AMY-8	1.62	1.88	1.12	2.25	2.50	1.87	1.12	2.00
AMY-16	2.62	2.12	2.00	1.62	1.62	1.75	2.75	2.38
N-0	6.62	8.00	9.25	8.62	7.62	10.25	11.62	11.38
N-4	2.88	3.88	5.25	3.62	5.38	4.38	9.62	11.62
N-8	3.38	2.50	5.50	4.88	7.00	9.12	7.00	10.25
N-16	7.00	10.50	9.38	13.12	11.75	12.88	16.50	18.12

Table 2. Mean Avoidance for Amygdaloids (days 9 to 16) and Normal Controls (days 1 to 8) on 1st 8 days of Drug Acquisition

	Sessions							
Groups	1	2	3	4	5	6	7	8
AMY-0	2.00	2.25	3.38	3.62	3.50	4.75	4.50	4.38
N-0	6.62	8.00	9.25	8.62	7.62	10.25	11.62	11.38
AMY-4	11.62	10.88	12.00	14.25	14.25	15.50	14.62	15.88
N-4	2.88	3.88	5.25	3.62	5.38	4.38	9.62	11.62
AMY-8	8.88	12.50	13.50	14.75	16.50	15.75	16.25	15.75
N-8	3.38	2.50	5.50	4.88	7.00	9.12	7.00	10.25
AMY-16	14.62	15.12	16.50	17.88	18.38	19.75	18.75	19.75
N-16	7.00	10.50	9.38	13.12	11.75	12.88	16.50	18.12

Table 3. Mean Avoidance for Amygdaloids and Normal Controls for the last 8 days of Acquisition

	Days							
Groups	9	10	11	12	13	14	15	16
AMY-0	2.00	2.25	3.38	3.62	3.50	4.75	4.50	4.38
AMY-4	11.62	10.88	12.00	14.25	14.25	15.50	14.62	15.88
AMY-8	8.88	12.50	13.50	14.75	16.50	15.75	16.25	15.75
AMY-16	14.62	15.12	16.50	17.88	18.38	19.75	18.75	19.75
N-0	13.00	12.00	13.50	14.62	14.50	14.75	14.38	14.75
N-4	9.38	9.12	8.00	9.75	9.50	10.88	13.25	13.38
N-8	12.00	11.00	8.62	11.50	12.38	10.88	10.62	10.75
N-16	16.00	13.12	17.25	18.00	17.62	17.88	18.62	19.00

Table 4. Mean Avoidances during Post Drug Retraining

	Days					
Groups	1	2	3	4	5	6
AMY-0	5.25	5.25	6.12	4.88	3.75	4.25
N-0	16.62	15.25	16.75	14.50	17.00	17.88
AMY-4	11.75	11.38	11.75	13.38	13.00	11.62
N-4	8.38	9.12	7.75	10.12	10.38	10.88
AMY-8	9.12	10.50	12.25	10.62	12.75	13.12
N-8	10.75	10.88	12.12	12.00	13.00	12.75
AMY-16	10.00	11.38	12.00	12.00	12.50	13.75
N-16	7.50	9.50	13.50	14.62	15.12	16.62

Table 5. Mean Latencies for first 8 days of Training

	Days							
Groups	1	2	3	4	5	6	7	8
AMY-0	6.58	5.79	6.18	5.54	6.08	5.15	5.15	5.34
AMY-4	6.18	5.43	5.30	5.34	5.42	5.43	5.17	5.10
AMY-8	5.97	5.23	5.32	5.14	4.97	5.22	5.19	5.11
AMY-16	5.77	5.63	5.21	5.03	5.10	5.26	5.04	5.23
N-0	6.43	5.19	4.98	5.48	5.03	4.90	4.38	5.18
N-4	6.70	7.22	4.79	7.00	5.16	4.45	4.25	4.35
N-8	5.80	6.85	5.30	6.17	4.99	4.23	4.51	3.08
N-16	4.60	3.32	4.58	3.68	3.67	3.38	2.62	2.67

Table 6. Mean Latencies for Amygdaloids (days 9 to 16) and Drug Controls (days 1 to 8) on first 8 days of Drug Acquisition

	Sessions							
Groups	1	2	3	4	5	6	7	8
AMY-0	5.28	5.39	5.12	5.37	5.22	4.94	5.04	5.10
N-0	6.43	5.19	4.98	5.48	5.03	4.90	4.38	5.18
AMY-4	4.22	4.36	4.17	3.80	3.72	3.65	3.67	3.60
N-4	6.70	7.22	4.79	7.00	5.16	4.45	4.25	4.35
AMY-8	4.16	3.69	3.58	3.59	3.43	3.29	3.15	3.46
N-8	5.80	6.85	5.30	6.17	4.99	4.23	4.51	3.08
AMY-16	4.06	3.87	3.32	3.17	3.07	2.66	3.06	3.00
N-16	4.60	3.32	4.58	3.68	3.67	3.38	2.62	2.67

Table 7. Mean Latencies for last 8 days of training

Groups	Days 9	10	11	12	13	14	15	16
AMY-0	5.28	5.30	5.12	5.37	5.22	4.94	5.04	5.10
AMY-4	4.22	4.36	4.17	3.80	3.72	3.65	3.67	3.60
AMY-8	4.16	3.69	3.58	3.59	3.43	3.29	3.15	3.46
AMY-16	4.06	3.87	3.32	3.17	3.07	2.66	3.06	2.99
N-0	4.09	4.54	4.09	4.19	3.50	3.62	3.41	3.24
N-4	4.98	4.60	4.70	4.37	4.45	4.42	4.15	3.80
N-8	3.86	4.62	4.44	3.85	3.69	3.78	3.88	3.74
N-16	3.61	3.90	3.07	4.58	3.01	3.07	2.94	2.95

Table 8. Mean Latencies during Post Drug Retraining

Groups	Days 1	2	3	4	5	6
AMY-0	4.90	4.90	4.93	4.77	5.04	4.88
N-0	3.56	3.97	3.77	4.30	3.76	3.67
AMY-4	4.21	4.87	4.89	4.41	4.63	4.56
N-4	4.77	4.66	5.07	4.96	4.45	4.78
AMY-8	4.22	4.39	4.21	4.32	4.13	4.24
N-8	4.21	4.30	4.35	4.35	4.16	4.56
AMY-16	4.42	4.42	4.14	4.15	4.30	4.28
N-16	5.26	4.18	3.99	4.04	3.50	3.59

Table 9. Mean Intertrial Responses / day for first 8 days of Training

	Days							
Groups	1	2	3	4	5	6	7	8
AMY-0	37.25	20.38	24.25	21.62	20.38	20.25	20.88	20.38
AMY-4	55.75	43.00	35.25	24.75	27.12	25.38	27.25	31.50
AMY-8	43.12	28.38	19.75	28.00	23.12	30.25	16.38	22.88
AMY-16	51.50	42.62	38.88	38.25	33.38	34.25	29.88	28.25
N-0	40.00	43.12	26.12	25.38	39.25	20.38	24.38	24.62
N-4	22.62	23.75	56.00	22.62	21.75	21.75	27.75	31.38
N-8	34.88	29.88	27.12	32.00	35.25	42.62	33.88	47.75
N-16	46.00	86.75	54.62	62.12	53.12	43.38	66.88	73.12

Table 10. Mean Intertrial Responses for Amygdaloids (days 9 to 16) and Drug Controls (days 1 to 8) on first 8 days of Drug Acquisition

	Sessions							
Groups	1	2	3	4	5	6	7	8
AMY-0	23.38	19.12	20.38	27.50	22.38	30.75	24.50	25.00
N-0	40.00	43.12	26.12	25.38	39.25	20.38	24.38	24.62
AMY-4	54.25	46.12	58.00	59.00	56.88	65.50	64.38	69.50
N-4	22.62	23.75	56.00	22.62	21.75	21.75	27.75	31.38
AMY-8	72.25	61.62	76.75	56.62	58.12	73.50	91.88	57.25
N-8	34.88	29.88	27.12	32.00	35.25	42.62	33.88	47.75
AMY-16	80.75	83.50	62.38	73.12	77.00	69.75	72.25	59.00
N-16	46.00	86.75	54.62	62.12	53.12	43.38	66.88	73.12

Table 11. Mean Intertrial Responses for days 9 to 16 (AMY's and Controls)

	Days							
Groups	9	10	11	12	13	14	15	16
AMY-0	37.25	20.38	24.25	21.62	20.38	20.25	20.88	20.38
AMY-4	54.25	46.12	58.00	59.00	56.88	65.50	64.38	69.50
AMY-8	72.25	61.62	76.75	56.12	58.12	73.50	91.88	57.25
AMY-16	80.75	83.50	62.38	73.12	77.00	69.75	72.25	59.00
N -0	14.75	12.12	16.75	15.25	13.50	11.25	11.50	8.50
N -4	14.75	22.50	21.75	23.12	17.38	16.25	12.75	12.50
N -8	62.38	45.50	56.75	39.50	36.88	42.75	40.25	37.12
N -16	56.88	45.00	30.88	28.50	30.88	32.25	34.12	28.62

Table 12. Mean Intertrial Responses during Post Drug Retraining

	Days					
Groups	1	2	3	4	5	6
AMY-0	28.75	26.25	18.12	24.25	22.50	21.38
N-0	32.50	22.62	23.25	18.50	20.88	30.62
AMY-4	40.75	88.00	65.75	50.62	50.00	49.38
N-4	20.62	18.50	14.50	15.62	17.00	17.62
AMY-8	28.62	30.50	28.12	27.50	21.88	22.50
N-8	37.38	37.75	46.50	46.12	34.00	37.25
AMY-16	39.00	38.75	35.75	32.38	28.38	31.75
N-16	34.50	46.00	45.38	36.88	34.25	44.12

Table 13

Mean Response Probabilities for Intertrial Responses (ITR) and Percentage of Correct Avoidance (AAR) per Session on Day 9 and 16 of Drug Acquisition for Individual Ss from the Four Lesioned Groups (AMY-0,48 & 16)

Day	Measure	Subject No. 1	2	3	4	5	6	7	8	$\bar{X}$
					AMY - 0					
9	ITR	.07	.11	.11	.08	.12	.05	.02	.009	.08
	AAR	4	4	20	8	12	12	4	0	8
16	ITR	.04	.09	.08	.15	.11	.05	.05	.05	.08
	AAR	0	28	24	20	40	8	20	0	18
					AMY - 4					
9	ITR	.29	.12	.17	.21	.18	.18	.12	.05	.16
	AAR	44	16	44	84	24	52	72	36	.44
16	ITR	.16	.08	.24	37	.20	.23	.16	.10	.19
	AAR	84	40	84	100	12	84	84	20	64
					AMY - 8					
9	ITR	.65	.06	.15	.16	.11	.17	.14	.33	.22
	AAR	40	24	40	48	28	36	20	48	30
16	ITR	.19	.17	.07	.25	.28	.09	.07	.27	.17
	AAR	84	72	32	88	80	28	24	96	63
					AMY - 16					
9	ITR	.38	.53	.19	.21	.16	.19	.06	.10	.22
	AAR	84	68	60	40	60	32	56	68	52
16	ITR	.37	.27	.32	.12	.05	.13	.07	.12	.18
	AAR	84	92	76	76	80	72	60	92	79

APPENDIX B

Analysis of Variance Tables for Acquisition and Retraining

APPENDIX B

Table 1

Analysis of Variance: Acquisition Avoidances, Days 1 to 8

Source	df	MS	F
Lesion (A)	1	5323.83	68.87***
Dosage (B)	3	311.18	4.03**
A X B	3	289.89	3.75*
Error	56	77.30	
Days (C)	7	114.99	12.77***
A X C	7	99.89	11.10***
B X C	21	10.66	1.18
A X B X C	21	9.25	1.03
Error	392	9.00	

Table 2

Analysis of Variance: Acquisition Avoidances, Days 1 to 8 (Normal Controls) vs. Days 9 to 16 (Amygdaloids)

Source	df	MS	F
Lesion (A)	1	1491.94	9.66**
Dosage (B)	3	1936.86	11.54***
A X B	3	1703.89	11.03***
Error	56	154.46	
Days (C)	7	249.96	20.71***
A X C	7	35.75	2.96**
B X C	21	19.81	1.64*
A X B X C	21	12.22	
Error	392		

* $p < .05$
** $p < .01$
*** $p < .001$

Table 3

Analysis of Variance: Acquisition Avoidances, Days 9 to 16

Source	df	MS	F
Lesion (A)	1	98.00	0.35
Dosage (B)	3	1627.46	5.85**
A X B	3	1344.98	4.83**
Error	56	278.19	
Days (C)	7	122.71	15.35***
A X C	7	18.44	2.31
B X C	21	9.05	1.13
A X B X C	21	9.83	1.23
Error	392	7.99	

Table 4

Analysis of Variance: Retraining Avoidances

Source	df	MS	F
Lesion (A)	1	612.59	2.43
Dosage	3	63.41	0.25
A X B	3	905.50	3.59*
Error	56	252.27	
Days (C)	5	67.55	6.84***
A X C	5	13.50	1.37
B X C	15	21.41	2.17**
A X B X C	280	9.70	0.98
Error		9.88	

* $p < .05$
** $p < .01$
*** $p < .001$

Table 5

Analysis of Variance: Acquisition Latencies, Days 1 to 8

Source	df	MS	F
Lesion (A)	1	2701824.0	7.22**
Dosage (B)	3	1943466.0	5.20**
A X B	3	1247232.0	3.34*
Error	56	373961.3	
Days (C)	7	1106212.0	20.62***
A X C	7	375332.6	7.00***
B X C	21	106849.5	1.99**
A X B X C	21	143823.2	2.68***
Error	392	53637.9	

Table 6

Analysis of Variance: Acquisition Latencies, Days 1 to 8 (Controls) vs. Days 9 to 16 (Amygdaloids)

Source	df	MS	F
Lesion (A)	1	3238656.0	7.55**
Dosage (B)	3	6865493.0	16.00***
A X B	3	1541717.0	3.59*
Error	56	429083.4	
Days (C)	7	1229092.0	21.73***
A X C	7	304896.0	5.39***
B X C	21	98755.0	1.75*
A X B X C	21	147163.4	2.60***
Error	392	56560.3	

* $p < .05$
** $p < .01$
*** $p < .001$

Table 7

Analysis of Variance: Acquisition Latencies, Days 9 to 16

Source	df	MS	F
Lesion (A)	1	26112.0	0.05
Dosage (B)	3	2036480.0	4.06**
A X B	3	1522346.0	3.03*
Error	56	501604.6	
Days (C)	7	351341.7	9.48***
A X C	7	49225.1	1.33
B X C	21	28964.6	0.78
A X B X C	21	41484.2	1.12
Error	392	37063.8	

Table 8

Analysis of Variance: Retraining Latencies

Source	df	MS	F
Lesion (A)	1	373504.0	0.75
Dosage (B)	3	282026.6	0.56
A X B	3	480085.3	0.96
Error	56	501051.4	
Days (C)	5	27443.2	1.40
A X C	5	49049.6	2.51*
B X C	15	48759.5	2.49**
A X B X C	15	31641.6	1.62
Error	280	19569.4	

* $p \leq .05$
** $p < .01$
*** $p \leq .001$

Table 9

Analysis of Variance: Acquisition Intertrial Responses, Days 1 to 8

Source	df	MS	F
Lesion (A)	1	9730.38	2.81
Dosage (B)	3	12514.12	3.61*
A X B	3	4378.66	1.26
Error	56	3461.88	
Days (C)	7	1146.57	2.22*
A X C	7	1305.59	2.52*
B X C	21	591.85	1.14
A X B X C	21	575.99	1.11
Error	392	517.35	

Table 10

Analysis of Variance: Acquisition Intertrial Responses, Days 1 to 8 (Controls) vs. Days 9 to 16 (Amygdaloids)

Source	df	MS	F
Lesion (A)	1	37060.00	7.16**
Dosage (B)	3	35093.66	6.78***
A X B	3	11365.00	2.19
Error	56	5179.30	
Days (C)	7	344.00	0.38
A X C	7	886.86	0.98
B X C	21	983.33	1.09
A X B X C	21	696.62	6.77
Error	292	902.38	

* $p < .05$
** $p < .01$
*** $p < .001$

Table 11

Analysis of Variance: Acquisition Inter-trial Responses, Days 9 to 16

Source	df	MS	F
Lesion (A)	1	101137.94	21.22***
Dosage (B)	3	39604.33	8.31***
A X B	3	5955.85	1.25
Error	56	4766.42	
Days (C)	7	629.89	0.98
A X C	7	661.33	1.03
B X C	21	664.45	1.03
A X B X C	21	259.34	0.40
Error	392	642.42	

Table 12

Analysis of Variance: Retraining Inter-trial Responses

Source	df	MS	F
Lesion (A)	1	6256.50	0.96
Dosage (B)	3	3625.98	0.56
A X B	3	11108.04	1.71
Error	56		
Days (C)	5	723.99	1.66
A X C	5	495.76	1.13
B X C	15	358.59	0.82
A X B X C	15	392.34	0.90
Error	280	437.35	

* $p < .05$
** $p < .01$
*** $p < .001$

Table 13

Analysis of Variance: Relation of damaged structures in regard to CAR performance during predrug acquisition

Source	df	MS	F
Lesion sites	3	267.26	N. S.
Error	28	122.41	

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APPENDIX C

Histological Analysis of Amygdaloid Ss. Sections From the König and Klippel (1963) Stereotaxic Atlas of the Rat Brain

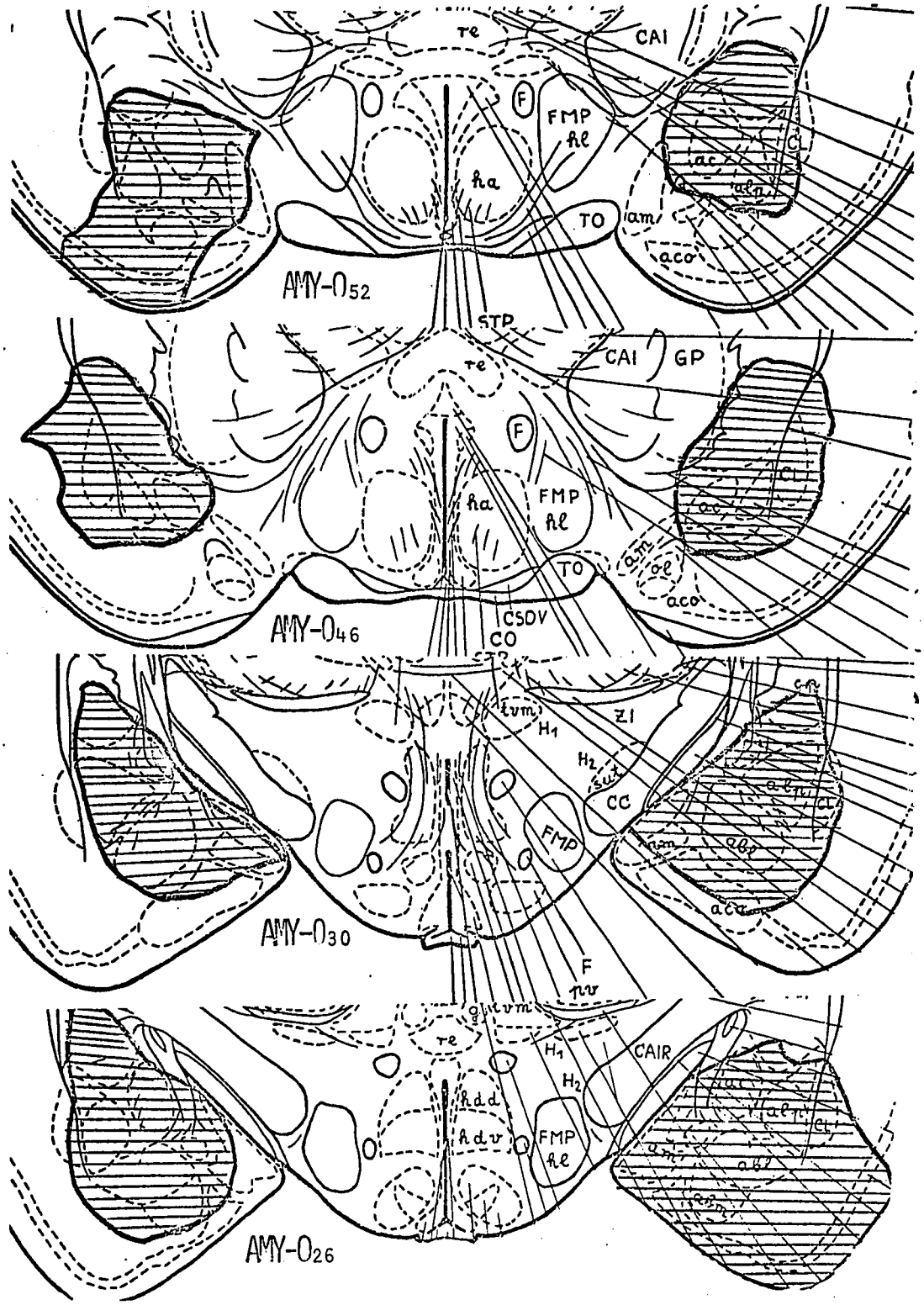

Figure 1 Reconstruction of lesions for individual animals of Group AMY-O

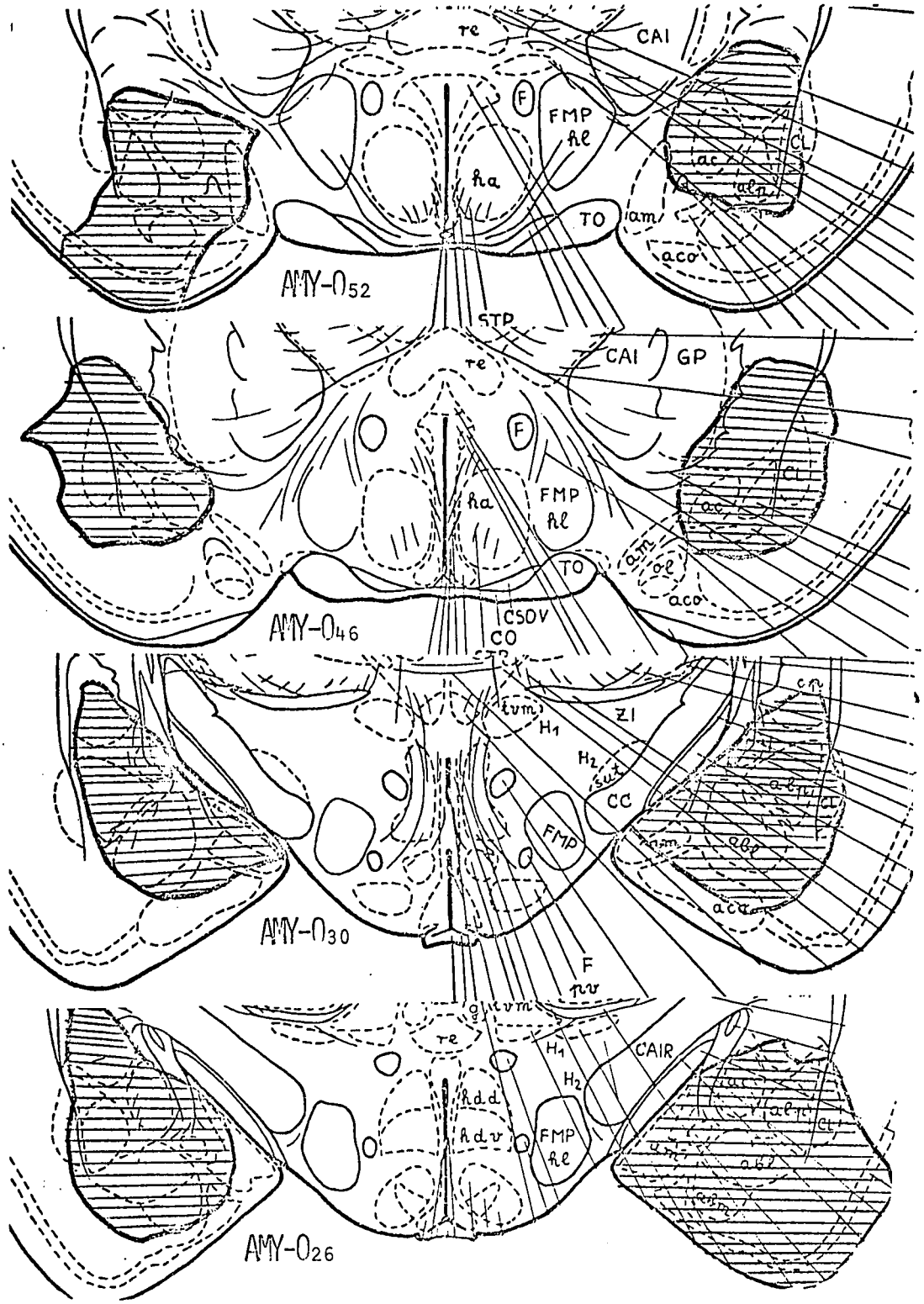

Figure 1 Reconstruction of lesions for individual animals of Group AMY-O

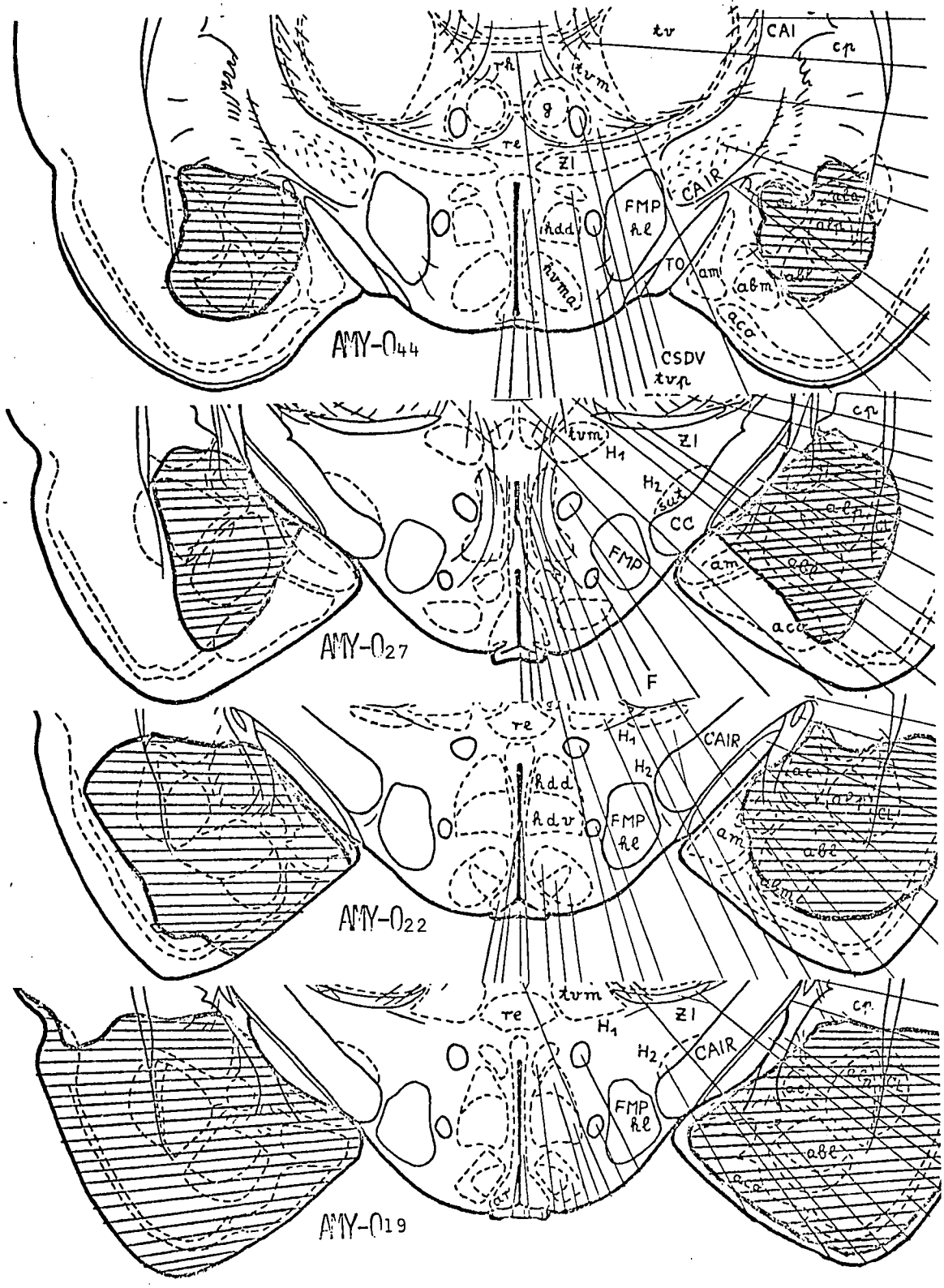

Figure 2 Reconstruction of lesions for individual animals of Group AMY-O

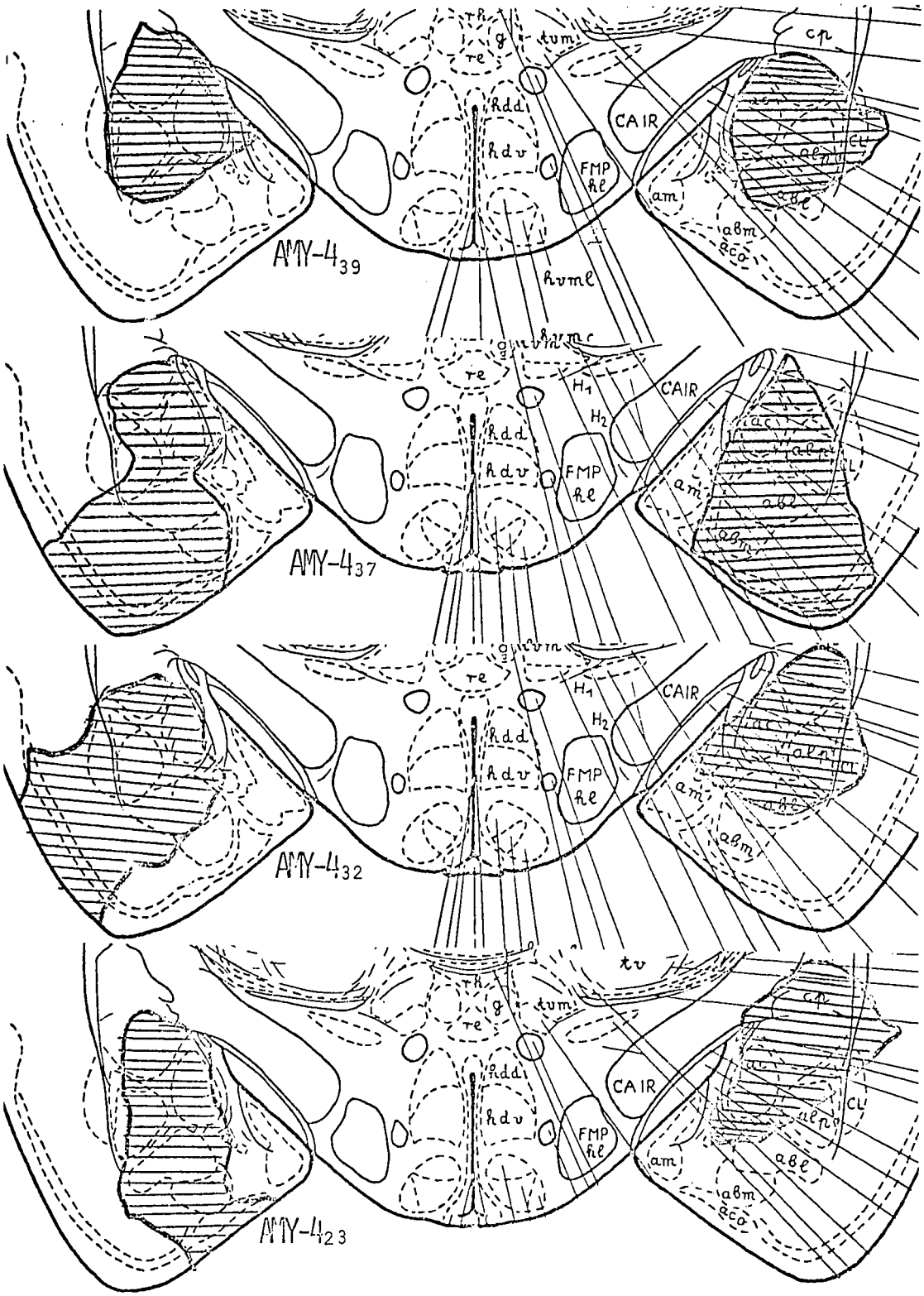

Figure 3 Reconstruction of lesions for individual animals of Group AMY-4

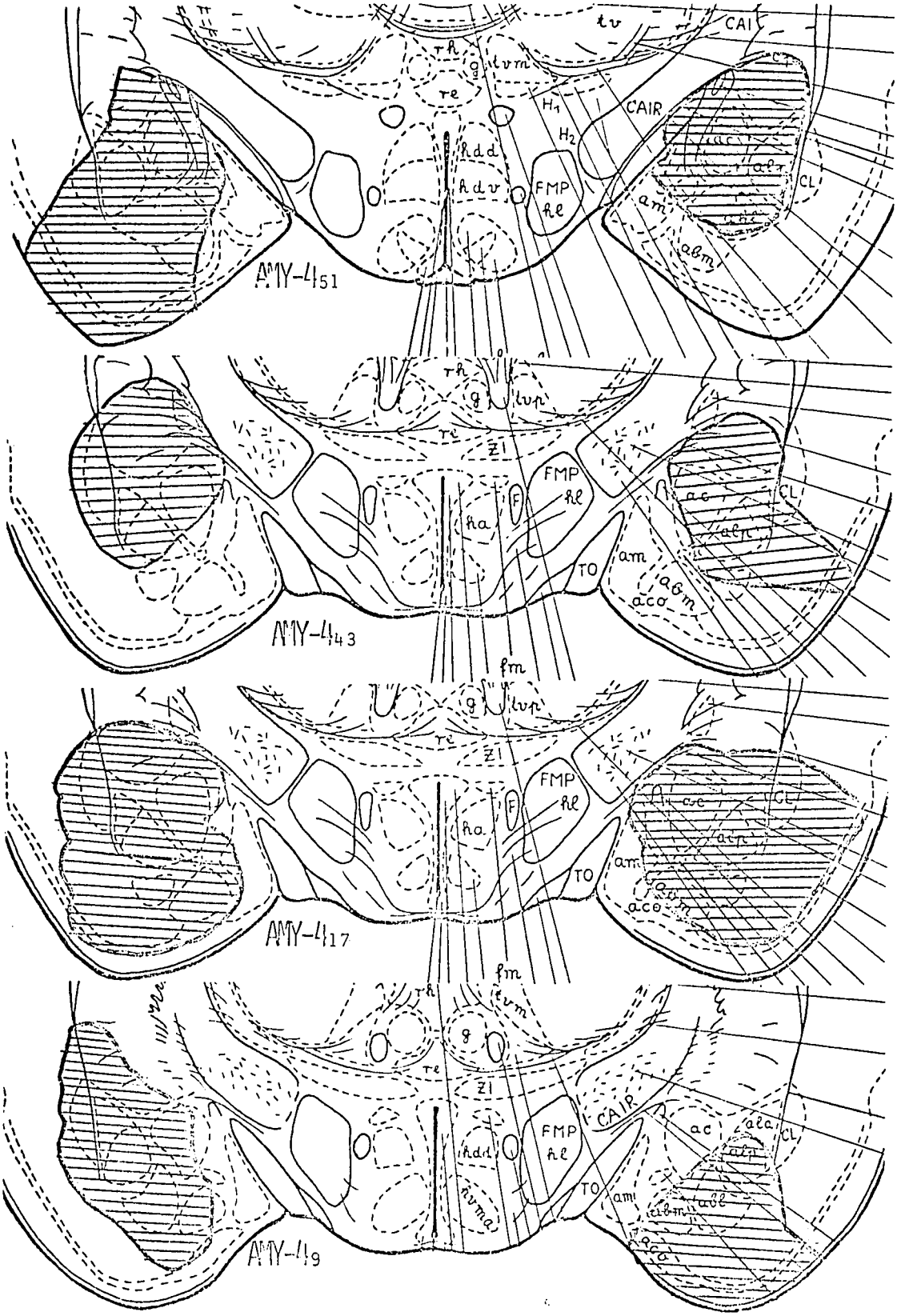

Figure 4 Reconstruction of lesions for individual animals of Group AMY-4

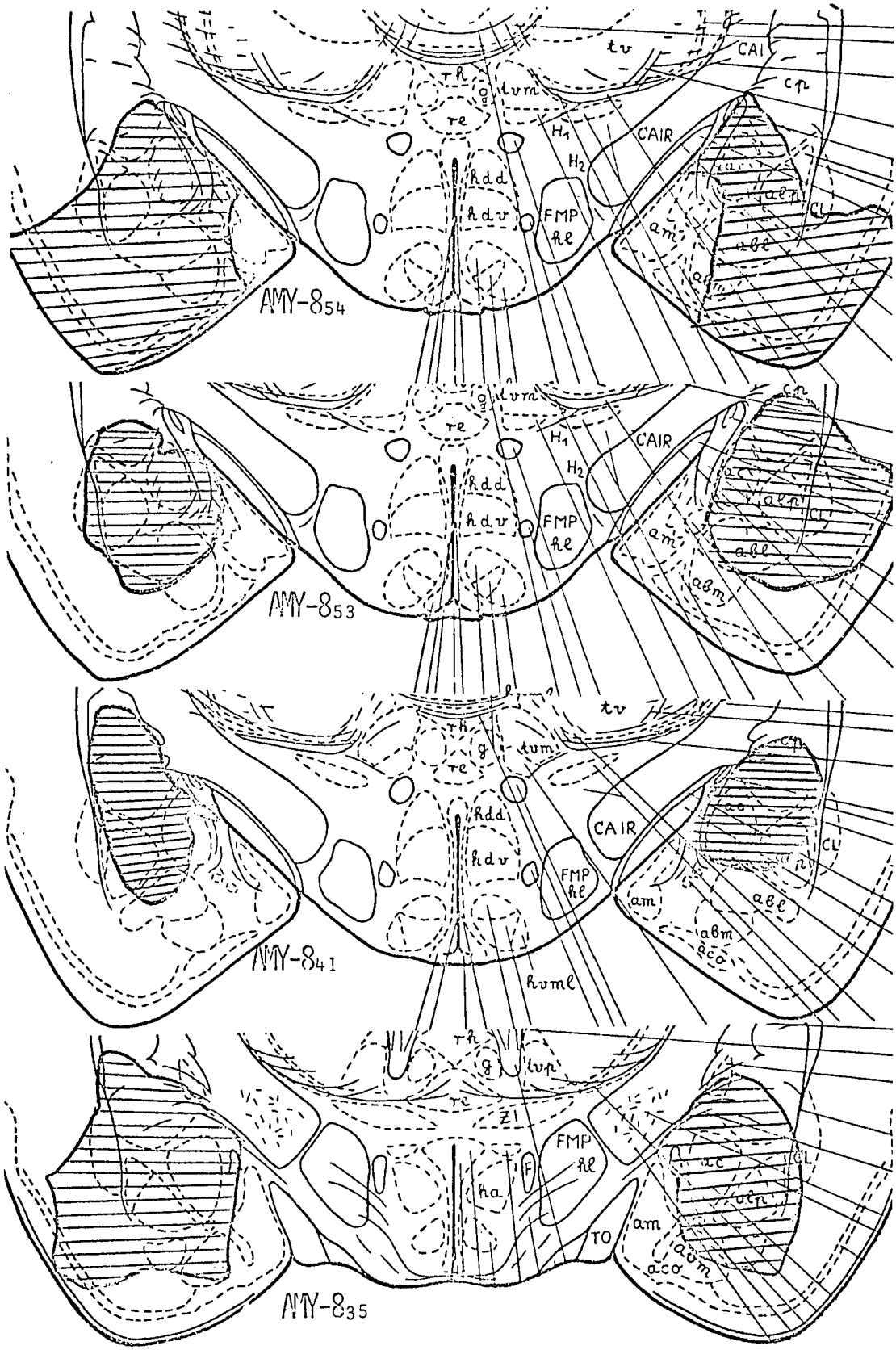

Figure 5 Reconstruction of lesions for individual animals

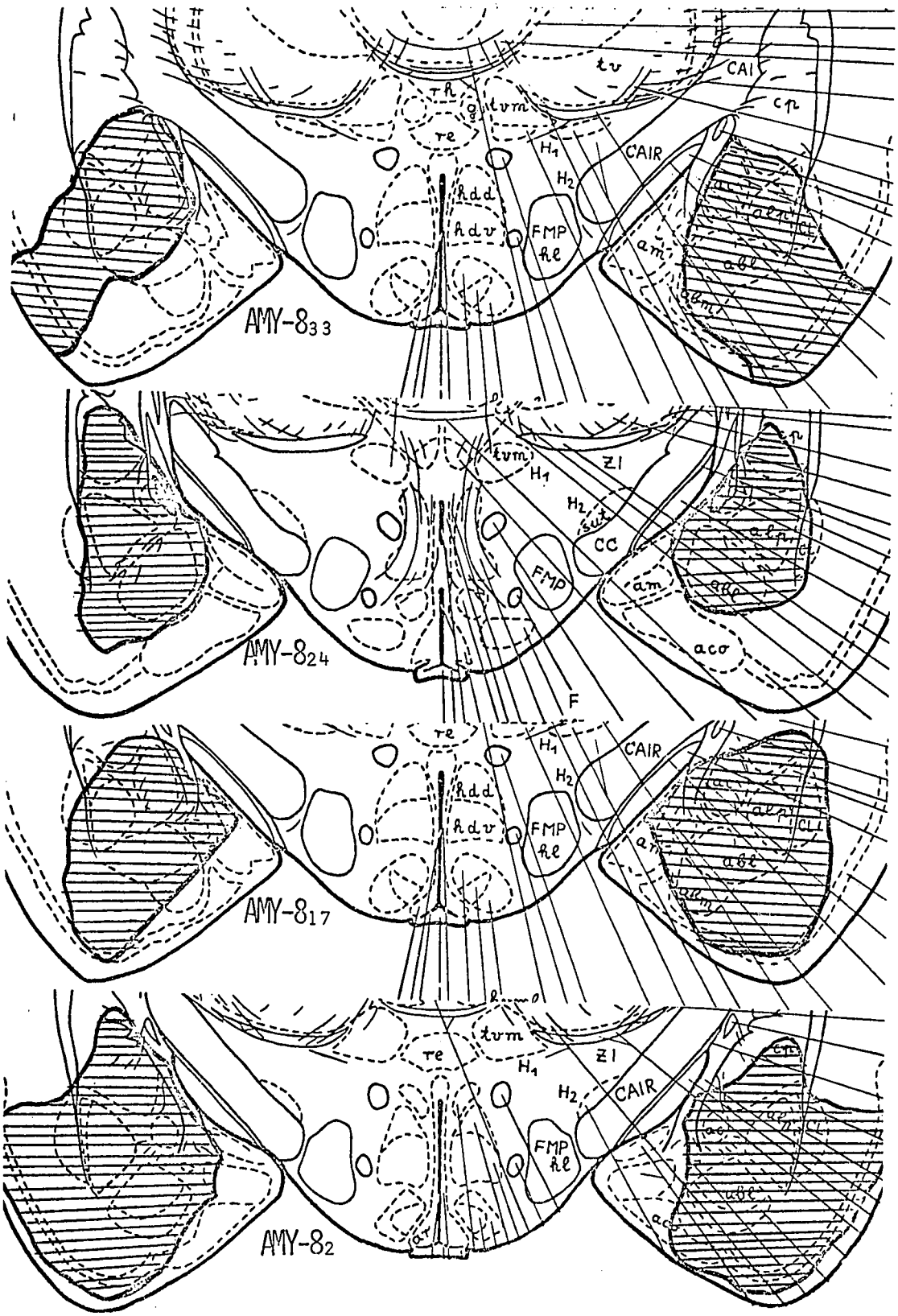

Figure 6 Reconstruction of lesions for individual animals of Group AMY-8

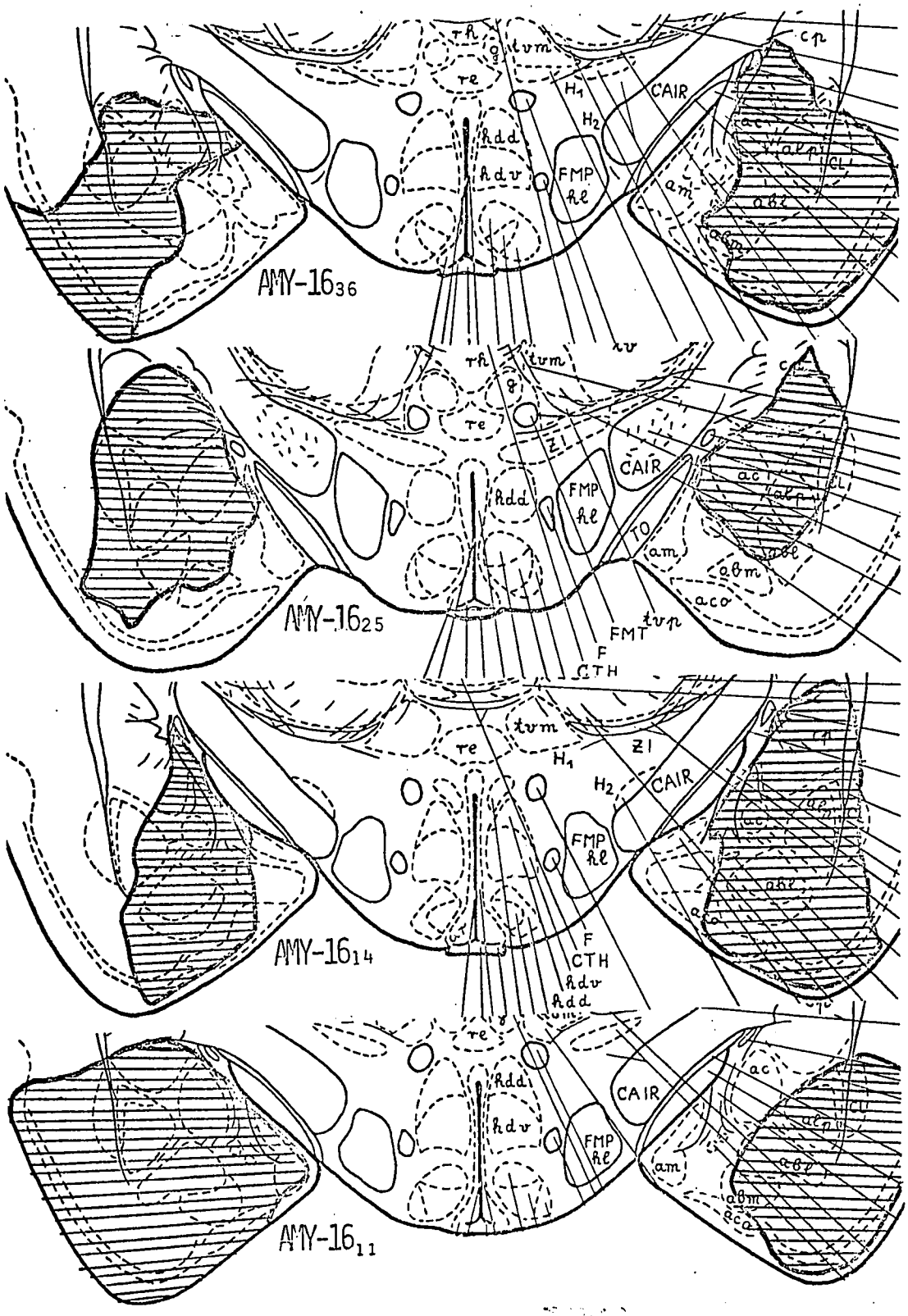

Figure 7 Reconstructions of lesions for individual animals of Group AMY-16

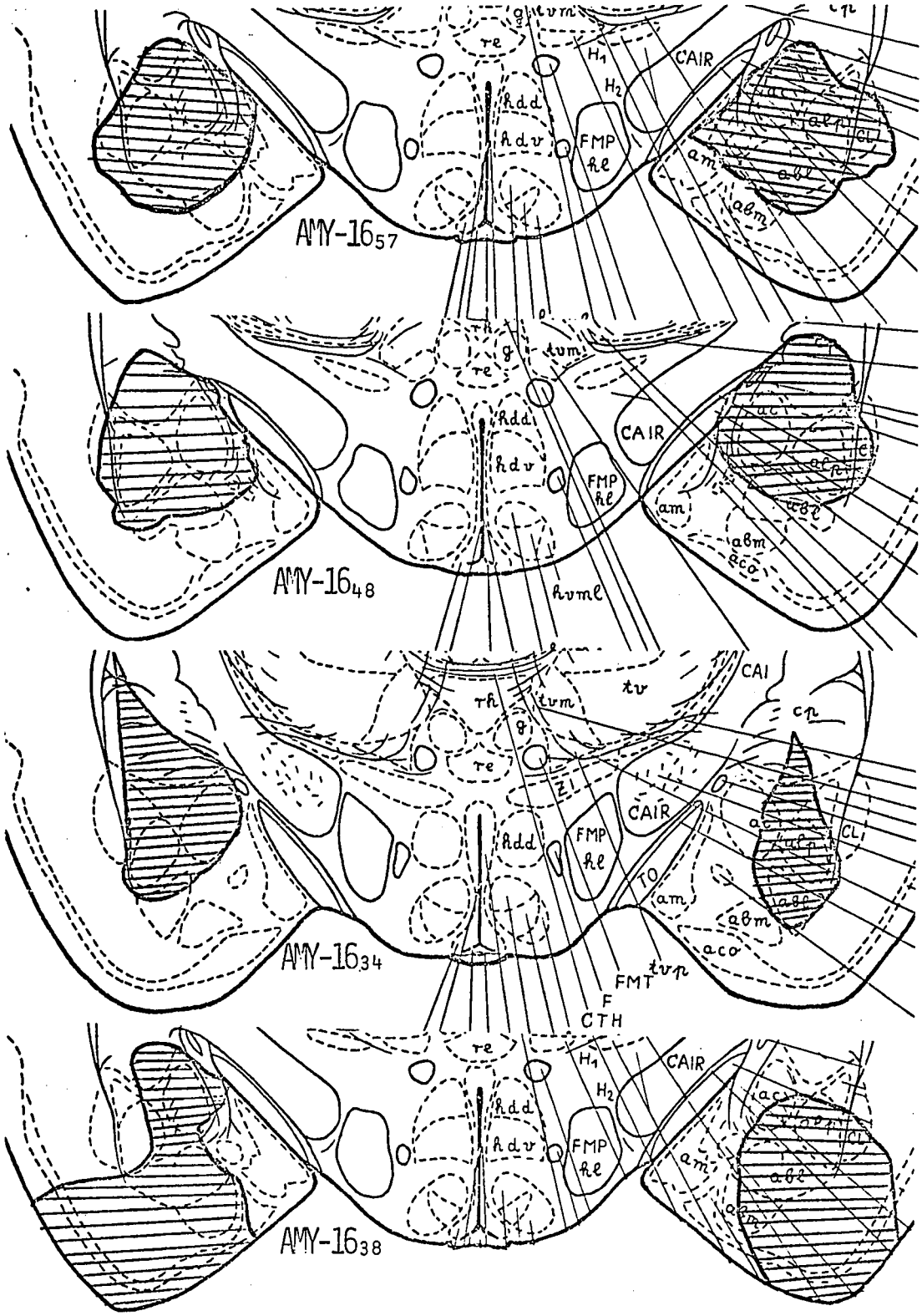

Figure 8 Reconstruction of lesions for individual animals of Group AMY-16