EFFECTS OF SEPTAL LESION ON GO, NO-GO DIFFERENTIATION
AND REVERSAL LEARNING IN RATS

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Abstract. Experiments were done on 24 Sprague-Dawley male albino rats. Acquisition of go, no-go differentiation and its reversal were compared between normal and septal animals. Rats were trained in Skinner boxes on a 30-s VI food reinforcement schedule. Differentiation sessions consisted of periods with flashing and steady light on, randomly distributed. In half the subjects of each group reinforcement was available only during the flashing light (CS⁺ periods) while during the steady light no reinforcement was delivered (CS⁻ periods). For the remaining subjects the allocation of stimuli as CS⁺ or CS⁻ was reversed. During reversal training the signalling properties of the stimuli were reversed. The experiments confirmed that there is lesion-induced increment in base-line response rate. During differentiation training septal damage had no significant effect on the proportion of total responses emitted during CS⁻, although it increased the overall rate of CS⁻ responding when the flashing light was used as CS⁻. During reversal training when the flashing light was used as CS⁻ septal animals both responded at a higher rate during CS⁻, and emitted a higher proportion of their responses during CS⁻, relative to controls. There were no lesion effects on CS⁻ responding when the steady light was used as CS⁻. Thus the septal deficit appeared when the to-be-extinguished habit was fairly strong and only under conditions of greater stimulus

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generalization. These results indicate that septal effects depend on a variety of experimental factors determining performance in any given test situation, among which stimulus intensity dynamism is one of particular importance.

INTRODUCTION

Septal animals appear to be impaired in their ability to reduce response output in the presence of a stimulus which is no longer reinforced. Septal lesions (particularly in the ventral portion of the medial septum and the diagonal band of Broca) produce deficits in inhibition of delay, manifested by a disruption of retention, as well as a deterioration in the acquisition of DRL performance (2, 4, 12, 16, 38). Septal lesions also reduce 'scalloping' in the responding of animals given food reinforcement on a fixed interval (FI) schedule (15). Septal rats trained on fixed ratio (FR) schedules continue to respond efficiently on ratios much higher than those which give rise to a breakdown in the behaviour of normal subjects (26). Total and medial septal lesions increase resistance to extinction after continuous reinforcement in the runway, while medial septal lesions sometimes even augment the partial reinforcement extinction effect in this situation (17, 18, 39, 43). Finally, septal lesions did not change or even facilitated the acquisition of a food-reinforced position habit, but caused a deficit in reversal of the position habit (7, 21, 22, 24, 46, 47, 48).

These results have been interpreted as a lesion-induced release or disinhibition of previously established behaviour (20, 33) and as grounds for treating the septo-hippocampal system as an anatomical substrate for behavioural inhibition (23). According to this hypothesis the medial septum, connected via the fornix-fimbria to the hippocampus, is responsible for the emotional and behavioural effects of frustrative non-reward. However, septal dysfunction does not usually affect either the acquisition or the reversal of non-spatial differentiation tasks (7, 41, 43), although deficits in brightness reversal tasks have recently been reported by Donovick's group (5, 45). Experiments in which the animal can respond so as to terminate its exposure to a stimulus (CS-) associated with the non-rewarded component of a multiple schedule in the Skinner box have also yielded little support for the frustration hypothesis, since the performance of lesioned animals was as good as that of intact animals (10, 25). But such experiments are inconclusive, since they have not included the necessary controls to show that the animal's responding is indeed maintained by the termination of CS-. Furthermore, when such controls are included, it has been demonstrated in
normal animals that there is little if any effect of this contingency (C. Preston, pers. comm., 1981). In other similar experiments it has been shown that septal animals develop behavioural contrast as well as normals (9, 10); but the development of behavioural contrast is now thought to depend on mechanisms unrelated to frustrative nonreward (40).

Experiments on the effects of septal lesions on the course of go, no–go differentiation (successive discrimination) have yielded inconsistent results. There is some evidence of an increase of responding during $\text{CS}^-$ after the lesion (10, 43). But in other studies the differentiation ratio, examined in a MULT VI/EXT paradigm, was the same for control and septal subjects (9). Thus this problem requires further investigation. There is also little evidence concerning septal effects on reversal learning after successive, go, no–go, differentiation. We decided, therefore, to examine the effects of septal lesions on both the acquisition and the reversal of such a differentiation.

Since it has been shown that the effects of brain lesions may depend on stimulus relations during the differentiation task (30, 51), in the present experiment the septal effects were analysed separately for two different stimulus arrangements: firstly, when the stronger of two stimuli was used as $\text{CS}^+$ and the weaker as $\text{CS}^-$; and secondly, when these stimulus conditions were the opposite.

Special attention was paid to the effects of septal lesions on the reversal of differentiation. The strength of the habit which undergoes extinction is greater during reversal learning than during the original differentiation training and therefore lesion-induced difficulties (if there are any) with the extinction of dominant but no longer reinforced behaviour should occur during reversal, even if no such effect is observed during the original training.

**METHODS**

**Subjects and surgery.** Twenty four Sprague–Dawley male albino rats were used, weighing 300–400 g at the beginning of the experiment. Surgery was carried out in a Kopf stereotaxic instrument under Equithesin anaesthesia (3 ml/kg). Lesions were performed using two monopolar electrodes made of 250 μm diameter diamel insulated wire aimed bilaterally with the following coordinates: 0.7 mm anterior to bregma, 0.7 mm lateral and 4.5 mm deep from dura for smaller septal lesions; and 0.8 mm anterior to bregma, 0.7 mm lateral and 5.0 mm deep from dura for a big septal lesion. To make smaller septal lesions ($n = 8$)
1 mA anodal d.c. current was passed for 10 s through each of the two electrodes in turn. To make a large septal lesion \((n = 8)\), both current and time of current passage were doubled. The circuit was completed by clipping the cathode to the rat’s ear. In sham-operated animals \((n = 8)\) the electrodes were surgically introduced as in lesioned subjects, but withdrawn without passing current.

All animals were allowed two to three weeks of post-operation recovery, during which the rats were regularly handled. During the first few days after the operation the animals had free access to food and water; they were then transferred to a 23-h food deprivation schedule.

**Apparatus.** Four identical Campden Instruments Skinner boxes were used, housed in sound attenuating cubicles. Each box contained a single lever and a recessed food-tray at floor level covered by a hinged perspex flap. Reinforcement consisted of a 45 mg food pellet automatically delivered into the tray, which was then illuminated for 3 s by a 1.2 W bulb mounted in a hole drilled in the rear edge of the perspex. A 2.8 W stimulus light was mounted above the lever and a dim house-light was placed in the centre of the ceiling. ANOVA computer was used for automatic programming of the experiment and for recording of the data.

**Procedure.** After magazine training, the subjects were shaped to press the lever and maintained for 1 h on a continuous reinforcement schedule. Then followed eight daily 1-h sessions under a 30-s VI food reinforcement schedule, resulting in the acquisition of stable lever-pressing behaviour. The preliminary training was carried out in the presence of the house-light only, while the stimulus light was not yet introduced. Afterwards, differentiation training began, wherein a single session consisted of 24 periods of 150 s duration each. The stimulus light was on steadily during half the periods and flashing (“on” and “off” intervals of 1 s duration) during the remaining periods. Periods with the steady or flashing stimulus light were separated by 2 s intervals, during which only the dim house-light was on. Arrangement of the periods was random with the restriction that periods with a given stimulus light on could not occur more than three times in succession. The order of stimulus light presentation changed from session to session. For half the animals reinforcement was available on a 30-s VI schedule during the steady stimulus light only, while during the flashing stimulus light no reinforcement was delivered. For the remaining subjects the allocation of stimuli was reversed. Periods in which responding was reinforced will be referred to as CS\(^+\) periods and those in which responding was not reinforced, as CS\(^-\) periods. Differentiation training lasted 14 days and was followed by a 3-week rest period.
Subsequently the animals were given 1 day of retraining and 14 days of reversal learning, during which the training CS$^-$ became CS$^+$ and vice versa.

The data recorded consisted of the number of lever-presses emitted by a rat during consecutive 150-s periods and the total number of responses emitted during CS$^+$ and CS$^-$ conditions independently in a given session.

**Histology.** After the experiment was completed, the animals were perfused with isotonic saline and 10% formalin. The brains were removed and left in a formol saline solution for about 10 days. Then brains were embedded in celloidin and sectioned at 50 μm, every fourth section being stained with cresyl violet. The sections were then inspected microscopically. Reconstructions of a series of coronal sections through the largest and smallest lesions are shown in Fig. 1.

Smaller total lesions extended from the genu of corpus callosum to the crossing of the anterior commissure. Typically the damage involved

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**Fig. 1.** Coronal sections through the smallest (R-28) and the largest (R-13) septal lesions.

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the medial nucleus of the septum, most of the lateral nucleus, sometimes the dorsal part of the vertical limb of the diagonal band of Broca and the dorsal tip of nucleus accumbens. Slight damage was usually also observed in the anterior hippocampus as well as in the nucleus fimbrialis septi and the dorsal fornix in the posterior direction.

The big septal lesions destroyed the medial and lateral nuclei completely, most of the diagonal band nuclei and the dorsal edge of nucleus accumbens. In the more anterior direction beyond the precommissural septum, the anterior hippocampus was damaged in all subjects, and in one subject the medial paraolfactory area was also destroyed. The posterior boundary of 5 out of 8 lesions was at the level of the ventral commissure of the fornix. In this direction, the damage involved typically the nucleus septalis fimbrialis, the nuclear triangularis septi, the descending columns of the fornix and the fornix itself.

RESULTS

For some time after the operation, all rats with big and some with smaller septal lesions showed the septal rage syndrome. Rats were regularly handled during the recovery period and the rage syndrome was much attenuated by the beginning of training.

At the beginning of the preliminary training, all rats had a similar baseline response rate. In the course of training response rate increased in all animals. ANOVA showed that the effect of session as well as the session x lesion interaction were statistically significant \(F(7,126) = 33.6, p < 0.001\), and \(F(14,126) = 2.9, p < 0.001\), respectively. According to the Duncan tests the increase in bar-pressing rate over sessions was significant in all groups. However, the greatest increase was observed in animals with big septal lesions and the smallest one in control subjects. The main effect of lesion was also significant \(F(2,18) = 5.9, p < 0.025\). Duncan tests confirmed that the response rate was significantly higher in both operated groups than in control animals. Lesioned groups did not differ significantly from each other.

In all groups, during differentiation as well as reversal learning, a decrease in the number of responses to \(CS^-\) was observed. ANOVA (performed on the absolute numbers of responses emitted during \(CS^-\) periods in successive blocks of 2 consecutive differentiation sessions) showed an insignificant effect of lesion and of stimulus; however, the lesion x stimulus interaction was significant \(F(2,18) = 3.86, p < 0.05\).

When a steady light was employed as \(CS^-\), between-group differences in \(CS^-\) responding were relatively small. Control subjects responded at a rate intermediate between those of animals with big septal lesions
(higher) and small septal lesions (lower). In contrast, when a flashing light was used as CS\(^{-}\), there was a large difference in the CS\(^{-}\) response rate between operated and control groups. The number of responses to the flashing light as CS\(^{-}\) was significantly greater in lesioned than in normal subjects, and the two lesioned groups did not differ significantly from each other. The effect of session as well as the session x lesion and session x stimulus interactions were also significant 

\[ F(6,108) = 35.52, p < 0.001; F(12,108) = 2.54, p < 0.001; F(6,108) = 3.44, p < 0.001, \text{ respectively}. \]

The decrease in CS\(^{-}\) responding that took place during differentiation training was more pronounced in lesioned than in control groups; in addition, the steady light as CS\(^{-}\) produced a faster decline in the number of CS\(^{-}\) responses than the flashing light as CS\(^{-}\). Despite the greater rate of extinction of bar-press responses to CS\(^{-}\) in septal than in normal subjects, the rate of CS\(^{-}\) responding was still higher in the former than in the latter. This was probably because operated rats entered differentiation training with a significantly higher level of base-line responding than control animals \((p < 0.05, \text{ Mann-Whitney test})\).

An analogous analysis of the data collected during CS\(^{-}\) periods in the course of reversal learning revealed a significant effect of session 

\[ F(6,108) = 10.76, p < 0.001 \]

and a significant session x lesion x stimulus interaction 

\[ F(12,108) = 1.89, p < 0.05. \]

During reversal learning, the quality of the negative stimulus affected the rate of decrease of CS\(^{-}\) responses differently depending on whether animals were lesioned or not. The reduction in CS\(^{-}\) responding was slightly faster with steady light than with flashing light as CS\(^{-}\) but it was so only in lesioned subjects. In normal rats no differences were observed in the rate of decrease of CS\(^{-}\) responding as a function of the kind of stimulus used.

In all animals, together with a decrease in the number of CS\(^{-}\) responses, a progressive increase in response rate during CS\(^{+}\) periods was noted. ANOVA used on the total numbers of responses emitted during CS\(^{+}\) intervals (in consecutive blocks of 2 differentiation sessions) showed nonsignificant effects of lesion and of stimulus and a significant effect of session 

\[ F(6,108) = 6.64, p < 0.001. \]

None of the interactions of these three factors was statistically significant.

ANOVA performed on the numbers of CS\(^{+}\) responses emitted during reversal training revealed a significant lesion x stimulus interaction 

\[ F(2,18) = 3.98, p < 0.05. \]

The analysis of this interaction showed that the number of responses to CS\(^{+}\) was significantly higher in operated than control rats, but only with the flashing light as CS\(^{+}\). With the steady light as CS\(^{+}\) the results were the reverse. Analysis of variance of CS\(^{+}\) responding during reversal learning showed a significant effect
of session \( F(6,108) = 15.93, p < 0.001 \), a significant session x lesion interaction \( F(12,108) = 1.79, p < 0.05 \), and a significant session x stimulus interaction \( F(6,108) = 8.93, p < 0.01 \). The increase in the number of CS+ responses observed in the course of reversal training was greater in lesioned than in normal rats and it was more pronounced with flashing than with steady light as CS+. One may ask why the experimental factors affected CS+ responding during the reversal but not during original differentiation training. This may be because CS+ responding was higher at the beginning of original differentiation training than at the beginning of reversal. This higher CS+ rate may have obscured the effects of the flashing light and the lesion by way of a ceiling effect.

Differences between lesioned and control animals in base-line responding during preliminary training might have affected the subsequently, observed between-group differences in responding to both CS+ and CS−. Therefore, we decided to analyse also the relative changes in CS− responding in the course of the experiment. The ratio of the number of responses during CS− to the total number of responses

![Fig. 2. Mean differentiation ratios during differentiation and reversal training in groups trained originally with flashing light as CS+ and steady light as CS−. Broken line, big septal lesion; broken line separated by dots, small septal lesion; solid line, control.](image-url)
emitted during both CS− and CS+ periods was computed for each subject and each session independently. A value for this ratio of 0.5 means that the response rate during the CS− periods was the same as during the CS+ components and the animal did not differentiate the stimulus conditions; values less than 0.5 indicate a decrease of response rate in the CS− with respect to the CS+ components.

Fig. 3. Mean differentiation ratios during differentiation and reversal training in groups trained originally with steady light as CS+ and flashing light as CS−. Denotations as in Fig. 2.

Figures 2 and 3, based on the mean differentiation rations, illustrate the course of differentiation and reversal learning in each group separately. As seen from the graphs, in all groups in the course of both differentiation and reversal training a decrease in differentiation ratios was observed. When the flashing light was used as CS+ and the steady light as CS−, no differences appeared between lesioned and normal animals in the course of original differentiation or reversal learning, and the lesioned animals were as good as, or even better than, the controls. The changes in the differentiation ratio were slightly slower in septal than in control subjects only when the flashing light served as a negative stimulus. The effect of stimulus arrangement on the course of differentiation appeared in all rats but it was more pronounced in lesioned animals. For both original differentiation and reversal
learning ANOVA confirmed a significant effect of session \( F(13,234) = 73.39, p < 0.001 \) and \( F(13,234) = 40.40, p < 0.001 \) respectively) and stimulus \( F(1,18) = 7.38, p < 0.025 \) and \( F(1,18) = 8.48, p < 0.001 \). However, the lesion \( \times \) stimulus interaction was significant during reversal learning only \( F(2,18) = 4.15, p < 0.05 \).

Duncan tests confirmed the lack of significant differences between groups when flashing light was used as CS\(^+\) and steady light as CS\(^-\). With the reversed stimulus arrangement differentiation ratios were significantly higher in rats with small septal lesions than in control animals.

It is worth pointing out that the resting period of three weeks after 14 days of original differentiation training had almost no effect on performance, either in normal or in lesioned rats.

**DISCUSSION**

The present experiment confirmed the septal effect on baseline response rate. An increment of free-operant responding in septal rats has been reported many times before and it has been shown that this higher response rate is not due to changes in primary drive, since septal lesions did not produce an increase in ad lib. food intake (11).

However, it was found that septal damage had no effect on go, no-go differentiation nor on reversal learning when flashing light was used as CS\(^+\) and steady light as CS\(^-\). A slight deterioration of differentiation was observed only during reversal training and only when a steady light was used as CS\(^+\) and a flashing light as CS\(^-\). Intermittent stimuli such as a flashing light have been demonstrated to be physiologically stronger and more reflexogenic than continuous stimuli such as a steady light (30, 36, 51). It has also been shown that stimulus generalization is greater and differentiation more difficult when a physiologically weaker stimulus is reinforced and a physiologically stronger stimulus extinguished than when the stimulus conditions are reversed (27, 28, 29, 30, 34, 35, 37, 49, 50, 51).

Thus, in the present study, the septal effect appeared only during reversal learning, when the to-be-extinguished habit was fairly strong, and under conditions of greater stimulus generalization.

Our results are only partially consistent with the results of other studies concerning the effects of septal lesions on successive go, no–go differentiation. Zucker (52) and Dickinson (10) found that septal damage decreased the rate of decline of CS\(^-\) responding but these authors analysed jointly data obtained under different stimulus arrangements.
In contrast, the present study shows that, if septal lesions decrease the frustrative consequences of nonreward, as suggested for example by Gray (23), this effect is strongly influenced by the kind of stimuli used in a given task (their strength and mutual relations) rather than by the character of the conditioned response itself.

The interaction between lesion and type of stimulus found in the present study is consistent with reports by others of septal hyper-reactivity to the eliciting properties of discrete stimulus events. Lorens and Brown (31) have shown that stimulation of the septal area attenuated electrically evoked cortical potentials. From this one might predict that septal lesions would have the opposite effect, increasing the magnitude of evoked potentials, and this has indeed been reported (42, 44). The effect of septal damage on an animal's reactivity to external stimuli is particularly pronounced under conditions of deprivation (19). An exaggerated influence of external stimulation on septal animals has also been shown in behavioural experiments. It has been shown for instance that impairment of spontaneous alternation occurred in septal animals only in the light (6) and that in this task septal rats, unlike those with dorso-hippocampal lesions, perseverated external stimuli rather than body turns (8). In other experiments, Zucker and McCleary (53) showed greater stimulus generalization in septal cats than in normals.

Overreactivity to external stimuli and consequently a broader stimulus generalization in septal subjects may cause poorer performance in more difficult differentiation tasks. Septal hyperreactivity may also underlie other behavioural deficits in septal animals, such as the impairment in DRL performance. The latter task is based mainly on time conditioning, the external stimulus conditions always remaining the same. In this situation, septal subjects, guided to a greater extent than normals by environmental stimuli, may have greater difficulties in performing efficiently. When, however, the force required to press the lever was gradually raised or lowered within the DRL interval, the performance of lesioned rats in this task was similar to that of control animals (1). The introduction of an external stimulus to indicate the end of the delay interval also ameliorated the DRL deficits after septal lesions (13, 32). Special shaping procedures in DRL training, such as a gradual increase of the DRL delay in the course of training (3) or a gradual decrease in the intensity of an external stimulus which sets the occasion for responding (14), also help to produce a sustained improvement in the performance of septal animals, which then continue to respond efficiently even after the removal of the cue. During shap-
ing, stimulus control can be transferred more easily across a range of changes in stimulus value.

Similarly, the acquisition of position reversals did not show any impairment in septal subjects when a visual stimulus relevant to the correct response was included (46).

The results presented in this paper, together with earlier findings concerning septal function, indicate that septal effects are rarely if ever all or none; they depend on a variety of experimental factors, among which stimulus intensity dynamism is apparently of great importance.

REFERENCES

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