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Brief Report

Action of Septal Lesions on Facilitation Rather Than Inhibition of Responding in Conditioned Suppression*

N. McNaughton

Department of Psychology and Centre for Neuroscience, University of Otago

Some of the effects of septo-hippocampal lesions have been characterised as resulting from a loss of response inhibition. In the present study septal lesions did not reduce the response inhibition seen early in conditioned suppression training, rather they appeared to potentiate the response facilitation which occurs later in training. This suggests that a variety of current theories of septo-hippocampal function need modification.

Septal lesions and hippocampal lesions have a wide variety of behavioural effects in common (Gray & McNaughton, 1983). However, there are no generalisations in terms of changes in some single simple underlying process that have so far accounted for the common behavioural profile of these lesions. As a result, a wide variety of hypotheses of septo-hippocampal function have been put forward over the last few years and the most successful of these, in terms of the mass of data accounted for, are large-scale theories which have required book-length exposition (Gray, 1982a; O'Keefe & Nadel, 1978). A common feature of many of the hypotheses put forward, and of the two large-scale theories, is the treatment of a subset of the behavioural effects of the lesions as being the result, at the descriptive level, of a loss of inhibition of prepotent responses. The differences between the various current theories can often be viewed as reflecting the different ways in which they predict apparent losses of behavioural inhibition and the different circumstances from which they predict there would be no such apparent loss.

For example, in the earlier of the two large-scale theories, O'Keefe and Nadel proposed that the hippocampus contains a cognitive map — which in animals is mainly concerned with spatial information. Apparent losses of behavioural inhibition are accounted for, in this theory, as a consequence of the use by the animal of "taxon" hypotheses (by ad hoc definition resistant to inhibition) after the loss of more malleable "spatial" hypotheses (O'Keefe and Nadel, 1978).

The more recent of the two large-scale theories has its origins in the remarkable similarity of the behavioural profile of septo-hippocampal lesions with that of anxiolytic drugs. It views the hippocampus as a critical structure for the elaboration of anxiety. This theory makes more explicit use of the concept of behavioural inhibition since it postulates that the hippocampus, in addition to other functions, is a critical component of a "behavioural inhibition system" (Gray, 1982).

However, even when an explicit or disguised form of behavioural inhibition is specifically excluded from theory construction (e.g., Rawlins, 1985), the descriptive, as opposed to theoretical, value of the concept of a loss of behavioural inhibition in relation to the effects of septo-hippocampal lesions is not questioned.

These, and a number of other competing views of septo-hippocampal function, all account for a large part of the lesion literature. Equally, all are open to criticism at specific points (e.g. see commentaries to target articles in Gray, 1982b; O'Keefe & Nadel, 1979; Rawlins, 1985). As Rawlins (1985) notes "the behavioural inhibition theory of hippocampal function has proved one of the longest-lasting, though various changes to the theory have been made as new data have emerged". Possibly because of this, most current theories take it as given that in the case where a release of suppressed responding is observed after septo-hippocampal lesions this can be described in terms of an effective loss of behavioural inhibition either as a primary deficit, or secondary to some other specified effect of the lesion. The present experiment suggests that this

*The writing of this paper was supported by a Senior Fellowship from the MRC of New Zealand. All correspondence should be addressed to: Dr N. McNaughton, Dept. Psychology, University of Otago, P.O. Box 56, Dunedin, New Zealand.

assumption, basic to virtually all of the theoretical approaches, may be mistaken.

Method

Subjects were male Sprague-Dawley rats. All had received stereotaxic operations under chloral hydrate/nembutal anaesthesia. Medial septal lesions were made by passing 1.0mA for 15s through a bipolar 200 micron diameter stainless steel electrode on the midline, 1.0mm A to bregma, 5.2mm below dura with the skull flat. Medial septal controls received identical operations but no current was passed. Lateral septal lesions were made by passing 0.5mA for 20s separately through each of two monopolar 250 micron wires (ears as cathode) located on opposite sides and 0.7mm L, 0.5mm A to bregma and 4.5mm below dura. Lateral septal controls received the same operation but no current was passed. All animals were allowed to recover for 10 days and were then gradually placed on a 23h food deprivation schedule.

They were autoshaped to lever press in Camden Instruments operant chambers with a random time 62s schedule and superimposed contingent continuous reinforcement for lever pressing. The reward cycle throughout the experiment consisted of retraction of the lever, illumination of the magazine for 5s and delivery of one 45mg Campden Instruments food pellet. After 10 reinforced lever presses, each reinforcement incremented the value of a contingent random interval schedule until RI42s was reached. All subsequent sessions used RI62s and lasted one hour. Three days of RI62s preceded the main experiment.

On the fourth and subsequent days of RI62s there was superimposed on this schedule conditioned suppression and time out intrusions in a fixed sequence of 5min blocks. Four minutes after the start of the session 3 stimulus lights (2.8W) were switched on, after 1min they were switched off and a 200ms shock delivered. After a further 4min the lever was retracted from the box for a period of 1min. This whole cycle was repeated 5 times and terminated with a final stimulus-shock block followed by 4 min of baseline RI62. For the first 5 days shock was the same for all rats and was 0.1, 0.15, 0.2, 0.2, and 0.2m A respectively. From the sixth day of shock (day 9 of RI62) shock was adjusted upwards as necessary for each rat individually, initially on a daily basis, with the aim of maintaining suppression ratios (see below) in the range 0.2-0.3. The amount of the adjustment depended on the experimenter's judgement of the trends in the individual rat's responding. For example, it can be seen from Figure 1 that over Sessions 3, 4 and 5 when shock was held constant most animals showed a steady increase in suppression (i.e. a decrease in the suppression ratio) — when any individual animal did not show such an increase after session 6, its shock level was increased immediately in anticipation of the rebound which invariably follows. The purpose of shock adjustment was to produce equivalent responding in the different groups before they entered an independent experiment in which the effects of pavlovian counterconditioning were to be assessed (Gray & McNaughton, 1983). In the context of the present experiment matching suppression ratios in an intermediate range has the advantage of removing any artefacts produced by individual ceiling or floor effects in response rates. Thus, once suppression ratio was matched between groups the mean shock delivered provides a good estimate of differential reactions to the schedule. Higher titrated shock level indicating a lesser tendency of the animal to inhibit its responding.

Lever presses were recorded for the two minutes before the presentation of each conditioned stimulus (divided by 2 to get pre-CS rate) and for the one minute duration of the conditioned stimulus (CS). Suppression ratios were then calculated as (CS rate)/(pre-CS rate + CS rate). Increases in this measure represent a lesser tendency of the animal to inhibit its responding. Shock levels were transformed to Log mA. Both variables were then submitted to analysis of variance with extraction of orthogonal polynomial components (Snedecor & Cochran, 1967) with separate analyses being carried out for the periods of consistent and individually adjusted shock levels respectively.

Lesions were histologically verified and are shown graphically in McNaughton and Gray (1983).

Results

Three medial septal lesion animals and one lateral septal lesion animal had unsatisfactory lesions and were excluded from analysis. There were no obvious behavioural differences between medial septal controls and lateral septal controls and these groups were therefore pooled to form a single control group. Separation between medial and lateral septal groups was not perfect in that about half of each group had damage which extended outside of one nucleus into part of the other. No firm conclusions will be drawn below about the specific contribution of the separate nuclei to the effects observed. Resultant N within group was control=15, medial=10, lateral=11.

Figure 1 shows the mean shock and suppression levels in the three groups. During the initial phase when all animals received the same shock level as each other there was a highly significant decrease in suppression ratio over sessions (linear trend $F\ (1,116) = 46.1, p < 0.0001$; quadratic trend $F\ (1,116) = 5.7, p < 0.025$; cubic trend $F\ (1,116) = 4.5, p < 0.05$). There was no significant deviation between groups overall, nor in trends between groups (all $F < 2.0$). In as much as there might be a lesion effect it would be a decrease in suppression ratio rather than the increase which

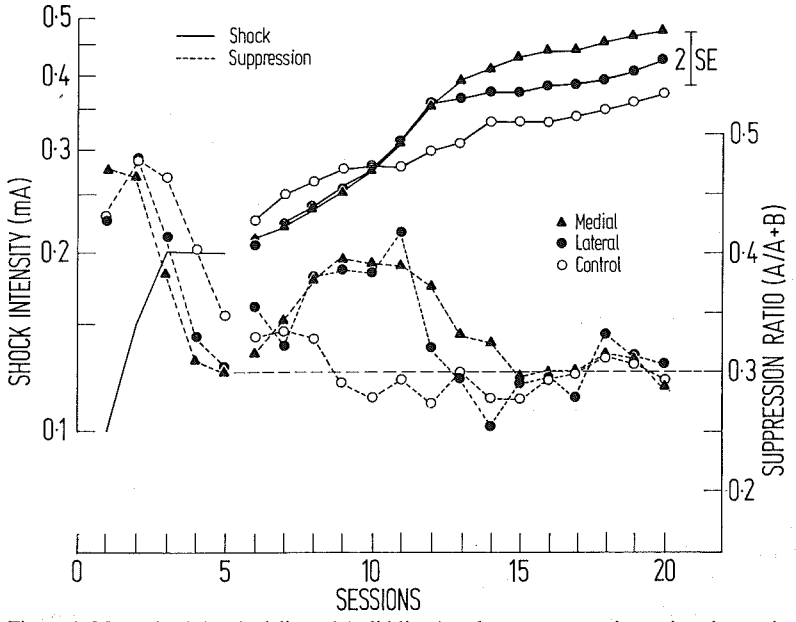

Figure 1. Mean shock levels delivered (solid lines) and mean suppression ratios observed (broken lines) in rats with predominantly medial septal lesions (filled triangles), predominantly lateral septal lesions (filled circles) or sham operated controls (open circles). Suppression ratios were calculated as A/(A+B) where A is the response rate in the 2 minutes preceding a one minute stimulus (the CS) which predicted an unavoidable shock and B is the response rate during the CS. From Session 6 shock was adjusted upwards, sometimes daily, for each rat individually to maintain a suppression ratio in the region of 0.3. The bar represents 2 standard errors for comparisons between groups on shock level values.

would be expected from a loss of response inhibition. We may conclude from this phase of the experiment that septal lesions do not reduce response inhibition which results from conditioned suppression training.

In the second phase of the experiment shock was adjusted individually for each animal. Because of the trend to greater suppression in septal animals up to Session 7 and subsequently faster rebound the results between Session 7 and Session 12 are complicated by insufficient shock increases applied to the septal animals. However, the overall conclusions are clear enough. Between Sessions 6-11, at the end of which time the mean shock levels are similar across groups, there is a decrease in suppression in the septal lesioned groups both with respect to controls and with respect to day 5. Between Sessions 12-20, at the end of which time mean suppression levels are similar across groups, there is an increase in the shock levels received by the septal lesioned groups. The initial separation and subsequent conjunction of suppression ratios is demonstrated statistically by significant nonlinearity in the differences between the groups across sessions (quadratic, F (1,406) = 4.5, p <0.05; cubic, F (1,406) = 6.8 $p < 0.01$). The steady separation in shock level of the groups over sessions is demonstrated by a significant linear trend difference (F (1,406) = 49.5, $p < 0.0001$).

The adaptation of the control animals to shock which, with constant shock levels, would have led to decreased suppression, is shown by the steady increase in shock levels between Sessions 6-20 required to maintain consistent suppressions ratios.

Discussion

It is clear from the present results that septal lesions do not impair inhibition of responding per se. This is shown unambiguously by the results in Sessions 1-5 of Figure 1. This is despite that fact that, with no change in the imposed behavioural schedule, by Session 20 of Figure 1 the usual reduction of suppression in septal animals has occurred — in this case demonstrated by the higher shock levels required to produce comparable suppression ratios to controls.

It is unfortunate that during Sessions 6-10 shock levels are somewhat higher in the controls as this

complicates precise interpretation of the variation in suppression ratios between the groups. It seems not unreasonable, however, to suggest that the septal lesions, rather than impairing response inhibition, are facilitating the rebound release of responding that typically occurs in control animals after their initial experience of shock regimes. (The lack of rebound as indexed by mean suppression ratios in the present controls is due to the anticipatory increases in shock level applied by the experimenter to individual animals — the comparable increases applied to individual septal animals were clearly insufficient to control their rebound to the same extent. Individual control animals showed a clear tendency to rebound).

Both experimental groups had lesions restricted to the septum and which caused extensive damage to the target nucleus. However, medial lesions extended partly into the lateral nucleus and lateral lesions extended partly into the medial nucleus. It is not possible, therefore, to be certain which nucleus is the source of the observed effects. However, the medial septal group had less tissue damage overall and appear to have a greater release of suppression than the lateral septal group; and they definitely had more extensive medial and less extensive lateral septal damage. It is most probable therefore that the source of the lesion effects is the medial rather than the lateral septal area. However a contribution from the lateral septal area cannot be ruled out.

The critical conclusion from the present study is that the observed reduction of conditioned suppression produced by septal damage may not be describable in terms of a loss of behavioural inhibition. Rather, it seems attributable to a potentiation of the behavioural facilitation of suppression, or adaptation to shock, which occurs in unlesioned animals in conditioned suppression experiments after they have learned the stimulus-shock contingency. It is possible, however, that the observed initial facilitation of inhibition of lever pressing is due to the release of some competing prepotent response by the lesion.

The implication of the results, especially if they can be shown to be equally true of hippocampal lesions and of other behavioural paradigms, is that current theories of septo-hippocampal function would require modification which in some cases may be quite extensive.

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