# How do Fornix-Fimbria Lesions Affect One-Way Active Avoidance Behavior?

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## Introduction

There have been at least 17 studies of the one-way shock avoidance behaviour of hippocampal-area lesioned rats. The question typically focused on is whether the lesioned subjects show a deficit in learning the task, relative to some lesioned or non-lesioned control group. To answer this a single measure—shocks or trials to some criterion—is usually employed. Other measures—latency, freezing, orientation, etc., are rarely reported.

One problem with this approach is that there is *no simple answer* to the deficit question. Sometimes deficits appear; sometimes they don't. Sometimes *facilitation* is reported. In the specific cases of total lesions of the fornix, Worsham (1975) reports facilitation, Ross et. Al. (1975) report no difference, and de Castro and Hall (1975) report a deficit.

Further, there is no guarantee that even gross behavioral differences will be reflected by, or be well described by, the number of learning trials required to reach some arbitrary criterion. Differences in motivation level, or in strategy, may have their strongest effects on variables other than the number of shocks administered. Normal and lesioned animals may *continue* to behave *very* differently long after they've taken their last shock.

In this study, the most striking result is as follows: Normals showed clear orientation to the door separating the dangerous side of the apparatus from the safe side. Fornically lesioned rats didn't show this at all. Normal rats appeared to be using a place, or cue strategy, while the lesioned rats appeared to be using a response strategy.

## Our Experiments

(FIRST SLIDE HERE: shows sections of a normal (operated control) brain.)

This slide shows sections of a more or less normal male hooded rat's brain. This animal, and all of the ones I call normal in this talk, underwent a control operation: the knife (actually it is more like a pair of scissors) was inserted into the brain but not closed. This control operation generally produces very little or no visible damage to the brain. A few structures of interest:

- This is the septum, just anterior to the fornix.
- The blue area here is the fornix.
- At the tails of the area, we have the fimbria.
- The small bit in the dip here is the stria terminalis.

- This bump is the stria medullaris, and across this region, there are a number of thalamic nuclei.

(NEXT SLIDE: Lesioned rat's brain.)

This is not the brain of one of this study's animals. The lesion technique is consistent in this lab's experiments, so only one lesion slide has been made. This lesion looks very much like the lesions of the animals in this study.

This is obviously a lesioned rat's brain. Note that the septum is intact, if very slightly shrunken. The fornix and fimbria are completely gone—this is typical. There is unilateral damage to the stria medullaris, and probably to terminalis. In some of this study's rats, both of these nuclei were eliminated bilaterally. Rats with more extensive damage in the neighbourhood of the thalamus were excluded from the analysis.

We've also just completed running a third group, although neither the analysis nor the histology are complete. In this group, we tried for a smaller lesion, taking out medullaris, terminalis, and this top area of the thalamus, while leaving the fimbria and fornix as intact as possible. Most of the behavior differences discussed below can thus be attributed to the fimbria-fornix damage.

(NEXT SLIDE)

This is a diagram of our avoidance box. It was quite large: 80 cm x 30 x 30. The black side was about 30 cm long, while the white side was just over 50 cm. The white side—the dangerous side—had a grid floor. The black side had a pressboard floor painted black. All the walls were painted Plexiglas, the ceiling clear Plexiglas. The sliding door was Plexiglas, painted black facing the safe side and white facing the dangerous side. There was a hole in the door, about rat-nose level, about 6 cm x 1.5 cm. White noise was constantly emitted from a speaker about here, and a tone CS came from a speaker about here (both off to the side, and back of, the safe side.) The video camera was positioned about 75 cm above the box. All trials were videotaped, and all analyses were made using the tapes. The rest of the equipment—shock generator, video recorder, etc., was outside the room. The shock was 1 ma, a.c., unscrambled, generated by a Grason-Stadler constant current generator.

The procedure was as follows: The rats were given at least a minute of exploration with the door open. At the end of the minute, as soon as the rat entered the black side, the door was closed and the first trial was started. The rat was picked up and placed here in the wide side—at the wall furthest from the door, facing away from the door. About sixteen seconds later (timing done by hand) the door was opened and the tone was turned on. If the animal did not leave within five seconds of CS onset (automatically timed) it was shocked until it did leave. Once it got to the black slide, it was allowed to stay there for a minute. Then it was picked up, returned to the white side and the next trial began. The door was closed during the inter-trial interval. In summary, there as a 16 second pre-CS period, a 5 second CS-US period, and a 1 minute ITI. The rats were run to a criterion of nine avoidances in ten trials. After this, about 25 further trials were run, including some probes.

## Results

(NEXT SLIDE, Table 1)

Table 1. Performance Measures for Each Subject

| Subject | Trials to Criterion | Avoidances pre-criterion run | Immobility | Pre-CS latency to front[1,2] | Avoidance latency | Escape latency | Number of excreta[3] | Interaction with door[3] |
|---|---|---|---|---|---|---|---|---|
| Controls | | | | | | | | |
| CBC1 | 15 | 0 | 12.3 | 11.0 (2) | 0.99 | 0.42 | 1 | 0 |
| CBC2 | 19 | 1 | 5.2 | 4.3 (10) | 1.70 | 1.70 | 10 | 3 |
| KC60 | 10 | 0 | 10.7 | 2.7 (2) | 1.19 | 0.60 | 5 | 2 |
| KC61 | 11[4] | 0 | 5.7 | 2.9 (7) | 1.19 | 0.60 | 13 | 5 |
| KC62 | 14 | 0 | 5.7 | 3.8 (7) | 1.00 | 0.51 | 11 | 6 |
| KC63 | 13 | 0 | 3.0 | 4.6 (10) | 1.78 | 0.75 | 9 | 8 |
| KC64 | 14 | 2 | 6.2 | 3.9 (10) | 0.84 | 1.27 | 29 | 4 |
| KC65 | 16 | 1 | 8.6 | 3.4 (10) | 1.50 | 0.65 | 25 | 4 |
| Fornicals | | | | | | | | |
| CBF3 | 16 | 0 | 11.2 | 9.0 (1) | 2.39 | 0.69 | 7 | 0 |
| KF50 | 24 | 0 | 13.0 | 10.0 (2) | 2.21 | 1.11 | 18 | 0 |
| KF51 | 19 | 3 | 7.2 | 2.8 (10) | 1.44 | 1.51 | 17 | 1 |
| KF52 | 28[4] | 6 | 12.4 | 16.0 (1) | 1.73 | 0.91 | 17 | 0 |
| KF54 | 32 | 7 | 10.0 | 14.7 (3) | 2.11 | 0.98 | 24 | 0 |
| KF56 | 19 | 2 | 10.5 | 11.6 (7) | 3.38 | 0.83 | 16 | 0 |
| KF57 | 20 | 1 | 9.6 | 14.0 (1) | 1.44 | 0.66 | 21 | 0 |
| KF58 | 21 | 0 | 15.3 | -- (0) | 2.26 | 1.07 | 28 | 0 |
| KF59 | 22[4] | 5 | 13.3 | 15.0 (2) | 1.53 | 2.43 | 13 | 0 |
| KF60 | 21 | 2 | 12.2 | 19.0 (1) | 1.10 | 0.86 | 14 | 0 |

1. Based on criterion run trials. Latencies are in mean seconds.

2. Based only on those (number in parentheses) trials in which the subject actually reached the front of the box in the pre-CS period.

3. Based on all non-probe trials.

4. Plus one (two for KF59) avoidance(s) before the first shock.

Here are some of the basic results.

First, trials to criterion. All rats attained criterion performance. The normals required significantly fewer trials. All statistical tests are two-sided Mann-Whitney-Wilcoxon tests. In the next column, we have the number of avoidance responses before the rat started his criterion run. Normals typically kept avoiding shock once they started to, while fornix-lesioned rats typically did not. This is not significant on the two-sided test: $p = 0.57$. A related measure was reported by Coscina & Lash (1969). They found that normal rats emitted longer chains of avoidance responses than hippocampally lesioned rats.

As to latencies, the normals avoided shock significantly faster than lesioned subjects. This is consistent with 4 of 6 reports. There is no difference ($p$ is greater than 0.20) in escape latencies. This is consistent with 3 of 4 reports.

Normal rats were more mobile than lesioned rats during the pre-CS period. This complements de Castro and Hall's (1975) finding that fornix-lesioned rats froze more during the CS-US interval. The only other data on freezing comes from Liss (1968). He found no difference in freezing ON THE SAFE SIDE. Neither did we.

Number of excreta: boli and urination frequency—no significant difference. Niki (1962) also found this.

Now for the orientation measures.

It's a problem trying to operationalize the notion of orienting to the door, or of orienting to the safe side. Here's the prototypic behaviour of the normal and lesioned rats. Later I'll go back to the data and discuss the agreement between the descriptions and the numbers. These behavioural patterns all took a while to develop, so these data are based on criterion and post-criterion performance.

Normal rats typically ran right to the door very soon after placement. Once they got there, they stayed there, often biting the door, pulling at it, or sticking their nose through it. Remember, there's a small hole in the door. When the door opened, they typically went on into the safe side, although they sometimes jumped back a little bit, first, apparently as a startle response.

Lesioned rats typically stayed where they were put, or moved around a little, but in the back area. They rarely went up to the door before CS onset. When the CS came on, they turned and ran, usually along one wall, until they reached the safe side. If a lesioned rat did end up in front of the door at the end of the pre-CS period, he was very likely to turn, at CS onset, and run by at least half the length of the box, often to the very back. Lesioned rats did not, with only one exception, on one trial, nose, bite or pull at the door.

The prototypic normal is clearly orienting to the door. The hole is a very salient stimulus for him, as is, perhaps, the front of the box in general. It's impossible, in this experiment, to tell whether the animal is focusing simply on very specific cues in the environment, or whether he's orienting to the PLACE: safe side. In any case, something up here is controlling his behaviour.

The lesioned rat, on the other hand, does not appear to be orienting to the door. He's simply showing the same response pattern: stay put until CS onset, turn, run. Most dramatically, he does this even when he's at the front of the box, turning and running away from the safe side, and often taking shock as a consequence.

Now, back to the data:

(NEXT SLIDE: Table 1 again)

The first measure is latency to the front. This is how long, on average, the animal took to get within about a head's length of the door. The bracketed numbers are how often, during the nine or ten criterion run trials, the animal actually got that close to the door. Only these trials are included in the averages. Normals are significantly faster, and they get there significantly more often. The behaviour of six of the eight normals is very well described by the prototypic description. The description is also very good for all but one or two of the lesioned rats. If we look at door interactions, i.e. the number of criterion-run trials in which the animal bit, nosed, or pulled at the door, the same pattern holds up.

(NEXT SLIDE: Table 2)

Table 2. Pre-CS Behavior, Location at CS Onset, & post-CS Behavior[1]

| At or after CS onset: | Pre-CS | Control | Fornix |
|---|---|---|---|
| Does not run away from door, or runs by less than 1/2 box | Stays in back | 11.7 | 65.7 |
| | Leaves back and returns | 6.5 | 5.1 |
| | In center at CS onset | 13.0 | 10.1 |
| | Reaches, stays in front | 44.2 | 4.0 |
| | Reaches front, leaves, returns | 7.8 | 0.0 |
| Runs away by 1/2 box length or more | Runs from front | 10.4 | 9.1 |
| | Runs from center | 6.5 | 3.0 |
| Miscellaneous | | 0.0 | 3.0 |
| | | | |
| Totals | | 100% | 100% |

1. These percentages are based on all criterion run trials of all animals in a group combined.

We also classified the pre-CS behaviour, and the reaction to the CS. Table 2 is based on criterion run trials including escape trials. The numbers are percentages: we classified every criterion run trial of every rat in a given group, pooled across animals within the group, and calculated percentages. This is obviously not representative of some animals, but we couldn't think of any better concise mode of representation. No statistical tests were performed, due to the lack of independence within cell entries. Fortunately, the results were fairly clear.

Normals were at the front of the box, i.e. at the door, when the CS came on, in 48 (i.e. 62%) of the 77 trials. In 44 percent of the trials, they ran to the front and *stayed* in the front quarter. In eight of the 77 trials (10%), a normal rat ran *well* away from the door, sometimes right to the back of the box, at CS onset. These 8 trials, of 48 at the front, make up 17% of the total trials were at the front at CS onset.

The lesioned animals rarely ended up in the front: 13 trials total, of 99, or 13.1%. Given that they were at the door when it opened, they ran away 9/13 times: 70%. The typical behaviour of the lesioned rats (66%) was to stay in the back until CS onset.

## The Probe Conditions

In two of our probe trials, we placed the animals at the front of the box rather than at the back. There are thus 16 trials for the normals, 20 for the lesioned rats. Normals ended up in the front in 11/16 trials (69%). Fornix-lesioned rats were at the front in 13/20 trials (65%). Only one normal rat ran away from the door, once, in the 11/16 trials. Lesioned rats ran away 10/13 (of the 20) trials, for a difference of 9 versus 77%.

In sum, whether the rats walked to the door on their own, or were put there, ***if they were at the front at CS onset,*** normals exited directly, while lesioned rats usually turned around and ran away from the safe side, often being shocked as a consequence. These differences hold up long after criterion is achieved, i.e. long after the animals have all "learned" the task.

## Theoretical Interpretation

Given these patterns of behaviour—looking at all the orientation-related measures as a group: latency to the front, frequency to the front, avoidance latency, behaviour categorization, front probe placement behaviour—we feel justified in claiming that the normals used a place, or a cue strategy, while the lesioned rats typically used a response strategy. All of the measures point in the same direction.

These patterns of behaviour do not uniquely support one theory of hippocampal function. Some views, of course, are much more compatible with the data than others.

One such view is the spatial mapping hypothesis of hippocampal function. Black, Nadel and O'Keefe applied this view to avoidance learning in 1977. According to this view, normal subjects are capable of forming detailed internal representations, maps if you will, of the external environment, whereas hippocampally-lesioned animals are not. They argue, basing themselves partially on papers by Olton and Isaacson (1968; Olton, 1973), that normal rats *do* use this information in one-way avoidance tasks, i.e. they employ spatial strategies as well as cue and response strategies. Hippocampally-lesioned subjects, being incapable of using spatial strategies, are restricted to cue or response strategies. They are at a disadvantage with respect to normals, but they may or may not show a deficit, depending on the exact stimulus situation.

We were rather surprised that the lesioned subjects appeared to use few, if any stimuli as cues, relying instead on rigid response patterns, and we have no good explanation for why this was the case.

On the other hand, we were struck, time and again, by the degree to which normal animals seemed to know where they were going, while the lesioned animals mostly did not.

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