Descending post-commissural fornix lesions produce impaired spatial working memory in a 12-arm maze

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Introduction

The descending post-commissural fornix (dPCFx) conveys hippocampal efferents to the mammillary bodies within an extended hippocampal memory system (MB; see Figure 1). This fibre pathway should be critical for memory, by virtue of a hippocampal influence on brainstem components of memory circuitry. However, two previous studies have reported surprisingly mild, if any, effect of selective dPCFx lesions on spatial memory in an 8-arm radial arm maze (RAM) (Vann et al., 2011; Vann, 2013), with a significant dPCFx lesion impairment found only when a mid-trial rotation was included (Vann et al., 2011). Therefore, the dPCFx may play a less critical role in spatial working memory than would be suggested by its anatomical connectivity, or that increased task difficulty is required to sufficiently tax the system. To address whether greater task demand is necessary to produce mnemonic deficits we examined the behavioural impact of dPCFx lesions in rats in a 12-arm RAM across 20 days of testing. In addition, electrodes were implanted in key memory structures (hippocampus (HPC), anterior thalamus (ATN) and prefrontal cortex (PFC)) to test whether impaired memory function could be attributed to changes in electrophysiological neural patterns.

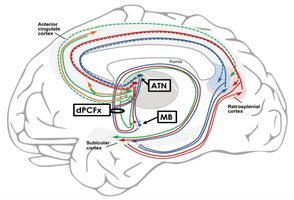


Figure 1. Structures and fibre tracts of the extended hippocampal system.
ATN: anterior thalamic nuclei
dPCFx: descending post-commissural fornix MB: mammillary bodies
Adapted from Child & Benarroch (2013).

Methods

1) dPCFx Surgery

- dPCFx lesion n= 10
- SHAM lesion n=11

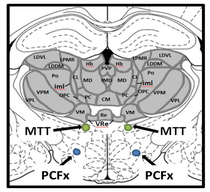


Figure 3. Magnified view of dPCFx lesion site. Adapted from Paxinos and Watson (1998).

Interim recovery period between lesion surgeries and electrode surgery ~ 2 months

2) Electrode Implantation Surgery

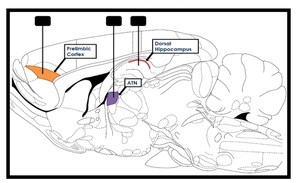
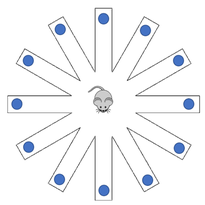


Figure 4. Sagittal view of electrode placement locations.

3) Behavioural testing in 12-arm RAM



Platinum tetrodes (PFC= 1, unilateral; Hippocampus=2, bilateral; ATN = 2, bilateral) inserted into the brain and silver ground wire secured above the cerebellum.

Results

Lesion Verification (preliminary)

Inclusion required total or near total bilateral dPCFx damage with minimal damage to adjacent structures or pathways. Some (N=4) dPCFx rats were removed from analysis due to incomplete lesions of the dPCFx. Following preliminary histology: sham (N=11); dPCFx (N=6).

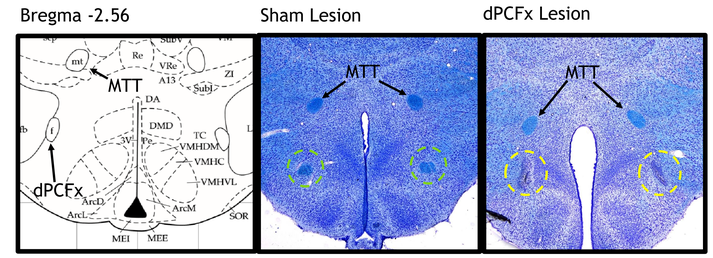


Figure 5. Example photomicrographs of a typical sham and dPCFx lesions stained with Luxol blue (myelin-specific) and cresyl violet (nissl). Intact dPCFx circled in green; complete bilateral lesion circled in yellow.

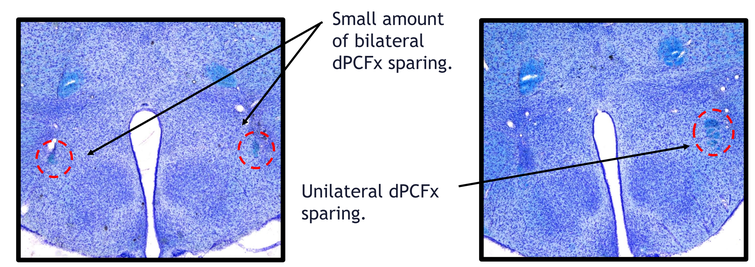


Figure 6. Example photomicrographs of lesions that did not reach inclusion criterion. Incomplete dPCFx lesions circled in red.

dPFCx Lesions impaired Spatial working in the 12-arm RAM

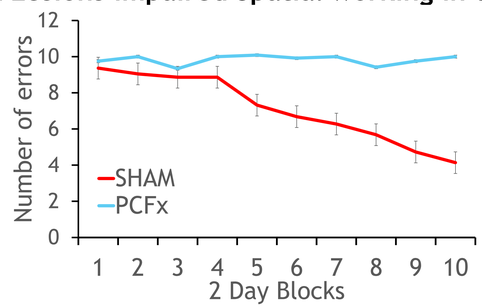


Figure 7. Mean ± SEM memory errors for the sham and dPCFx groups across the 20 days of RAM testing. dPCFx lesions produced a severe RAM impairment (Lesion effect, $F(1, 15)= 17.7$, $p<0.001$). Sham rats began reducing errors after only 8 days of testing, whilst dPCFx rats showed no evidence of improvement over the 20 days of testing (Lesion X Block, $F(9, 135)= 6.1$, $p< 0.0001$).

Conclusions

- dPCFx lesions severely impaired performance in the 12-arm RAM.
- The descending post-commissural fornix may be important for spatial working memory when task demands are high.
- The difficulty of this task is demonstrated by the failure of sham rats to begin reducing the number of errors made until day 8.
- It may be that the age (~21 months) of the rats used in this experiment contributed to the size of the mnemonic deficit but, since both sham and dPCFx rats were the same age, it is unlikely that this could account for the entire behavioural effect observed.

Further work

Electrophysiological activity, both within (power spectral density, PSD) and between (coherence) the PFC, ATN and HPC will be examined to assess whether lesion related changes in electrophysiological activity in the dPCFx contributed to the memory impairments observed in this study.

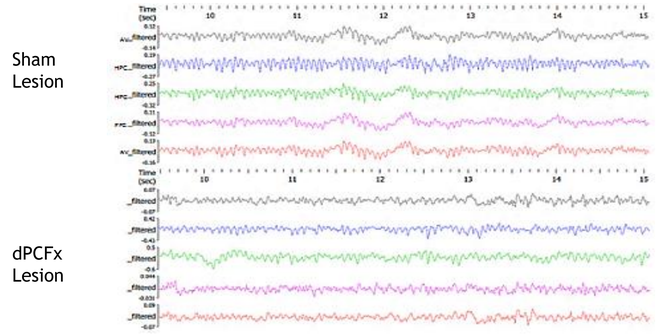


Figure 8. Example of raw electrophysiological neural recordings taken from a sham rat (top) and a dPCFx lesion rat (bottom). Recording scales have been optimized to provide a clear example of electrophysiological recordings.

References

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