The effect of Medial Septum Stimulation on Hippocampal Place Cells and Behaviour

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What is the Medial Septum?

The medial septum (MS) is anatomically and functionally connected to the hippocampus and essential to the maintenance of hippocampal oscillations .

It innervates the hippocampus with GABAergic, cholinergic and glutamatergic fibres which are intimately related to memory

Using optogenetic stimulation and electrophisiological recordings, we aimed to investigate how the MS is involved in reward-related behaviour and spatial memory processing.

MS stimulation induce place preference

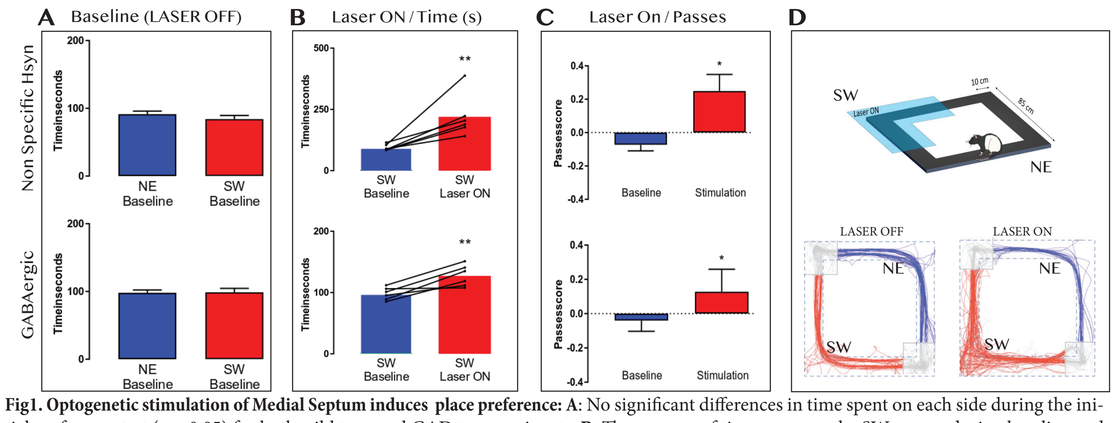
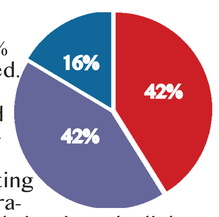


Fig1. Optogenetic stimulation of Medial Septum induces place preference: A: No significant differences in time spent on each side during the initial preference test ($p > 0.05$) for both wild type and GAD transgenic rats. **B**: The amount of time spent on the SW corner during baseline and stimulation. A paired t-test showed a significant increase of time during stimulation ($p<0.01$). **C**: The passes score ranged from -1 to 1, where 0 is the equal number of passes in both sides, 1 meaning all passes on stimulation side. A Wilcoxon matched-pairs signed rank test showed a slight preference for the SW side during stimulation. **D**: Schematic of the behaviour and examples of baseline and stimulation paths.

Is the Medial Septum modulating place cells activity in the hippocampus?

Intra Septal Effect

From 145 units recorded, 84% were affected. 42% were exited and 42% inhibited. Indicating an intra-septal circuit as the light only excites infected neurons.



76% of fast spiking theta modulated MS neurons were inhibited by MS stimulation. These cells have been described contribute to hippocampal theta.

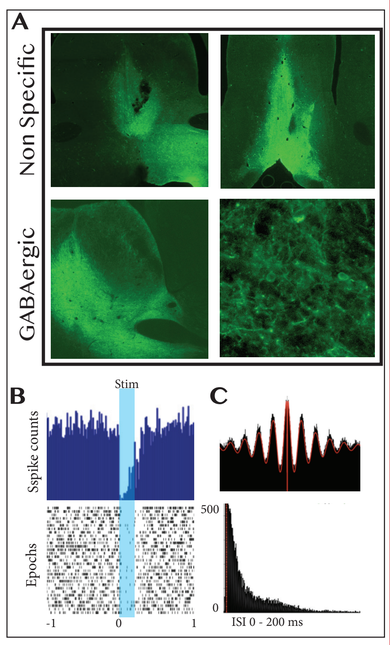
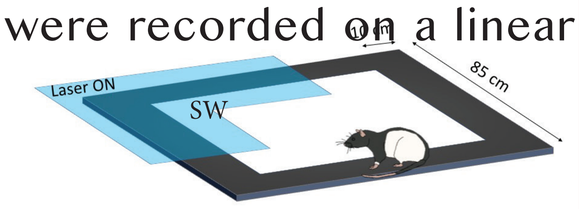


Fig2. Optogenetic stimulation of Medial Septum induces place preference: A: Expression of YFP into MS from both wild type and transgenic animals. **B.** Exemple of PSHT histogram and raster plot of an inhibited fast spiking theta modulated neuron. **C.** Autocorrelogram and ISI of the same unit with fitted sin function used to classify theta units.

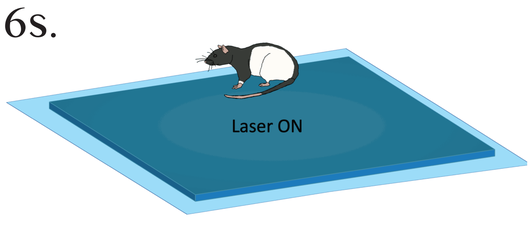
Our Approach

Wild type and transgenic GAD rats were injected with AAV virus to express channelrhodopsin 2 (ChR2) into MS.

Place preference and spatial distribuition of the place fields were recorded on a linear squared maze.
Laser was ON every time the rat entered the SW corner



MS neurons and CA1 activity were recorded during a Random Foraging Task. Where the MS was stimulated every 6s.



Effect on CA1 neurons and EEG

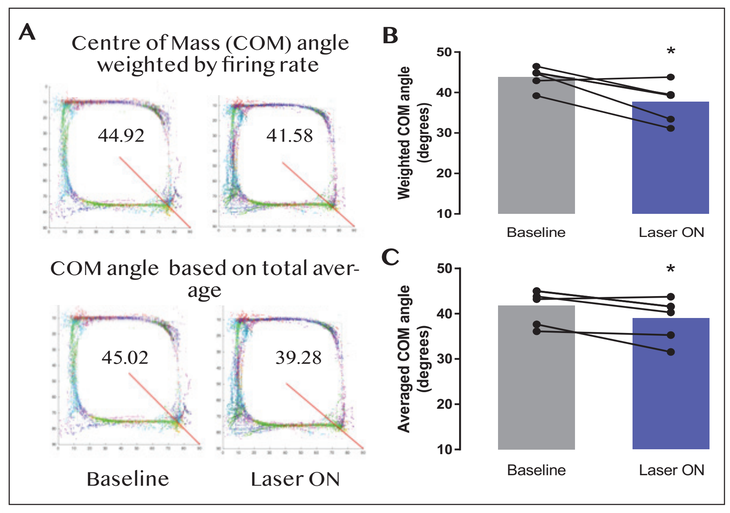
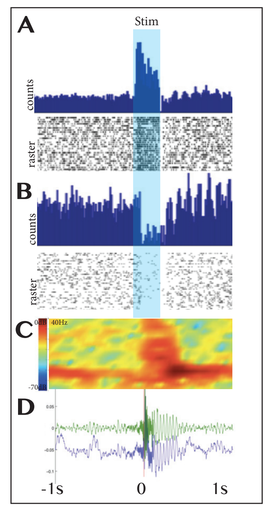


Fig3. Medial septum stimulation induce change on the place fields assembly. A. Examples of centr of mass angle calculated during 12 min baseline followed by 12 min stimulation of the SW corner on a linear squared maze. **B** and **C.** Paired t-test showed significant difference of the COM angle calculated by considering firing rates and also based on average number of place fields.



77% of CA1 interneurons affected MS stimulation were excited. And

64% of the 61 affected place cells were inhibited.
Moreover, 19% of the affected place cells remapped.

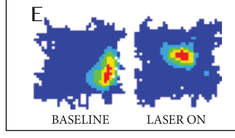


Fig4. Medial septum stimulation affected hippocampal EEG, interneurons and place cells. A and B. Example of histogram and raster plot of affect CA1 interneurons. **C.** Color coded spectrogram showing a peak in power in theta frequency. **D.** Example of EEG synchronization after MS stimulation. **F.** Example remapping place cells, 19% of affect place cells remapped during stimulation.

Conclusion

- Non-specific optogenetic stimulation of MS can induce place preference. A similar effect was observed during specific stimulation of MS GABAergic neurons;
- By calculating COM angle, we observed that the place field assembly moved towards the stimulation corner;
- 77 % of recorded interneurons and 64% of place cells were affected by MS

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