

Cellular organization of CA1 of the Hippocampus after Spatial Learning

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MAPS: Mapping Brain Circuits in Spatial Navigation

HBP Partnering Projects Meeting: Status quo & outlook

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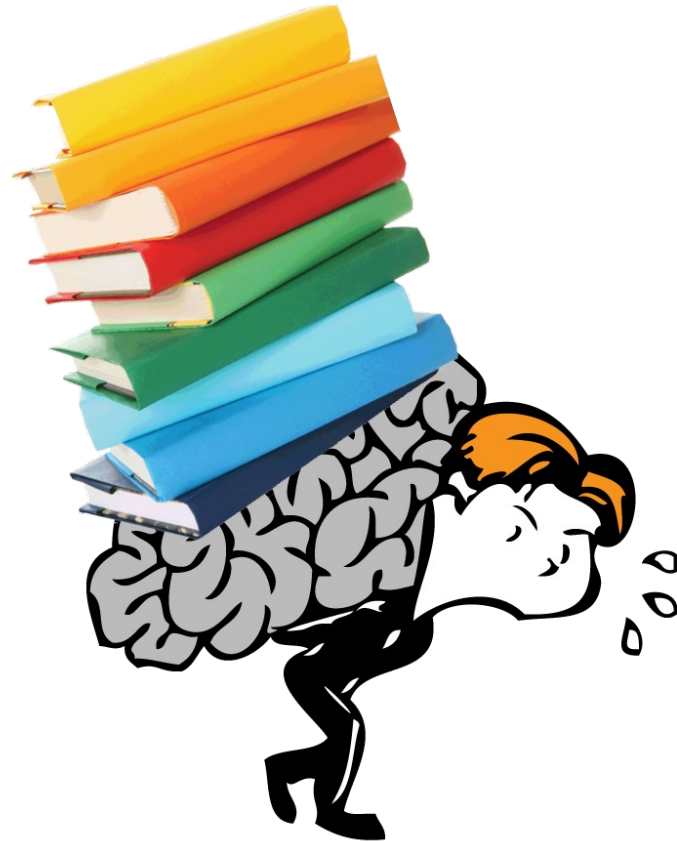


Scientific aim



Developing a network model to better understand brain dynamics during spatial learning

The spacing effect: general overview

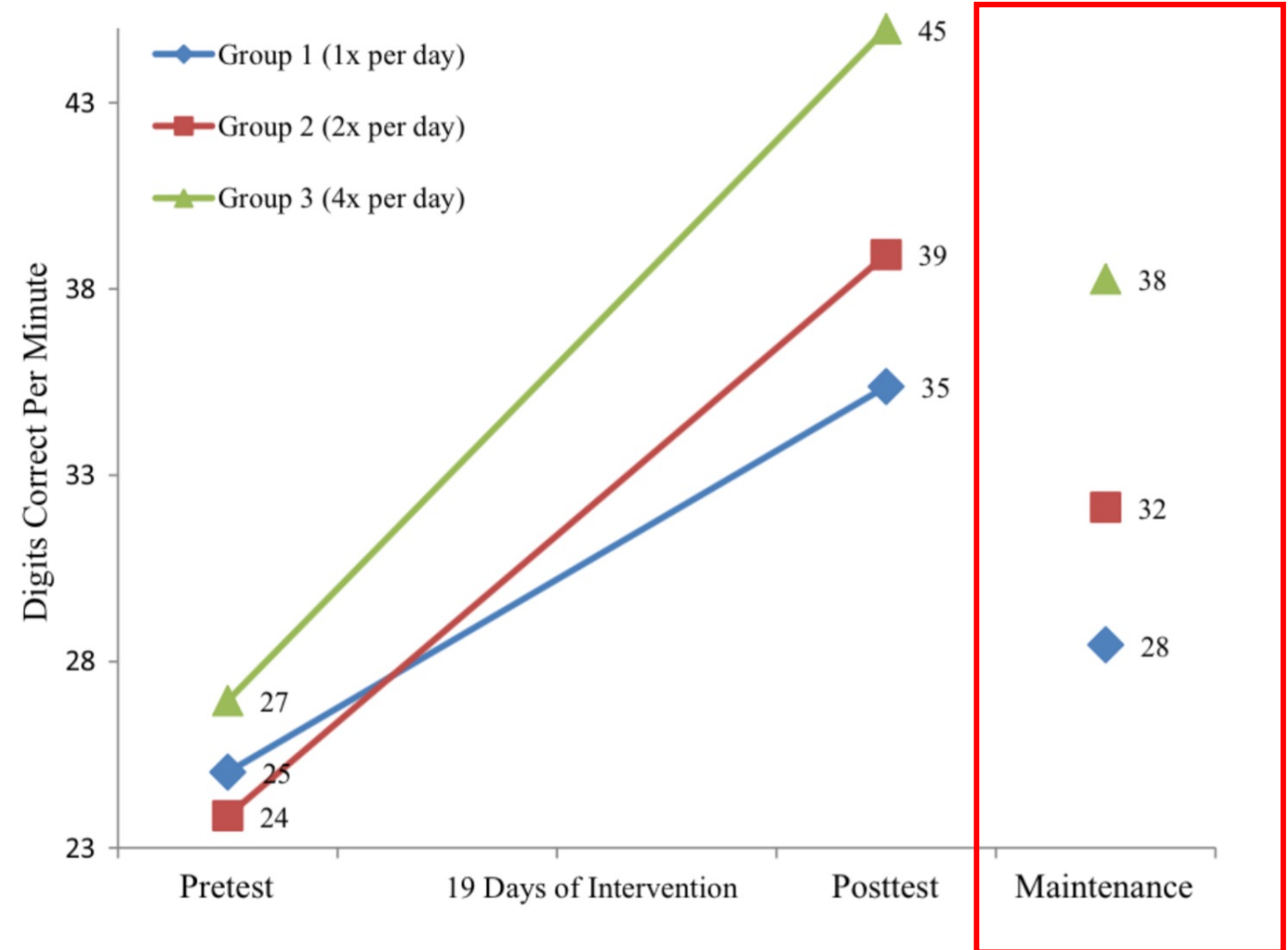


Don't strain the brain



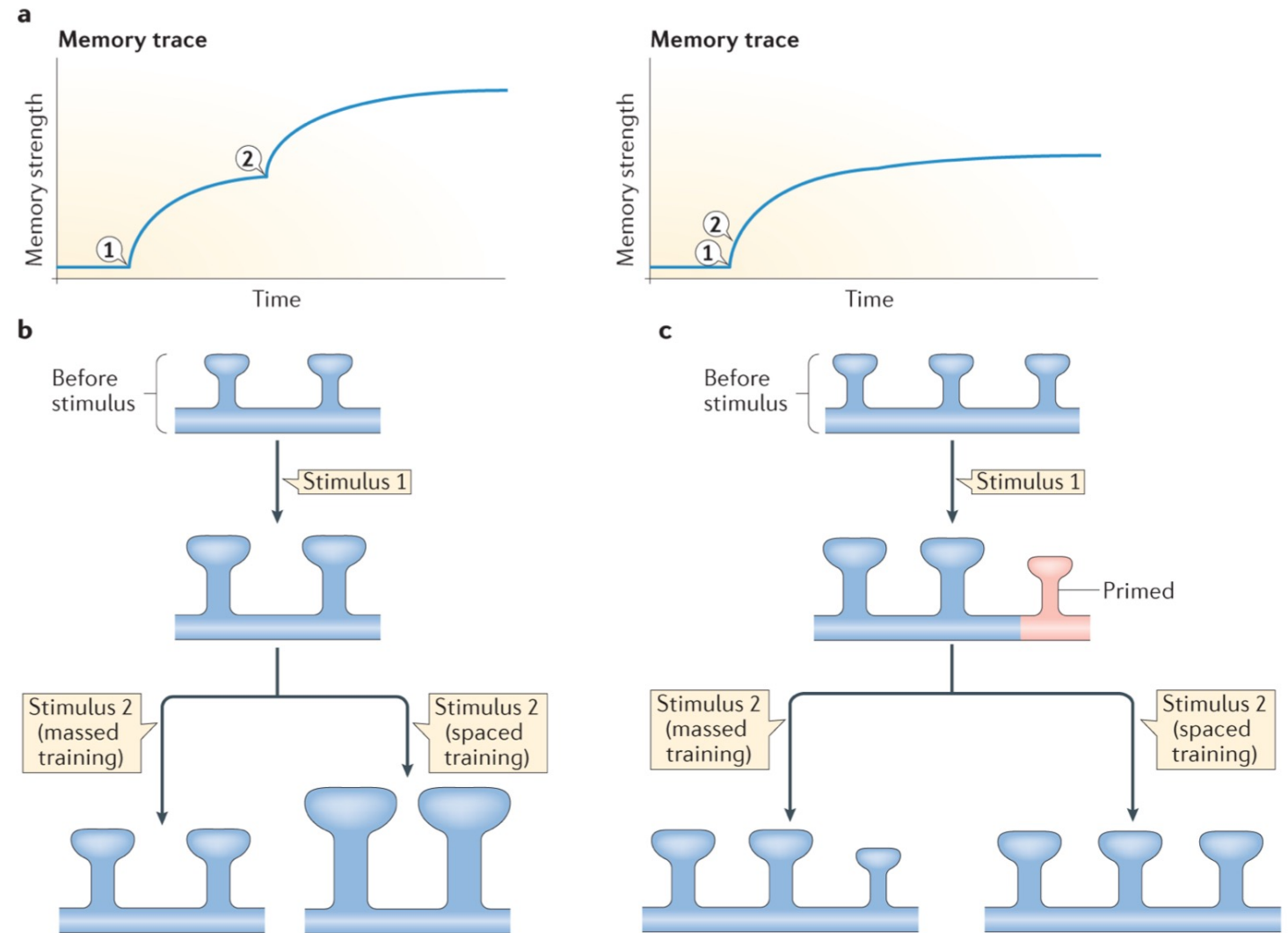
Train the brain

The spacing effect: human studies



Schutte et al., 2016 JSchPsyc

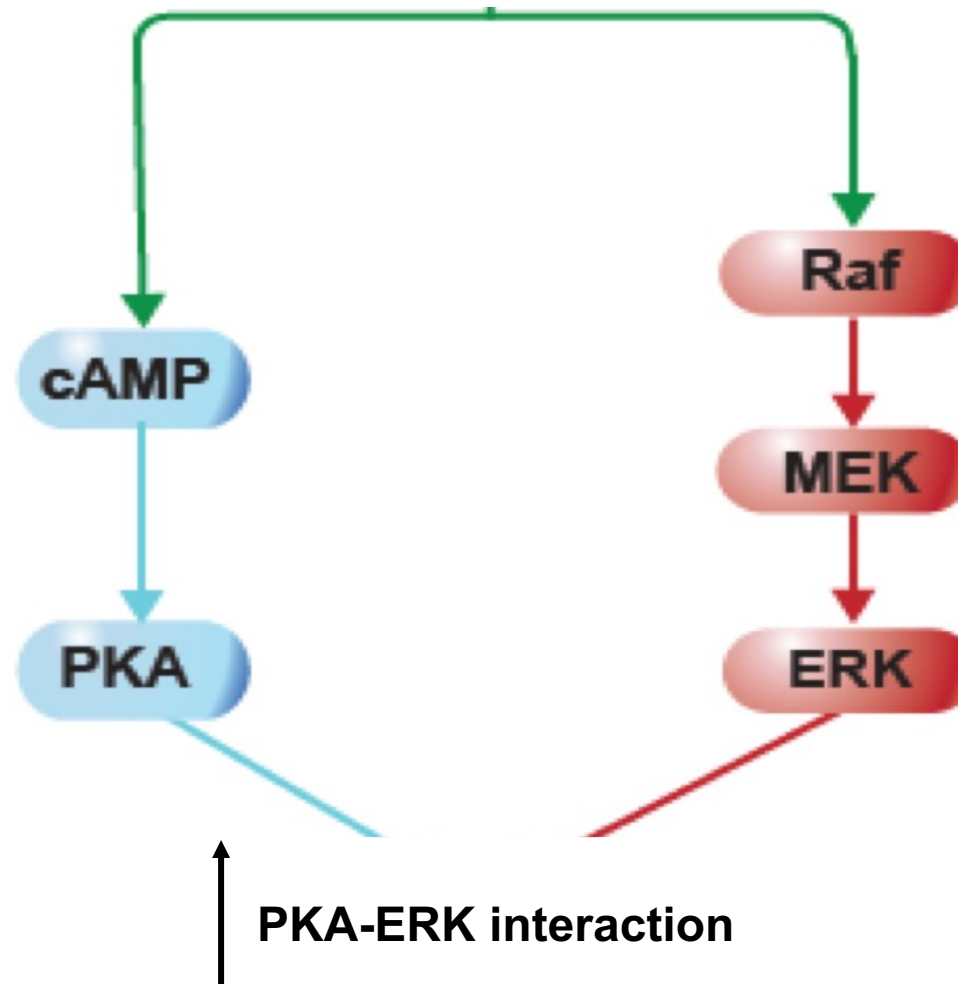
The spacing effect: synaptic plasticity



Smolen et al., 2016 Nat. Neuroscience

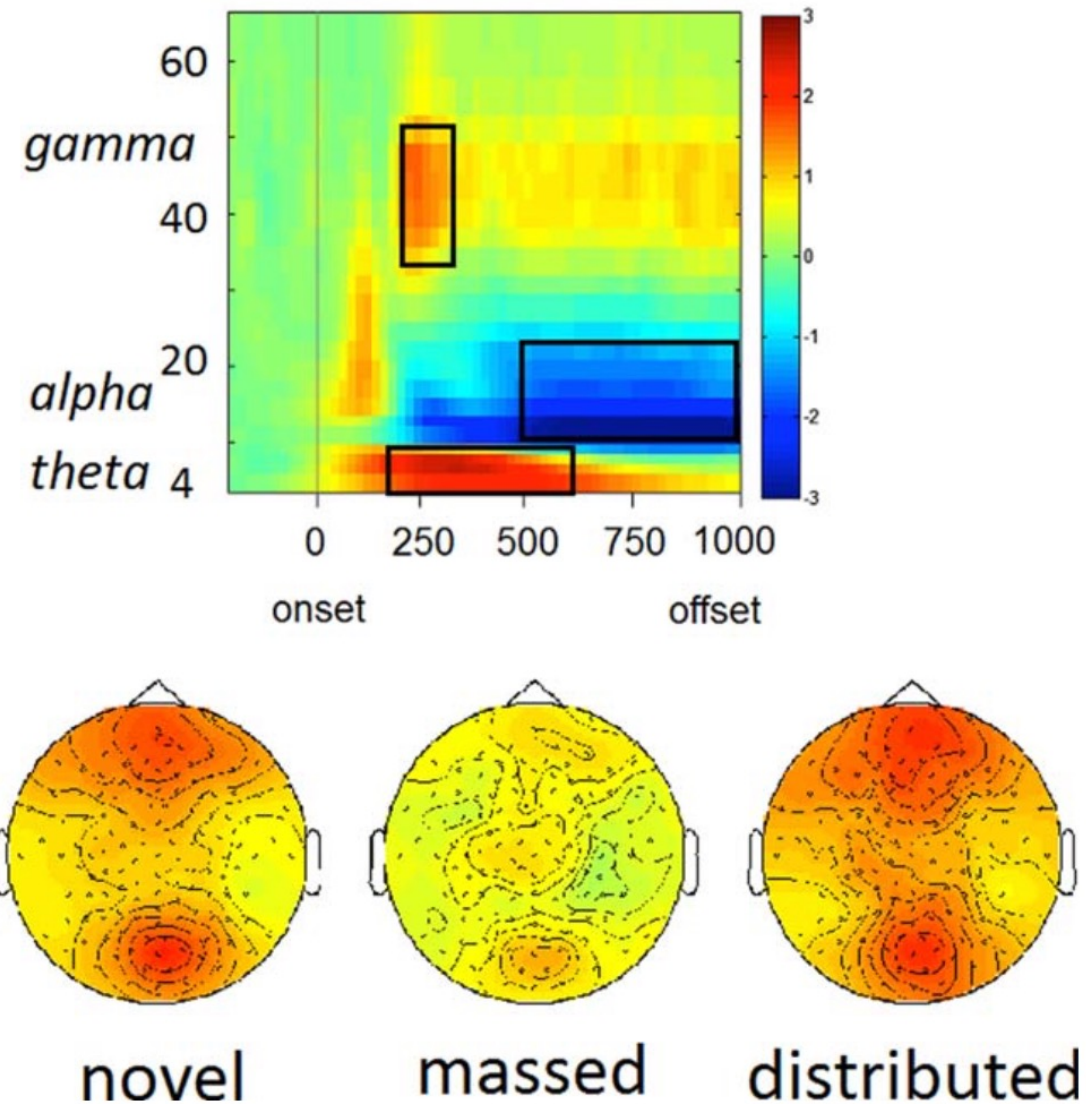
The spacing effect

Molecular and cellular mechanism



Smolen et al., 2016 Nat. Neuroscience

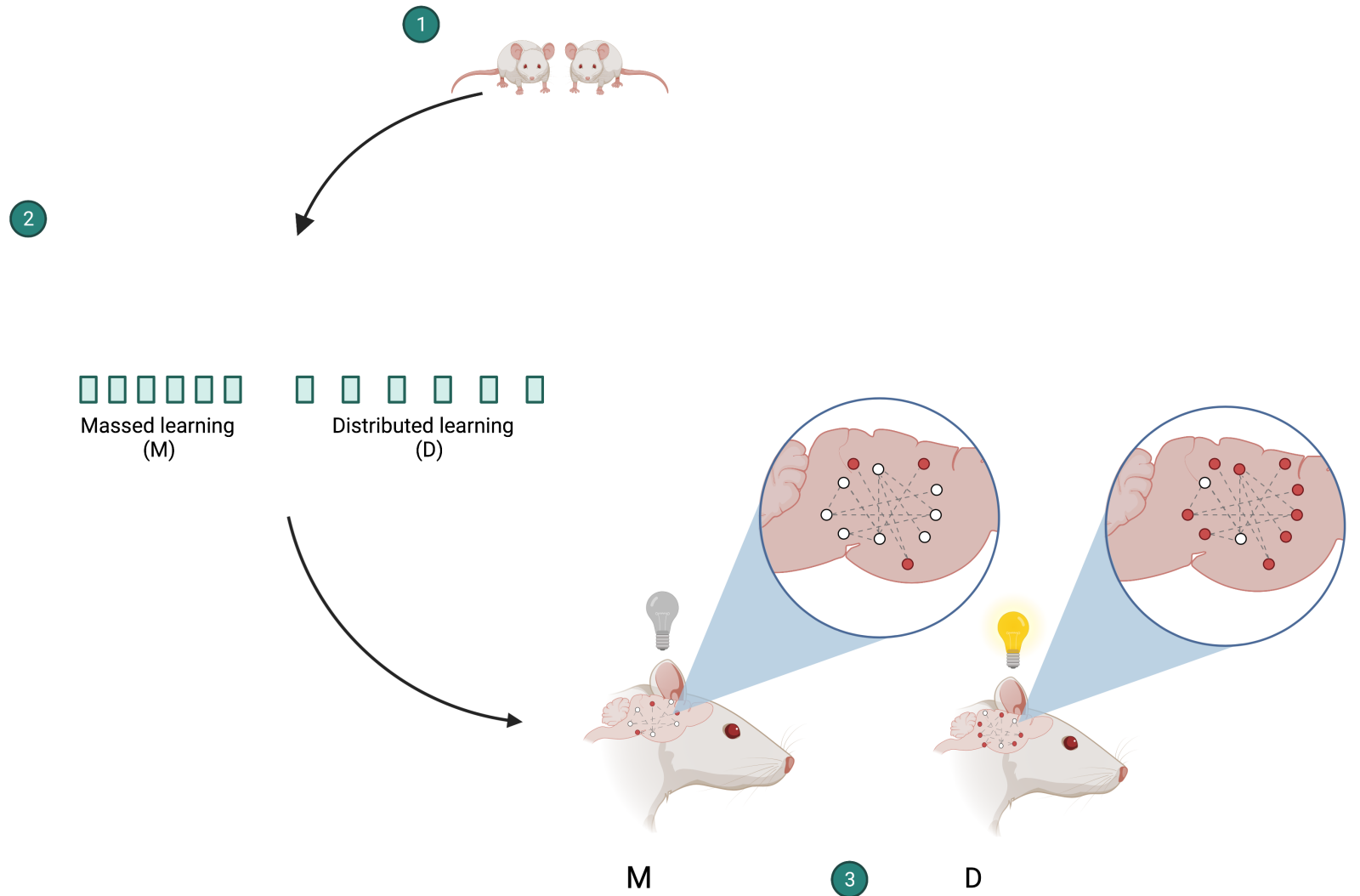
The spacing effect: human studies



Ferrari et al., 2015 SPR

2. The spacing effect:

Circuit dynamics
cellular topographical
organization



Mastrorilli, Centofante et al., 2022 PNAS

Aim



Investigating the cellular activation pattern of the hippocampus after a massed and a distributed spatial learning

The role of Hippocampus in memory consolidation

Reversible neural inactivation reveals hippocampal participation in several memory processes.

Riedel G, Micheau J, Lam AG, Roloff EL, Martin SJ, Bridge H, de Hoz L, Poeschel B, McCulloch J, Morris RG.

Retrograde amnesia: neither partial nor complete hippocampal lesions in rats result in preferential sparing of remote spatial memory, even after reminding.

Martin SJ, de Hoz L, Morris RG.

Interaction between dorsal hippocampal NMDA receptors and lithium on spatial learning consolidation in rats.

Parsaei L, et al. Brain Res Bull. 2016. PMID: 27444123

On the participation of hippocampal PKC in acquisition, consolidation and reconsolidation of spatial memory.

Bonini JS, Da Silva WC, Bevilaqua LR, Medina JH, Izquierdo I, Cammarota M.

Inhibition of mRNA synthesis in the hippocampus impairs consolidation and reconsolidation of spatial memory.

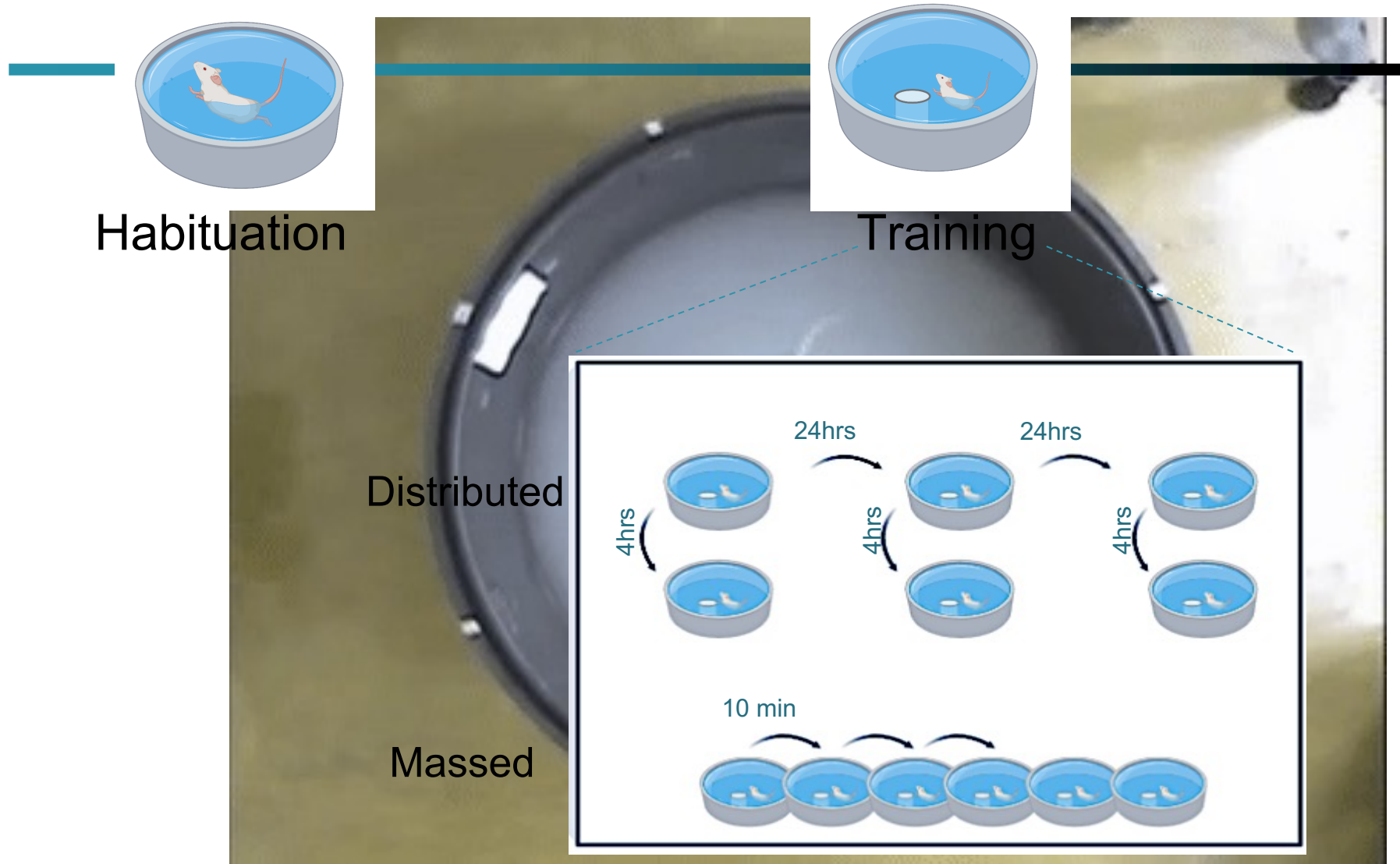
Da Silva WC, et al. Hippocampus. 2008. PMID: 17853412

Reversible hippocampal inactivation partially dissociates how and where to search in the water maze.

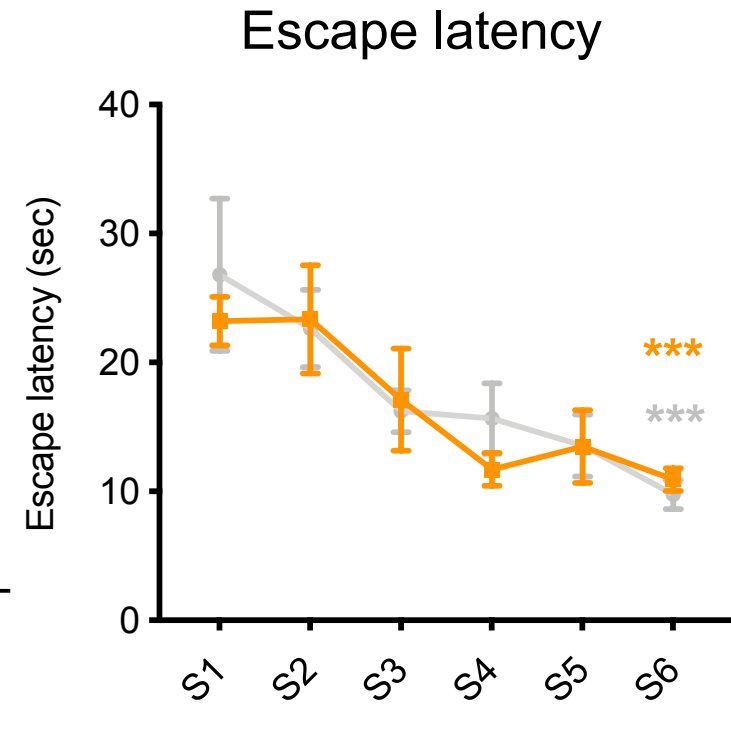
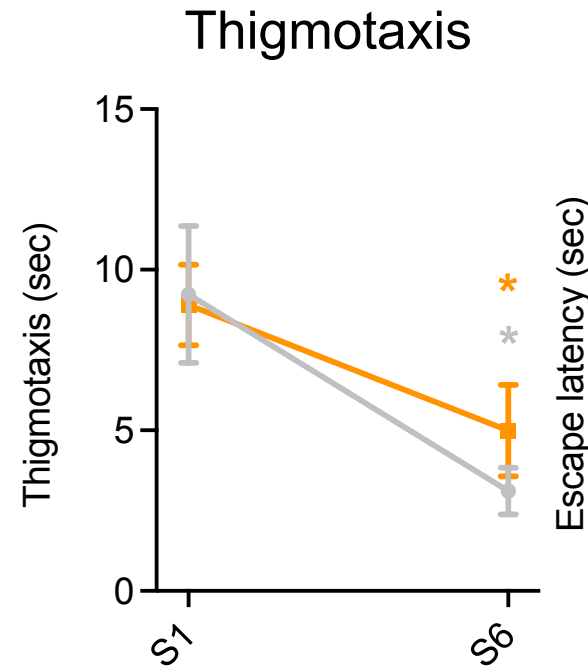
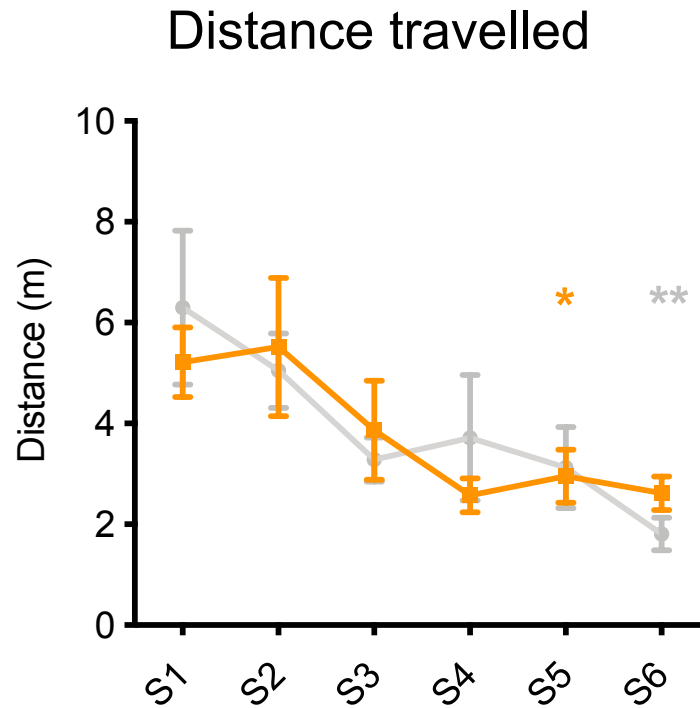
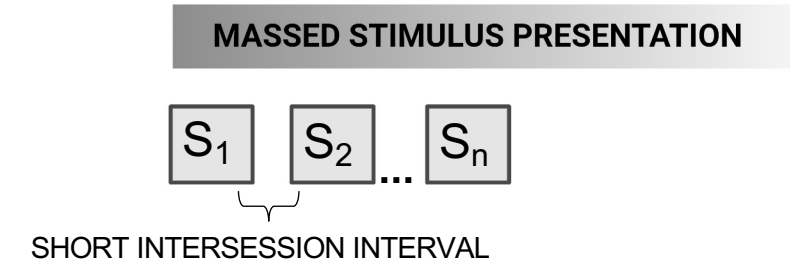
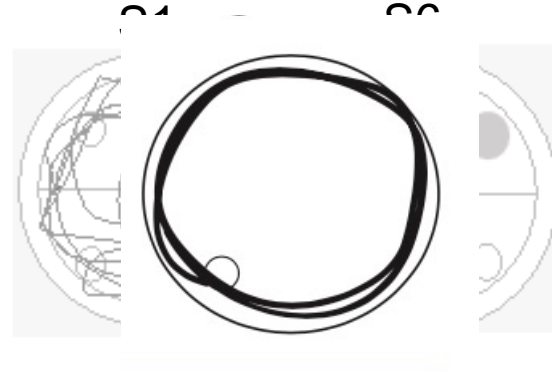
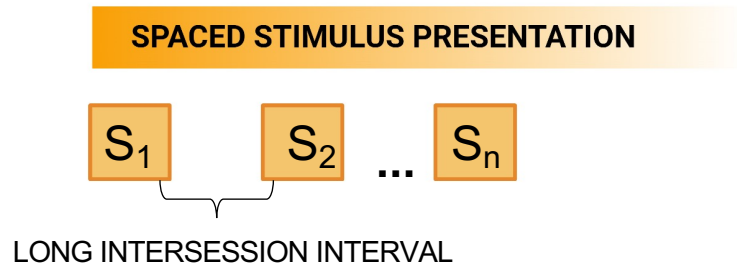
Micheau J, Riedel G, Roloff Ev, Inglis J, Morris RG.



Methods- Morris Water Maze



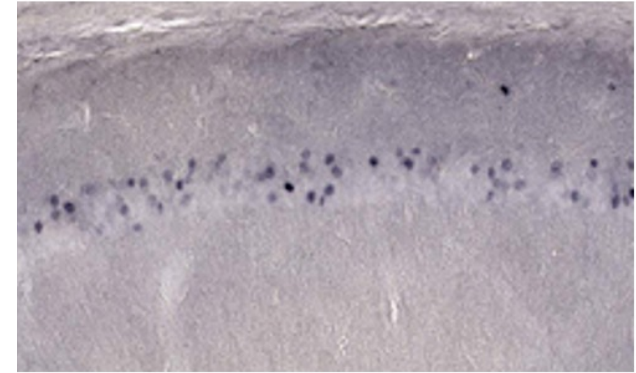
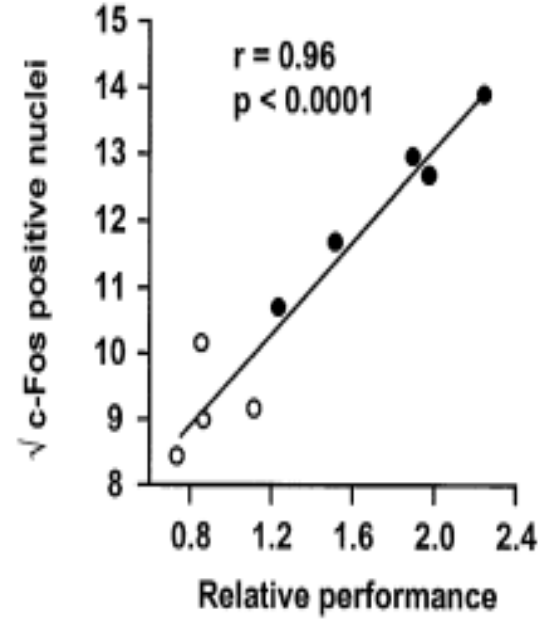
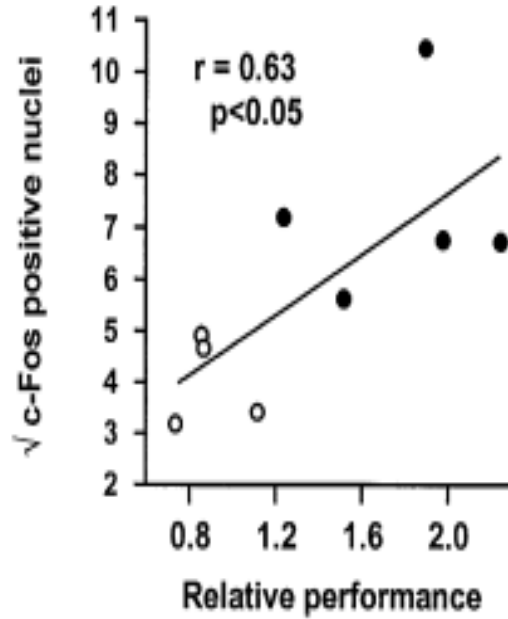
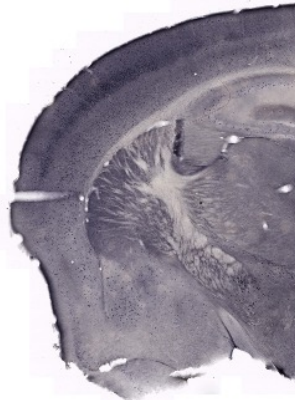
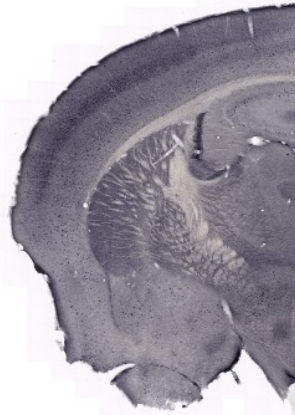
Both massed and distributed trained mice learn to locate the platform



Fos mapping in the dorsal CA1

Dorsal CA1

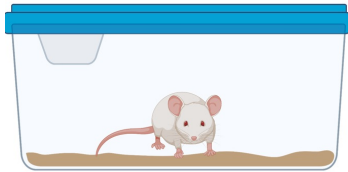
Ventral CA1



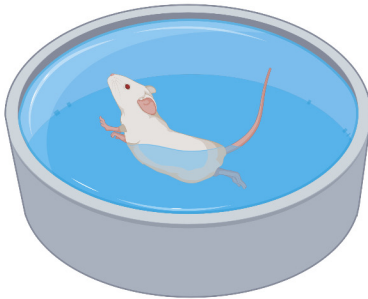
modified from Bertaina-Anglade et al., 2000

Fos mapping in the dorsal CA1

3 experimental groups:



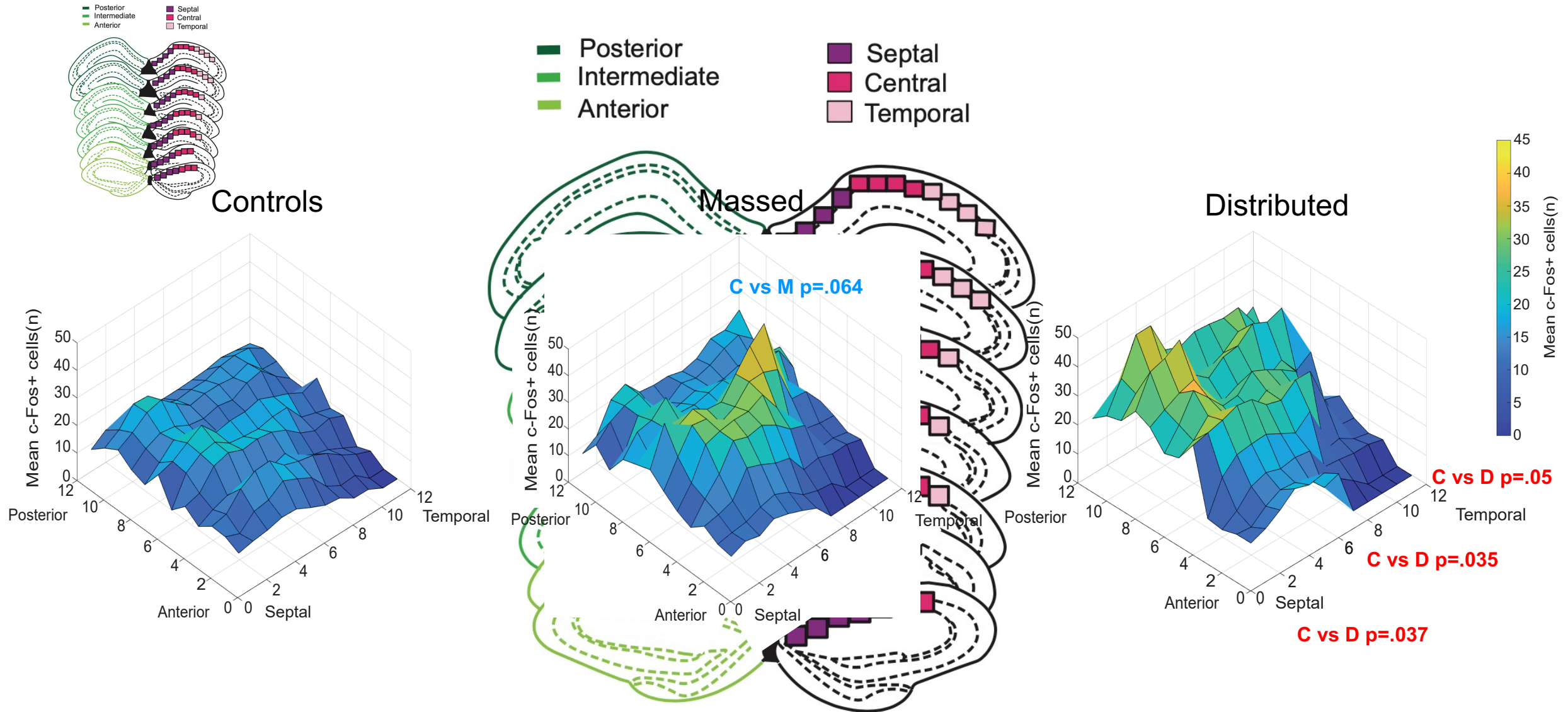
Control handled mice



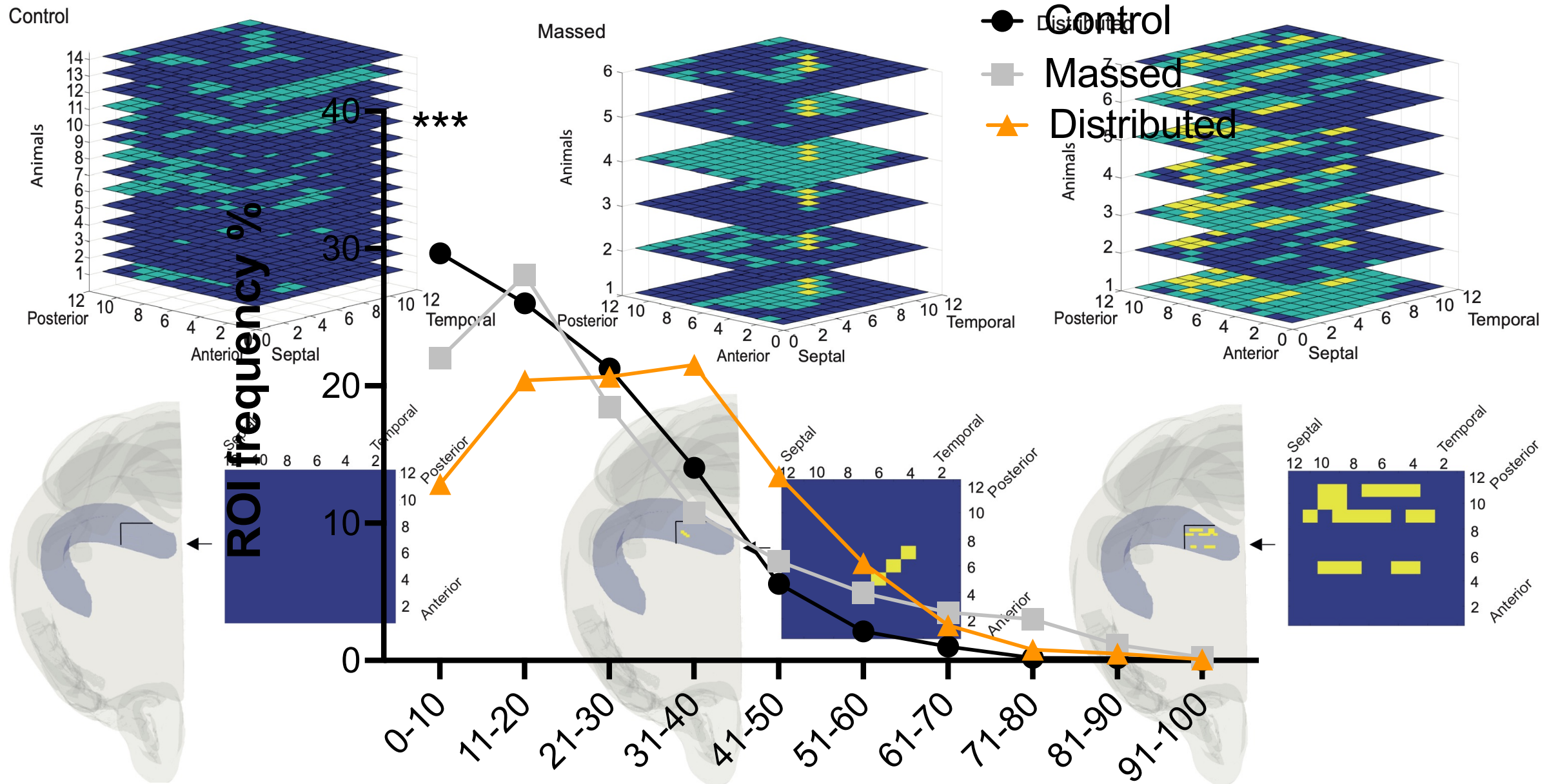
Massed trained mice

Distributed trained mice

Training procedure induce different fos expression pattern in the dorsal CA1

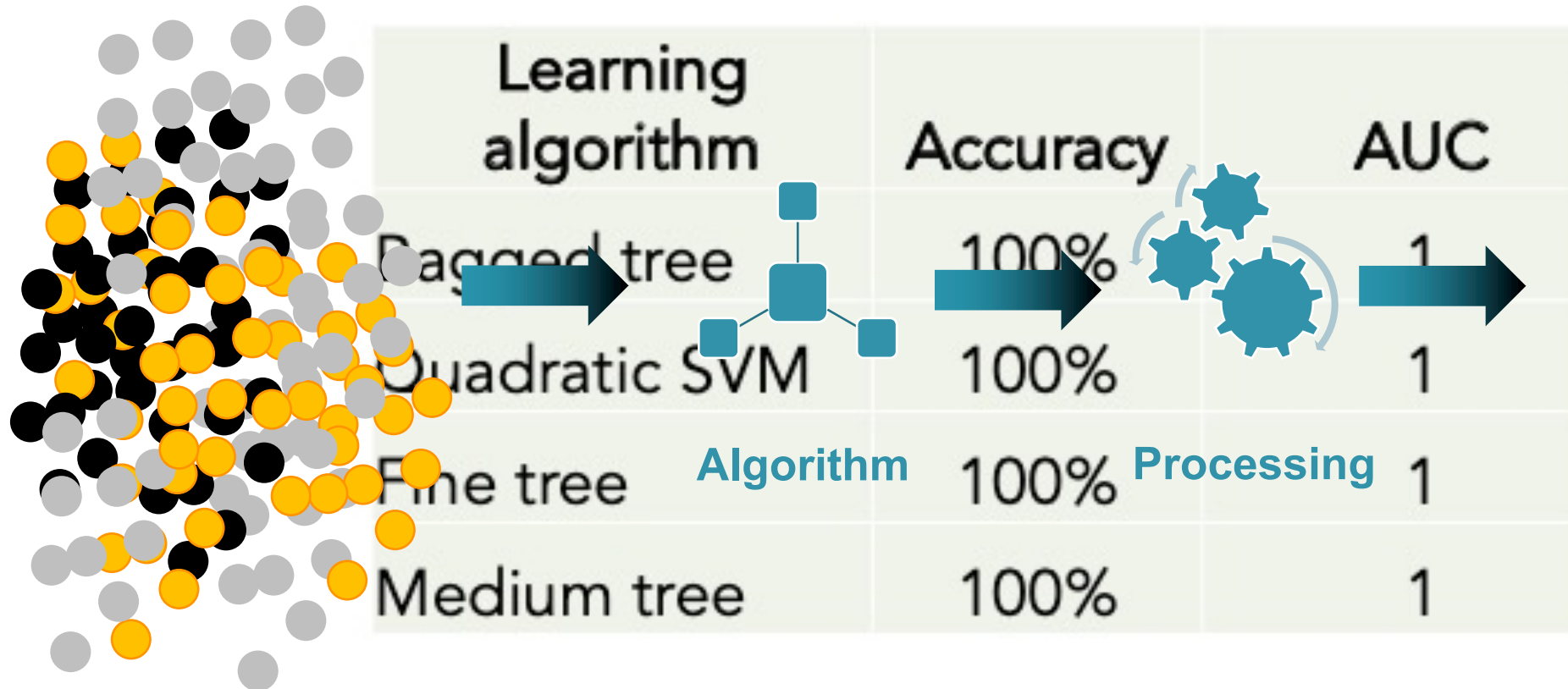


Trained mice shared all the same protocol- dependent cellular activation pattern

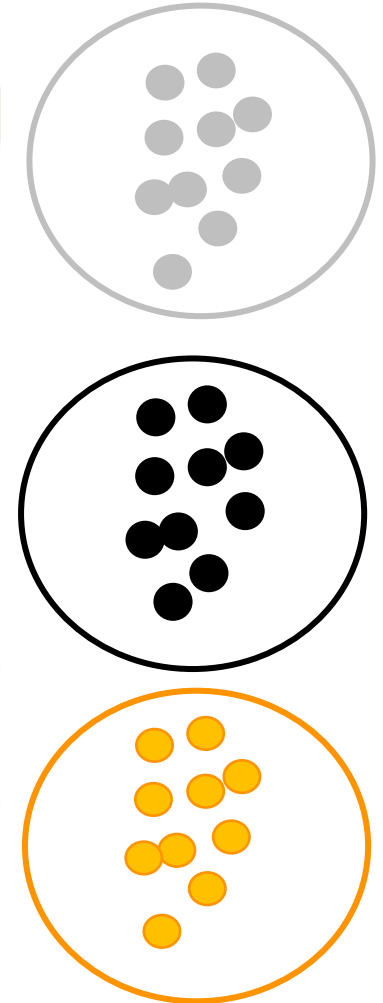


Training procedure can be decoded by the pattern of hippocampal neuronal activity

Raw data



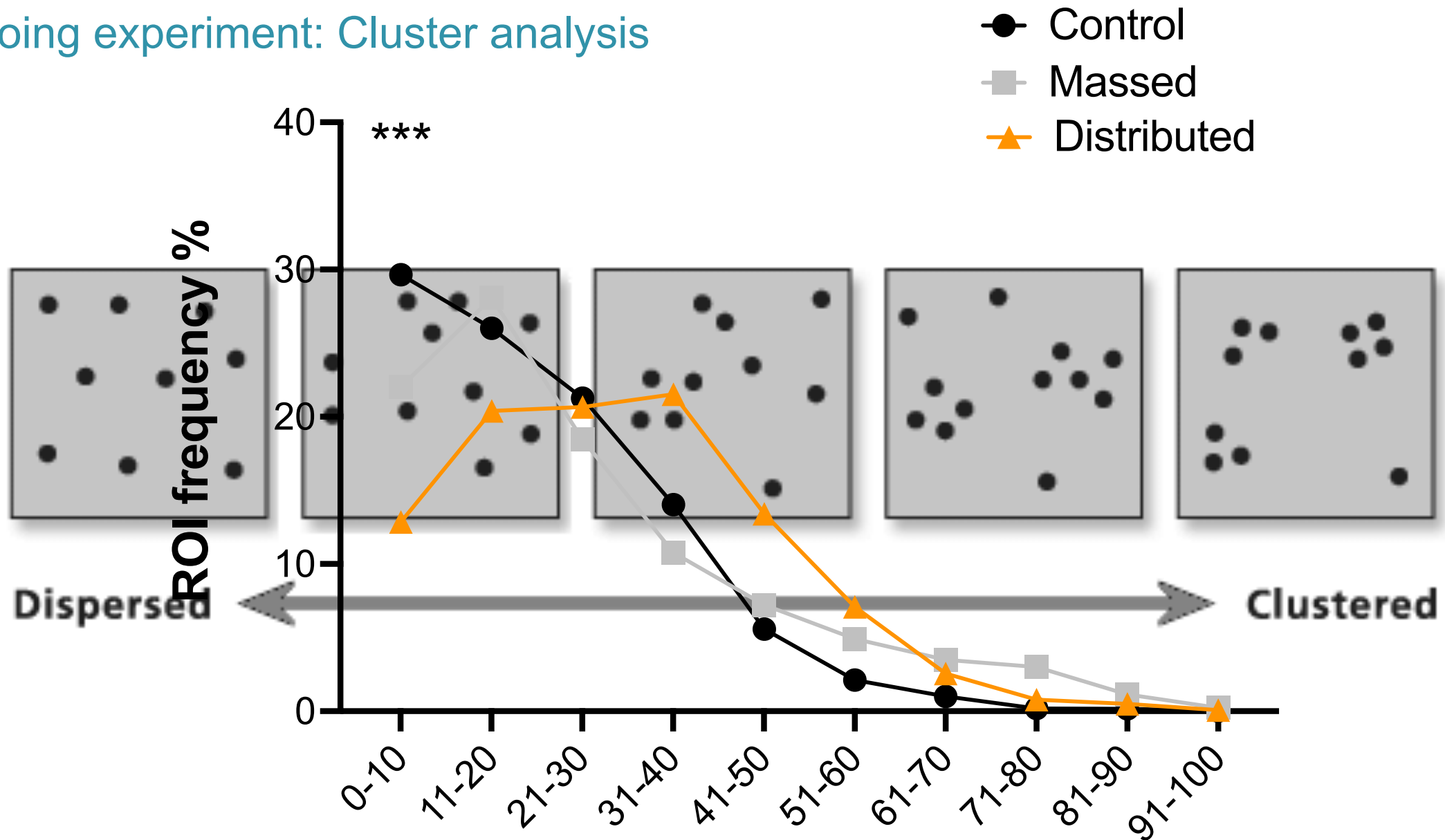
Output



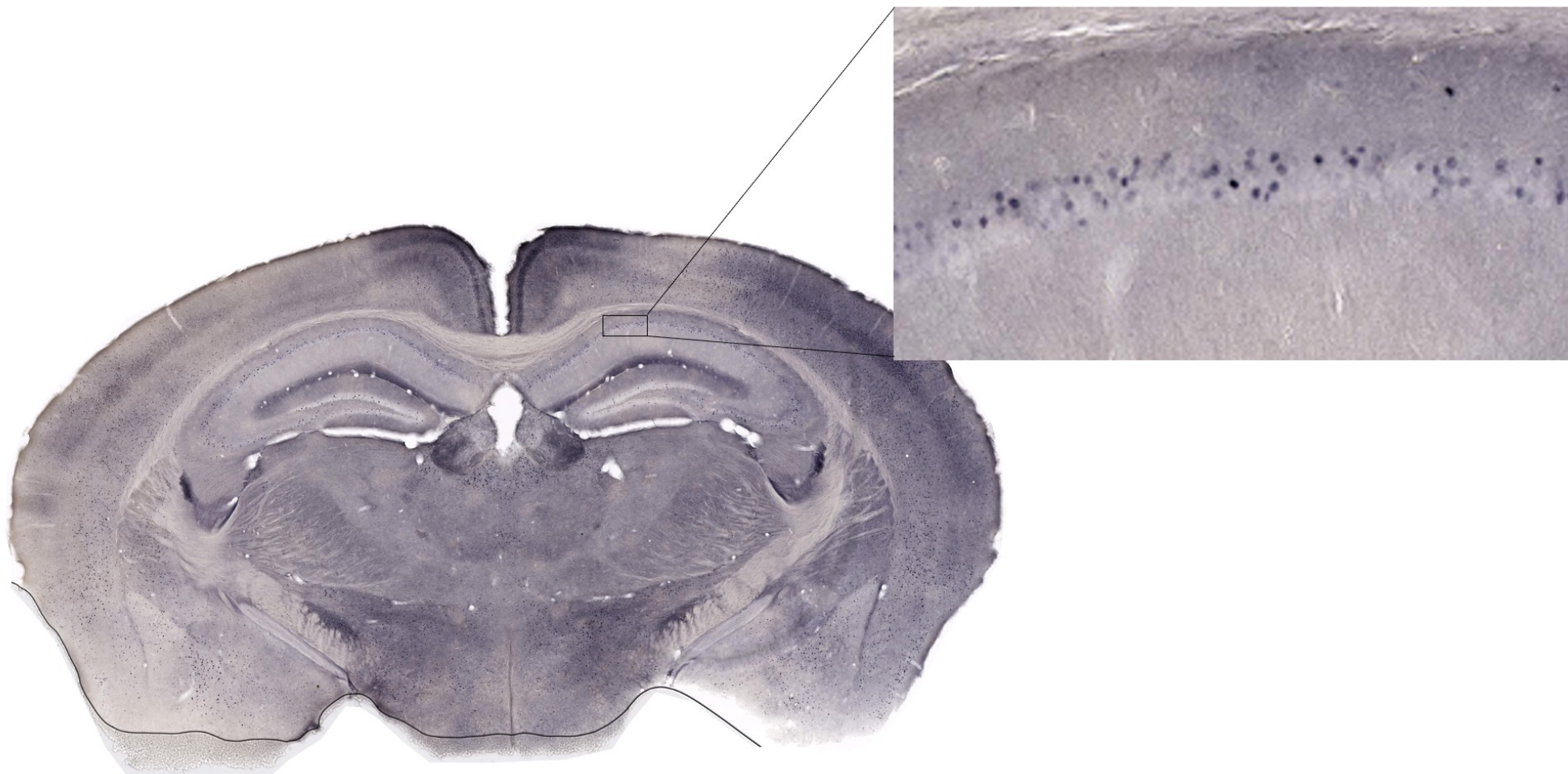
Conclusions

- Identification of CA1 subregions that are differentially active in massed and distributed trained mice.
- Identification of a consistent CA1 subregions, equally active in all the mice
- Identification of more CA1 subregions active in distributed compared to massed trained mice, suggesting a larger activation of the CA1, possibly explaining the superiority of the distributed training over a massed training.
- Identification of a unique cellular activation pattern in distributed and massed trained mice, strong enough to discriminate between the two groups using a learning algorithm.

Ongoing experiment: Cluster analysis



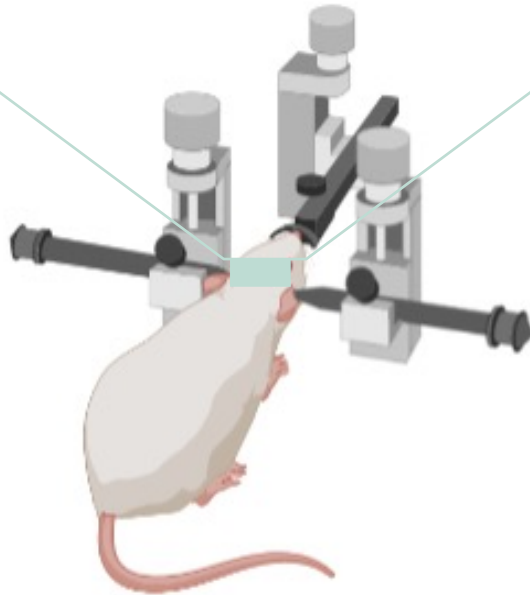
Ongoing experiment: Cluster analysis



Future prospective: Chemogenetic/optogenetic inhibition of the different CA1 subregions



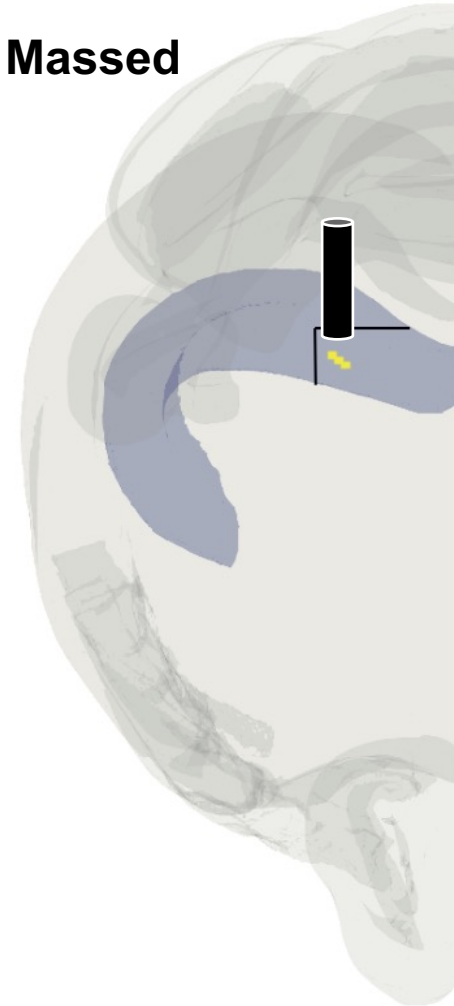
Adeno-associated (AAV) viral vector



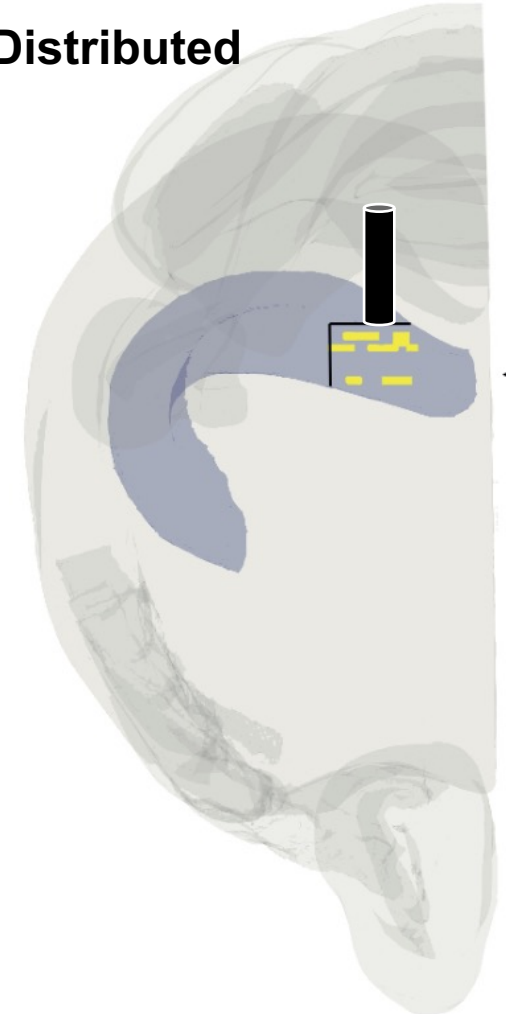
1. STEREOTAXIC SURGERY



Massed

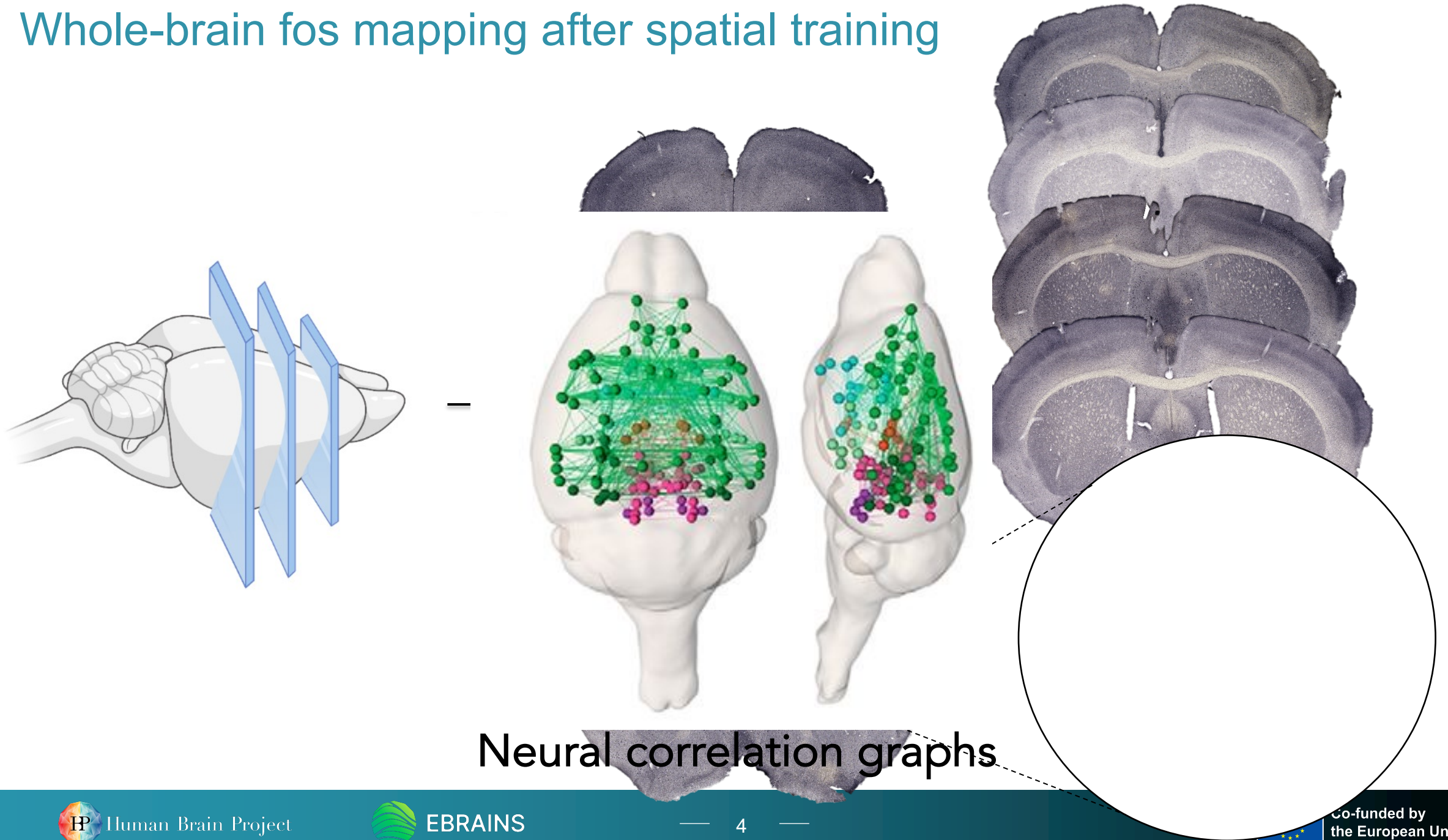


Distributed



2. FOCAL CNO ADMINISTRATION

Whole-brain fos mapping after spatial training





Human Brain Project



EBRAINS

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Thank you

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