Early life adversities alter dendritic spine density on ventral tegmental area neurons

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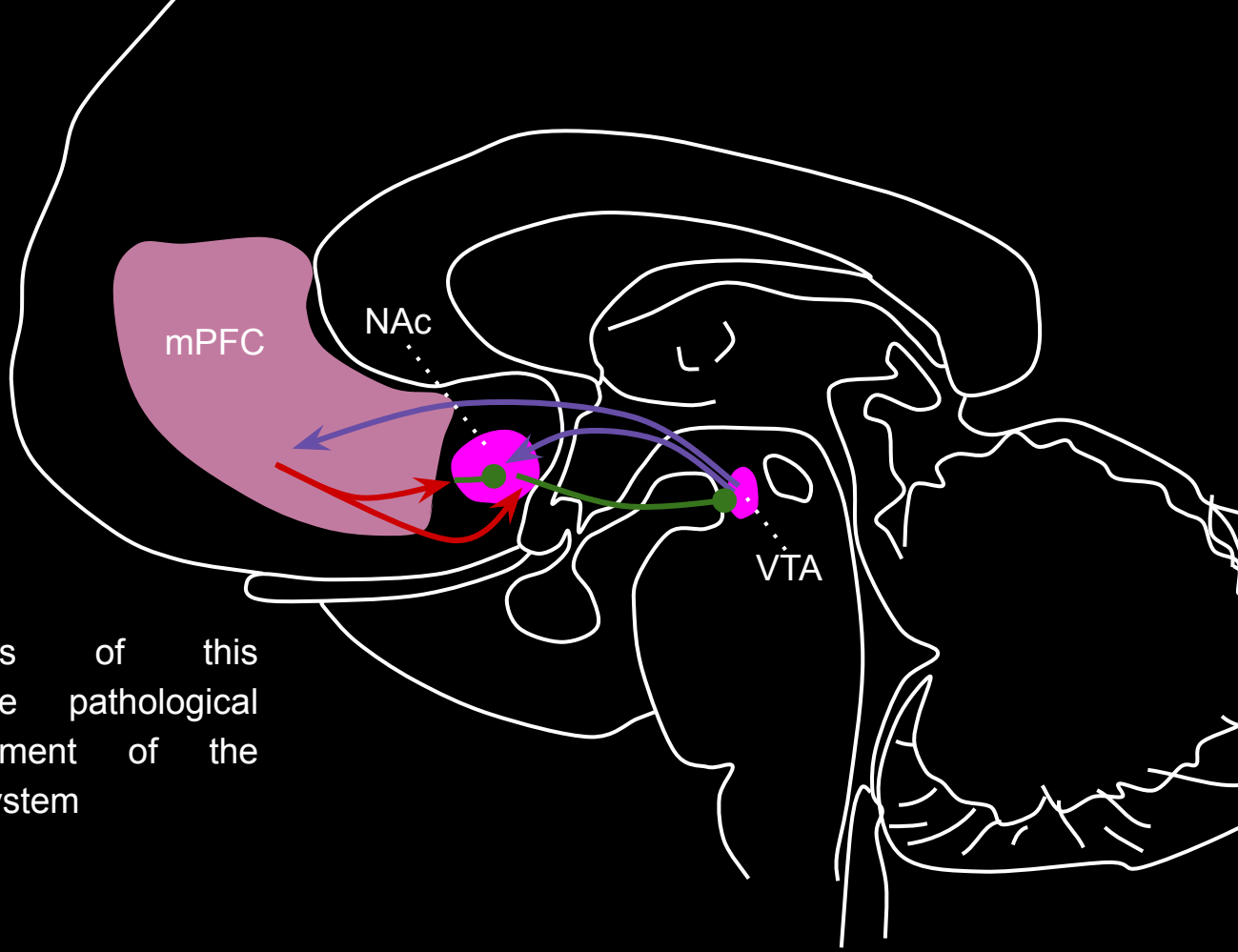
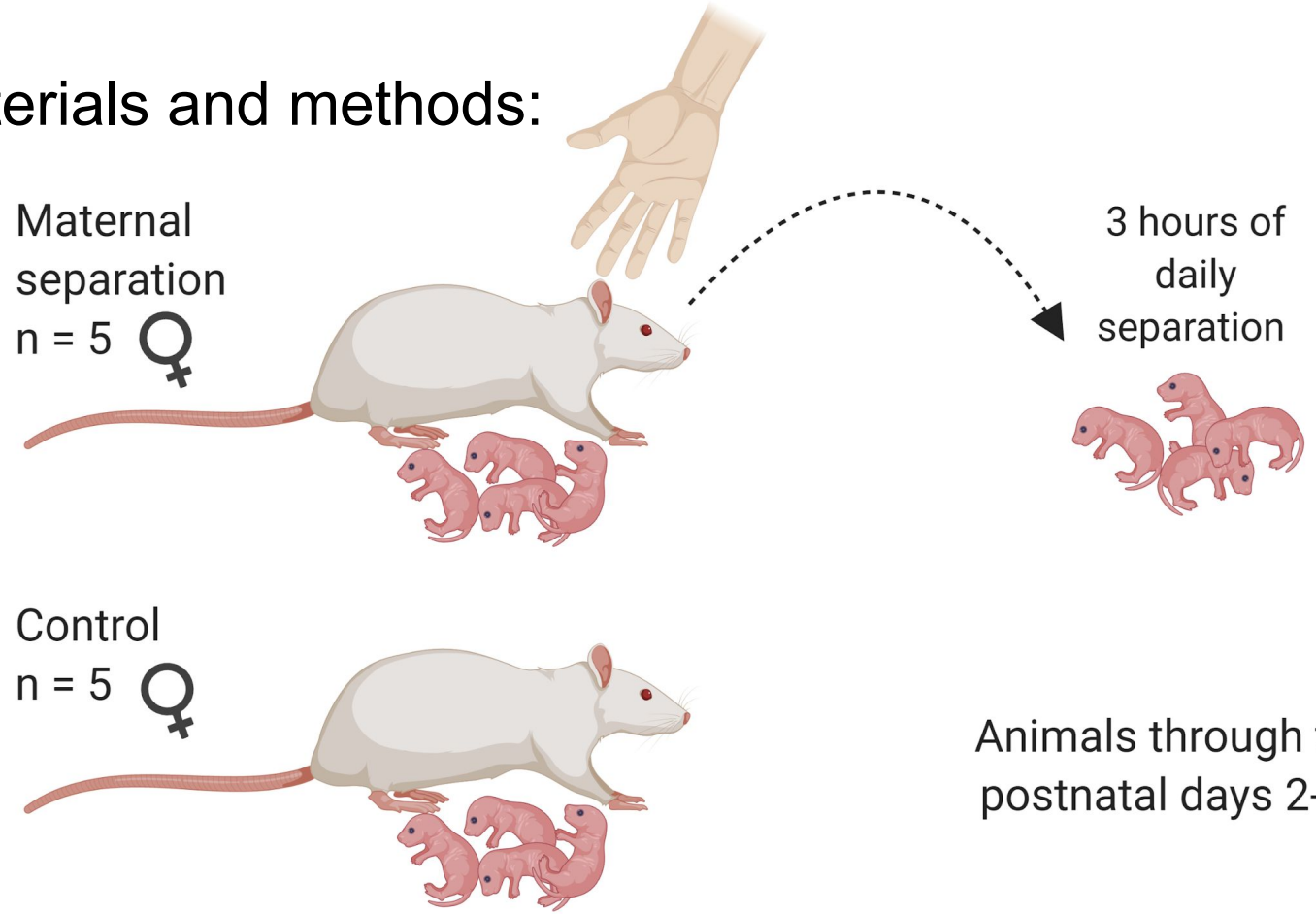
Stress experienced during the early postnatal period may have extensive and long-lasting consequences (psychiatric disorders, substance abuse susceptibility)

Potential explanations of this phenomenon might include pathological changes in the development of the mesocorticolimbic dopamine system

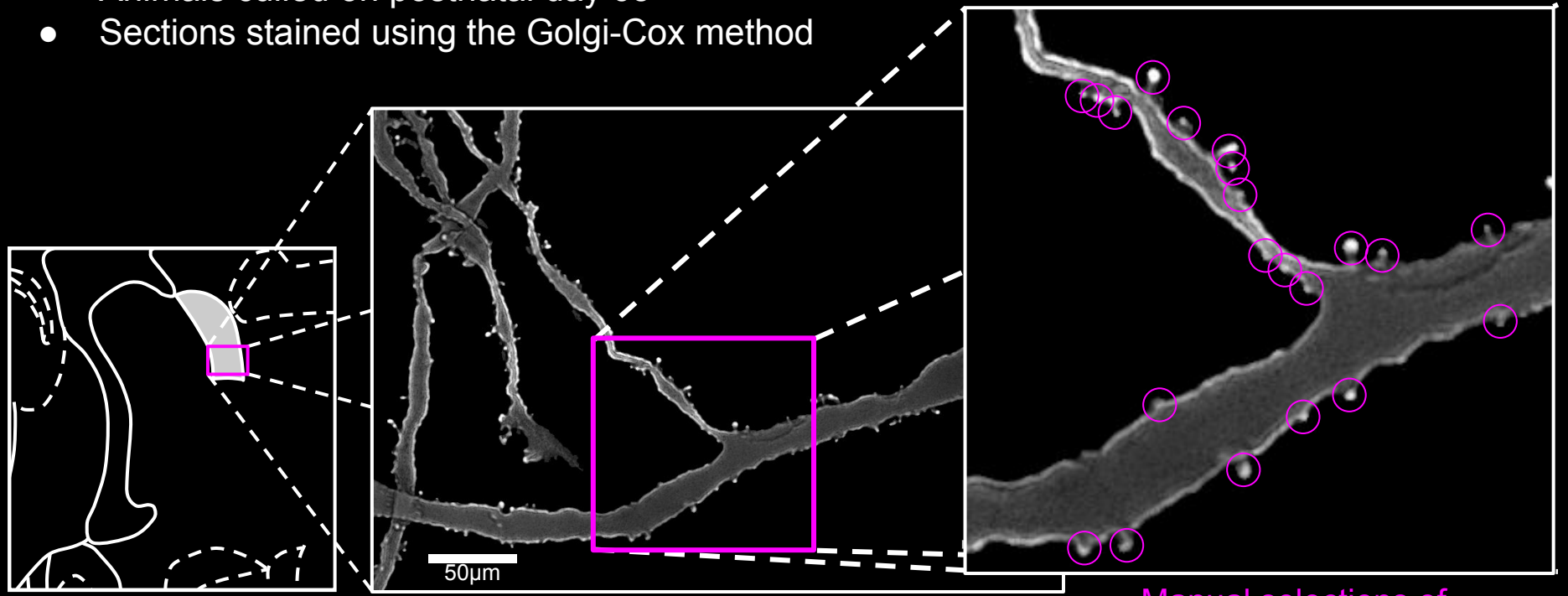


adapted from Stanton et al 2018

Materials and methods:



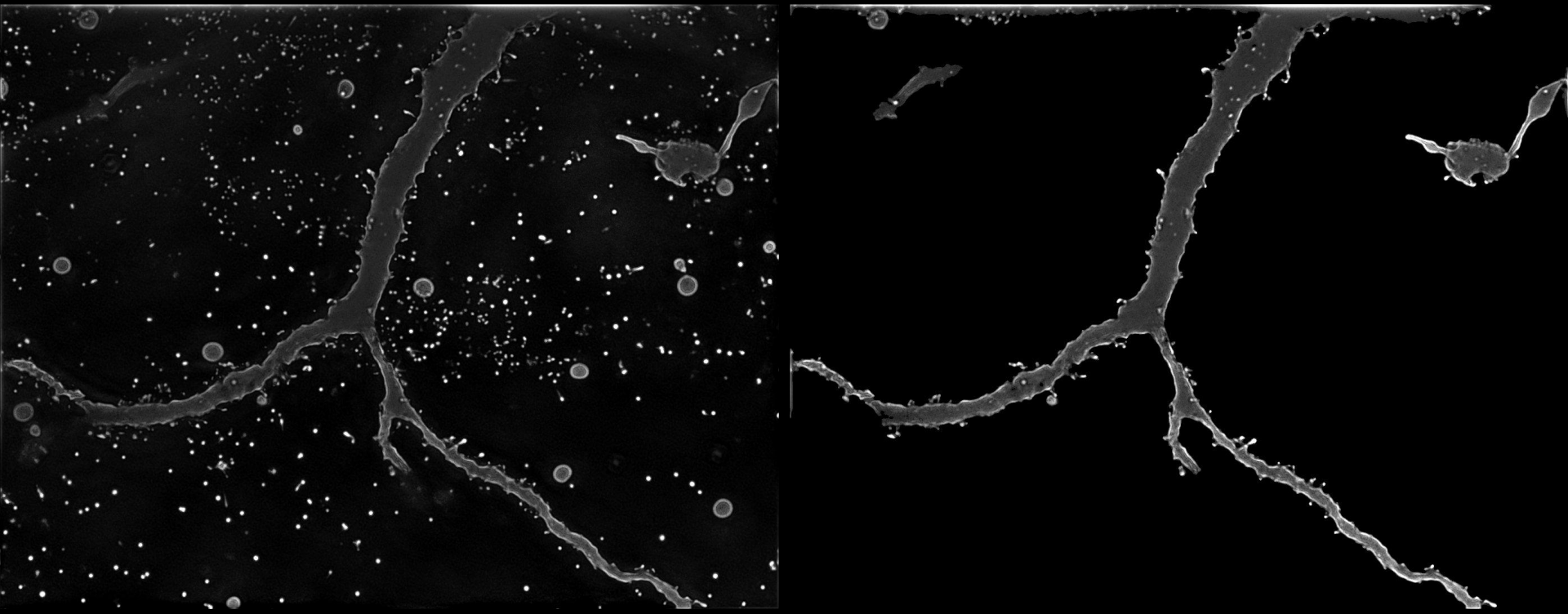
- Animals culled on postnatal day 65
- Sections stained using the Golgi-Cox method



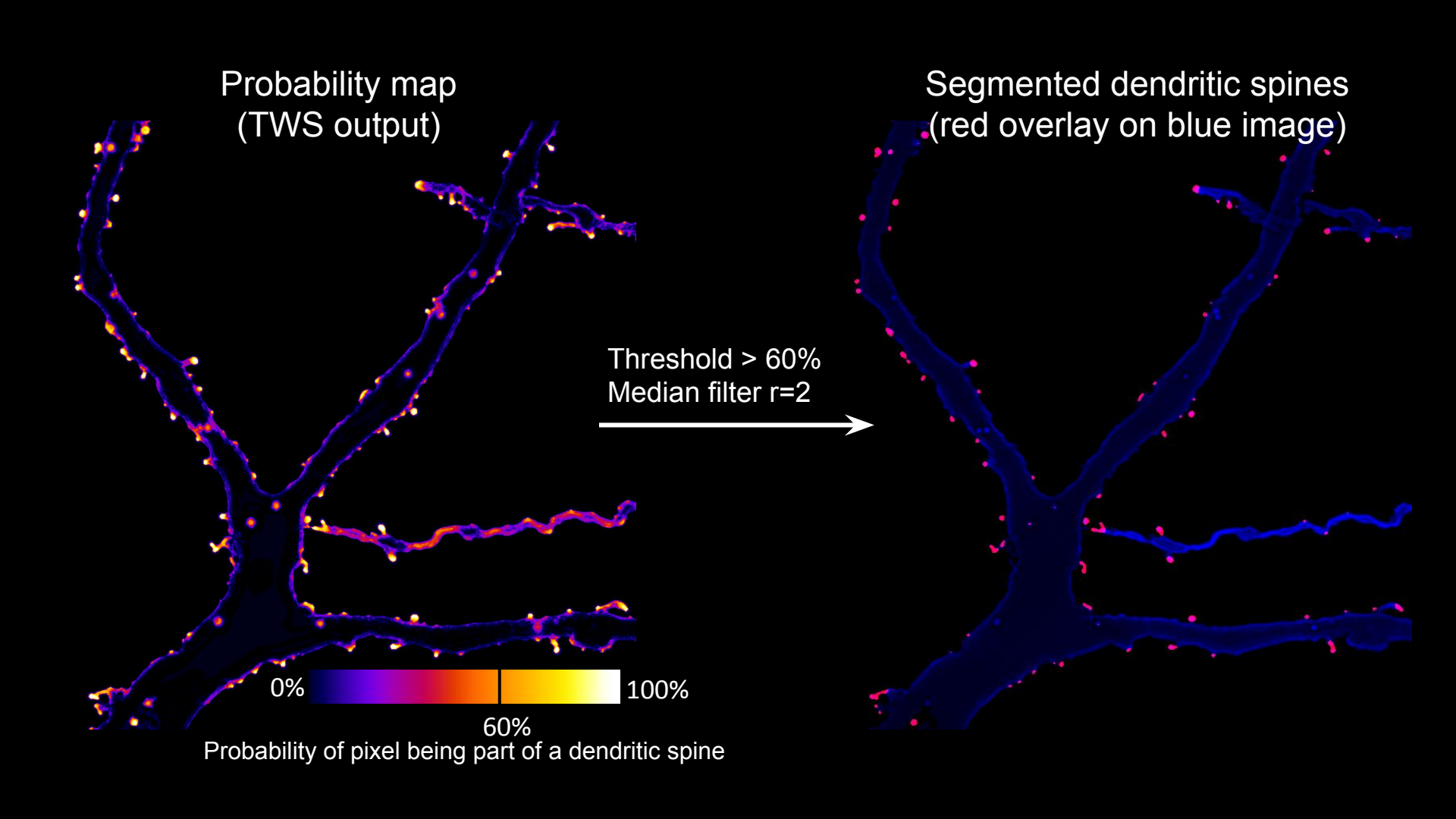
Dorsal VTA
(horizontal section)

Focus-stacked set of images
(Golgi-Cox stain)

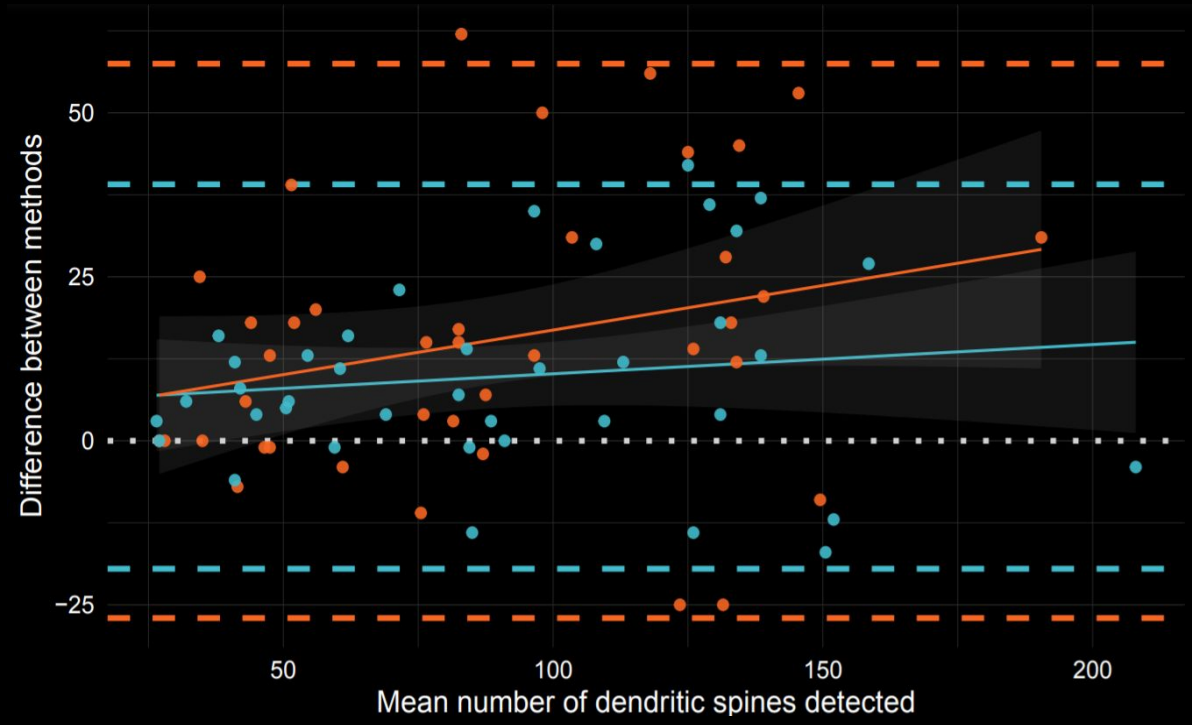
Manual selections of
dendritic spines



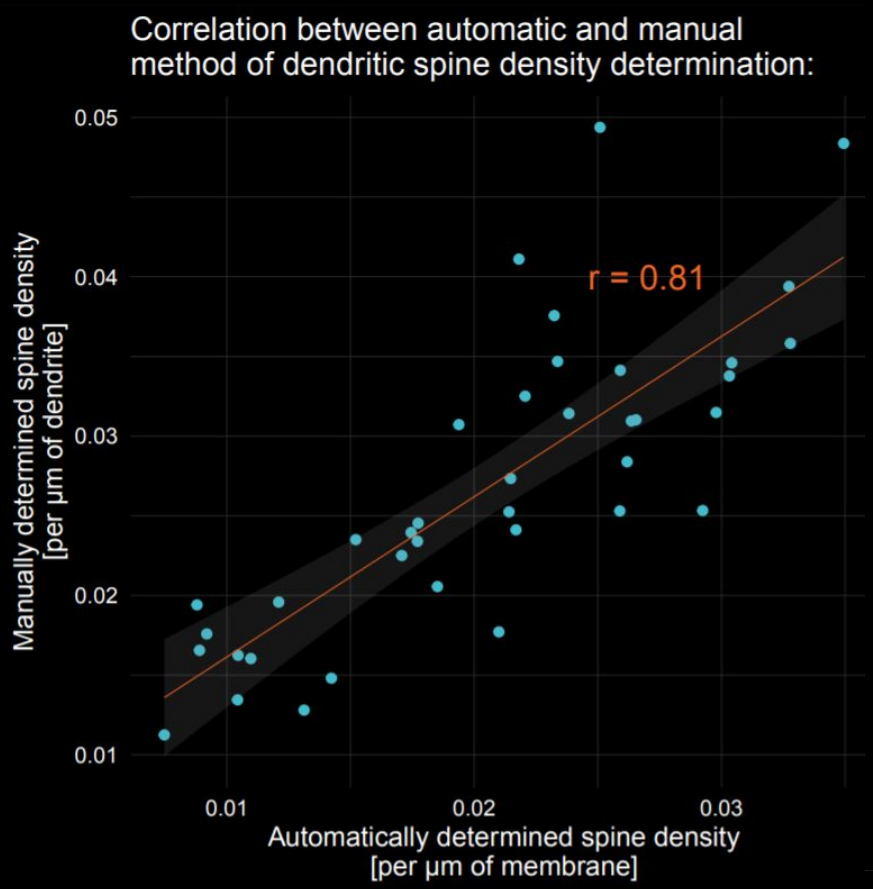
Before & after

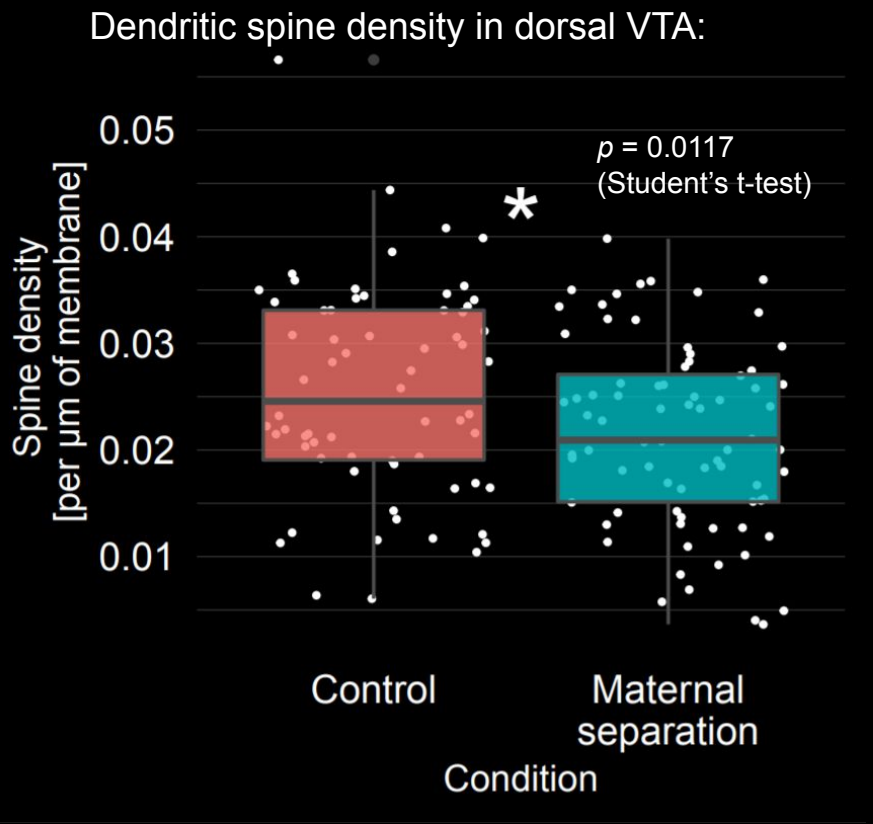

Probability map
(TWS output)
Threshold > 60%
Median filter r=2
Segmented dendritic spines
(red overlay on blue image)
0%
100%
60%
Probability of pixel being part of a dendritic spine

Bland-Altman plot of differences between methods of spine counting:



The Bland-Altman plot demonstrates the differences in the number of dendritic spines detected per image by different methods: orange points show the differences between manual counting performed by different condition-naive observers, blue demonstrate the difference between a trained observer and the automatic approach. Dashed lines show ± 2SD of differences between methods. The differences between manual counting are larger than differences between trained observer and the classifier.


Correlation between automatic and manual method of dendritic spine density determination:
r = 0.81
Manually determined spine density [per µm of dendrite]
Automatically determined spine density [per µm of membrane]
0.05
0.04
0.03
0.02
0.01
0.01
0.02
0.03


Dendritic spine density in dorsal VTA:
p = 0.0117
(Student's t-test)
*
Spine density [per µm of membrane]
0.05
0.04
0.03
0.02
0.01
Control
Maternal separation
Condition

- Arganda-Carreras I, Kaynig V, Rueden C, Eliceiri KW, Schindelin J, Cardona A, Sebastian Seung H. Trainable Weka Segmentation: a machine learning tool for microscopy pixel classification. Bioinformatics. 2017 Aug 1;33(15):2424-2426. doi: 10.1093/bioinformatics/btx180. PMID: 28369169.
- Stanton, Colin & Holmes, Avram & Chang, Steve & Joormann, Jutta. (2018). From Stress to Anhedonia: Molecular Processes through Functional Circuits. Trends in Neurosciences. 42. 10.1016/j.tins.2018.09.008.
- Carr CP, Martins CM, Stingel AM, Lemgruber VB, Juruena MF. The role of early life stress in adult psychiatric disorders: a systematic review according to childhood trauma subtypes. J Nerv Ment Dis. 2013 Dec;201(12):1007-20. doi: 10.1097/NMD.0000000000000049. PMID: 24284634.

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