3D Reconstructions of Neurons: Testing Structural Plasticity of CA3 Hippocampal Pyramidal Neurons in Response to Postnatal Maternal Exercise

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INTRODUCTION

Prolonged periods of stress can cause structural alterations to the neurons in the brain. Data suggests that exercise can normalize many of the effects of stress[1]. Parental environment and behavior can affect offspring development and behavior, likely through altered cytokine levels in breastmilk[2]. We have previously found that offspring of runner dams are resilient to acute stress-induced weight loss. We sought to clarify the effects of postnatal maternal exercise on structural changes, specifically dendritic branching through 3D reconstruction of pyramidal neurons in the CA3 region of the hippocampus.

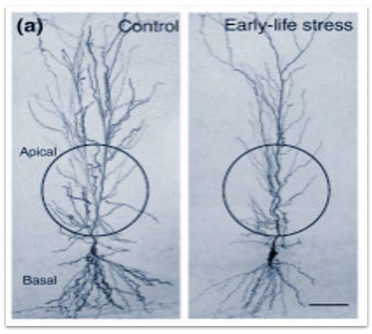


Figure 1: (a) Dendritic impoverishment in pyramidal cells of adult rats that experienced chronic early life stress (Maras and Baram, 2012) (b) Effects of running on neuronal structures (Trinchero et al., 2019)

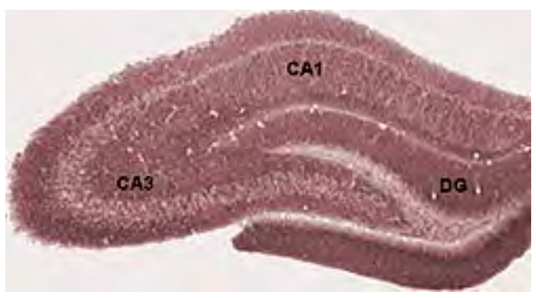


Figure 2: Neurons were sampled from the dorsal and ventral regions of the CA3 region.

FUTURE DIRECTIONS

- Overexpression of BDNF in the adult dentate gyrus promotes resilience and blocks the anhedonic effect of stress[4]. We will quantify BDNF and Trk-B expression within the hippocampus to probe for putative mechanisms.

RESULTS

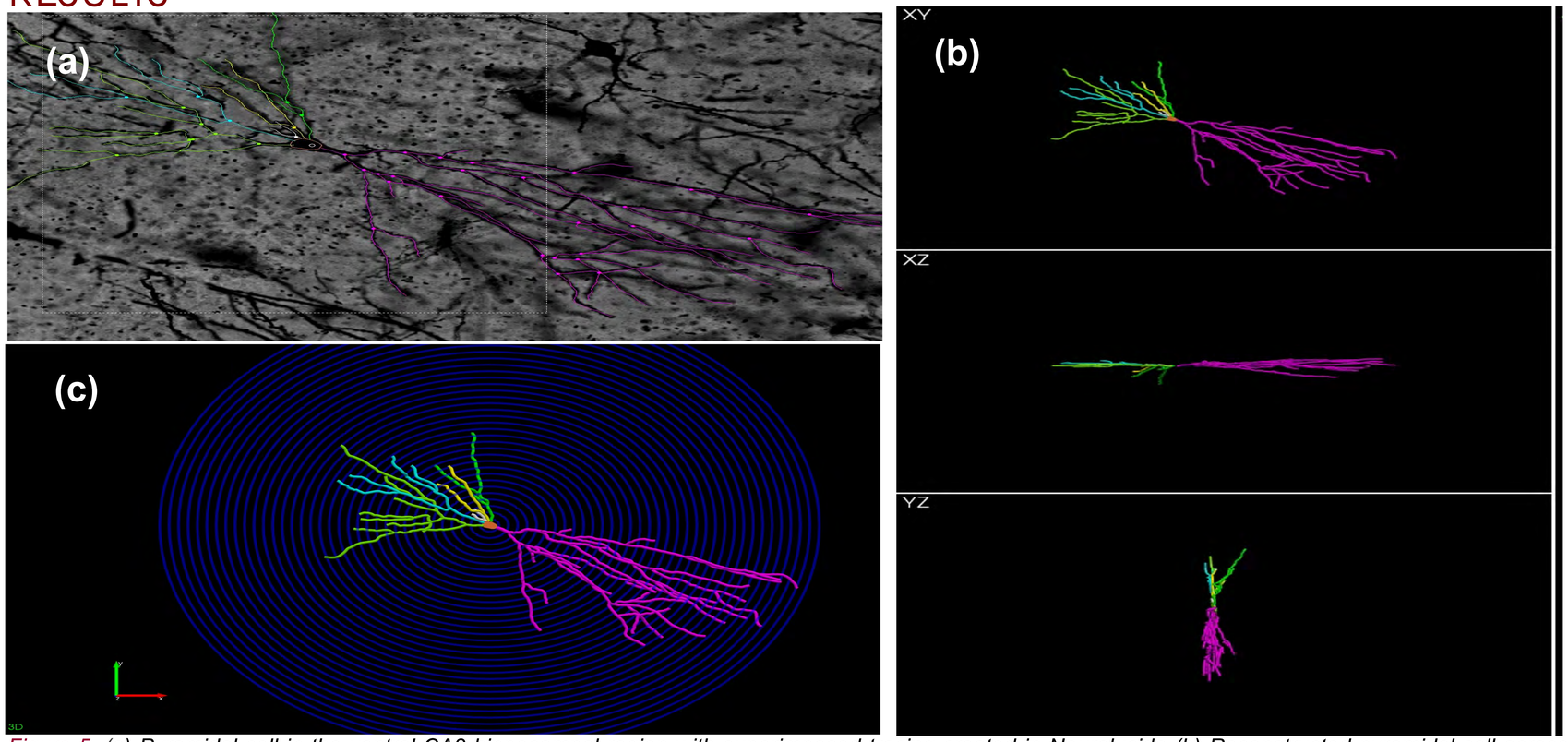


Figure 5. (a) Pyramidal cell in the ventral CA3 hippocampal region with superimposed tracing created in Neurolucida (b) Reconstructed pyramidal cell across the three axes (c) 3D reconstructions of pyramidal cells with Sholl rings created in Neurolucida Explorer (MBF BioScience)

Data suggests that there are two prominent types of neurons in the CA3 region that can be identified by the morphology of the apical dendrites. One is typified by a relatively long apical length between the soma of the cell and the first node, while the other has a shorter apical shaft[3]. We have identified and classified neurons into long- and short-shafted categories for further analysis of potential differences.

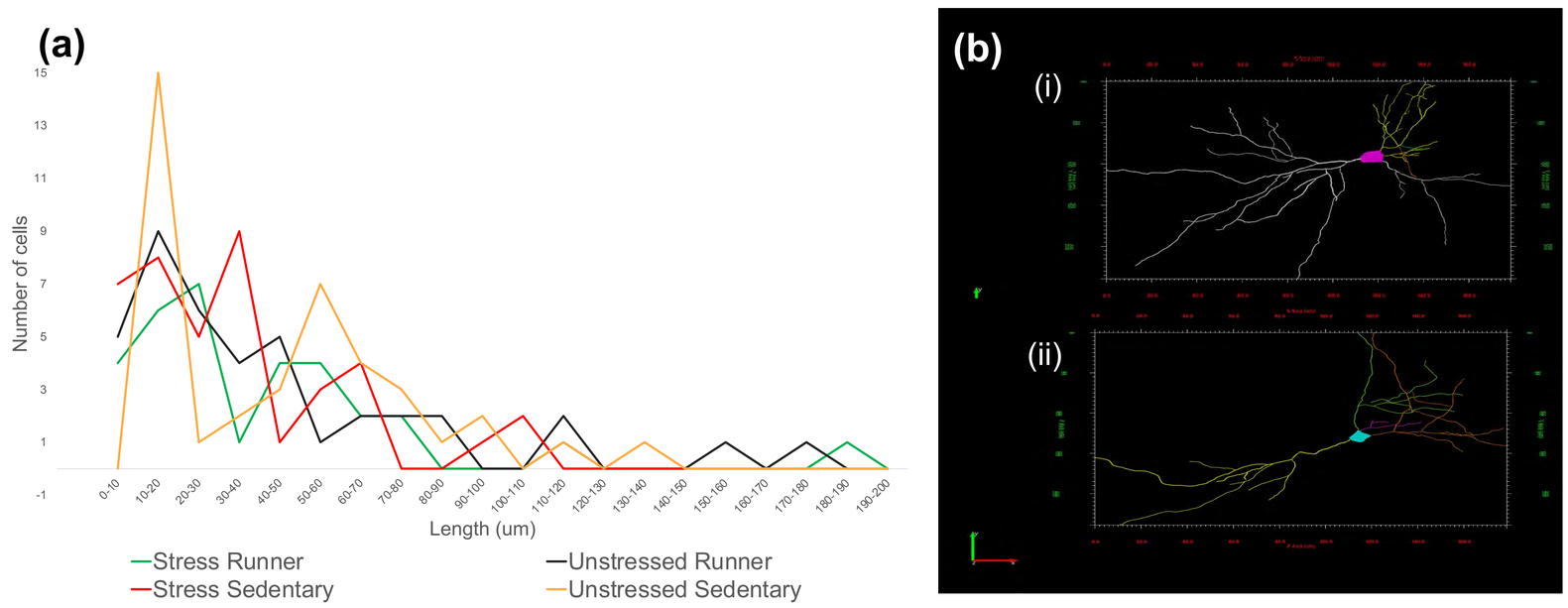


Figure 6. (a) Distribution of number of cells and length for treatment groups (b)(i) Short-shafted neuron and (ii) long-shafted neuron with scale bars

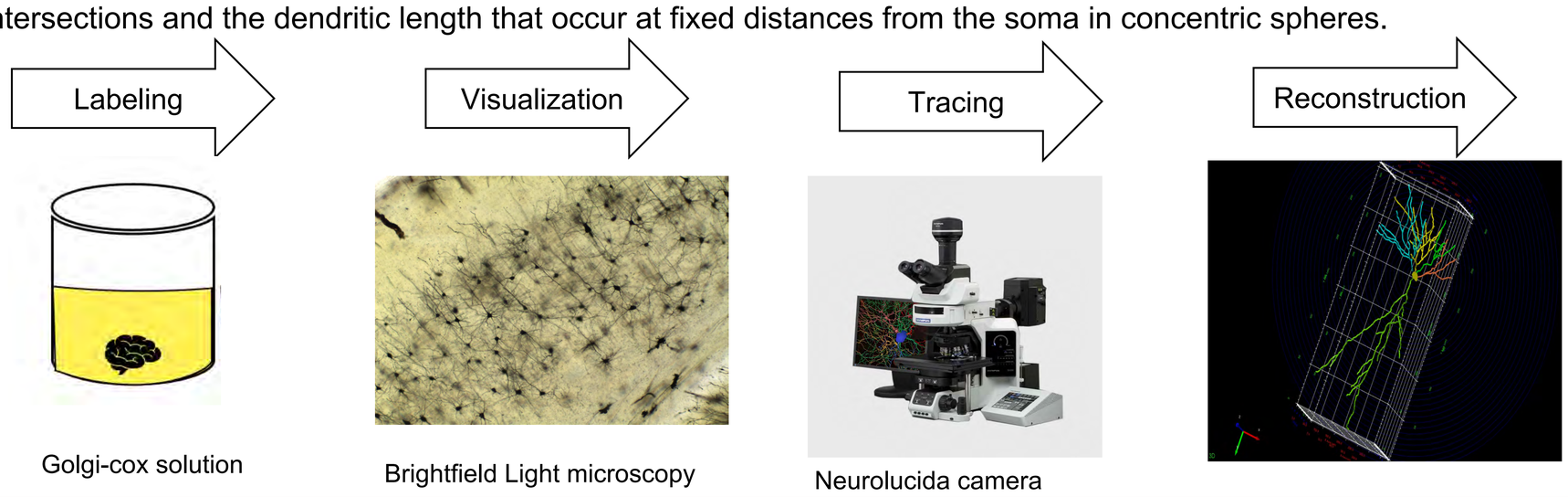
METHODS

Subjects: C57bl/6 male mice born from dams that had post-parturition access to a running wheel (runners; n= 9) or had a standard housing cage (sedentary; n= 10).

CUS Paradigm: Subjects were divided between control (runner, n= 4; sedentary, n= 5) and experimental (runner, n= 5; sedentary, n= 5) groups to undergo a 21-day CUS paradigm. Following CUS, mice were perfused and brains were Golgi stained[5] to study dendritic arborization within pyramidal neurons of the dorsal hippocampus CA3 region.

Reconstruction: A computer-based microscope system was used to delineate and reconstruct the axon, dendrites, soma, and other sub-cellular components of neurons, thereby creating a digital, geometric model of the neuron (n=152). Only relatively isolated neurons with completely stained and intact dendritic arbors from the middle third of the section were selected for analysis.

Analysis: Neurolucida explorer was used to conduct a Sholl analysis which reveals the number of dendritic intersections and the dendritic length that occur at fixed distances from the soma in concentric spheres.



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