The Effects of Early Life Stress in Different Stages of Adolescence on Perineuronal Nets in the Hippocampus and Amygdala

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Introduction

•Perineuronal nets (PNNs) are part of the brains extracellular matrix that wrap around neurons. PNNs are crucial for synaptic plasticity and structural support in regions like the Cerebral Cortex, Hippocampus, Amygdala, and Basal Ganglia.

•Studies show that early life stress (ELS) has a negative impact on PNN formation and can lead to reduced PNN intensity.[1] A decrease in PNN formation from ELS has been shown to result in significant implications for later neurodevelopment. Alzheimer's, bipolar disorder, schizophrenia, and other cognitive disorders have been associated with altered PNN formation.[2]

•This study compares ELS effects on PNNs in the hippocampus (CA3, CA1.2, DG) and amygdala between postnatal (PN) day 29 (adolescence) and PN day 44 (early adulthood) groups, alongside assessing hippocampal volume in PN day 29 and PN day 44.

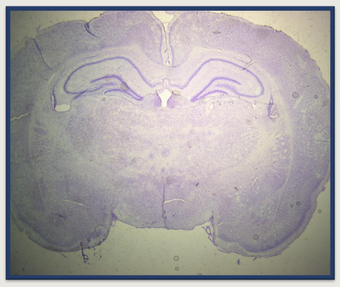
•Investigating PNNs in relation to ELS sheds light on neurodevelopmental resilience, cognitive disorders, and potential therapeutic strategies.

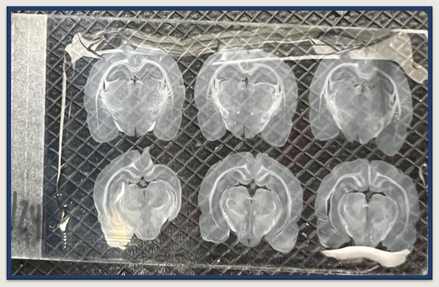
Methodology

Treatment rats underwent combination stress (limited bedding, maternal separation). Control subjects did not experience stress.

Wisteria floribunda agglutinin (WFA) Staining: 2 tissue slices from each subject in PN day 29 and PN day 44 were selected. These slices displayed the hippocampus and amygdala. The tissue was stained using a WFA staining protocol. 3 images were taken per each area of the hippocampus (CA3, CA1.2, and DG). 3 images were taken per each area of the amygdala. Do determine PNN percentages, the pixels from PNNs were counted using ImageJ.

Cresyl Violet Staining: 12 tissue slices from each of the PN day 29 and 44 subjects were selected. These slices displayed each of the hippocampal stages. The tissue was stained using the cresyl violet staining protocol. To determine hippocampal volume, cells were counted using ImageJ.





Results

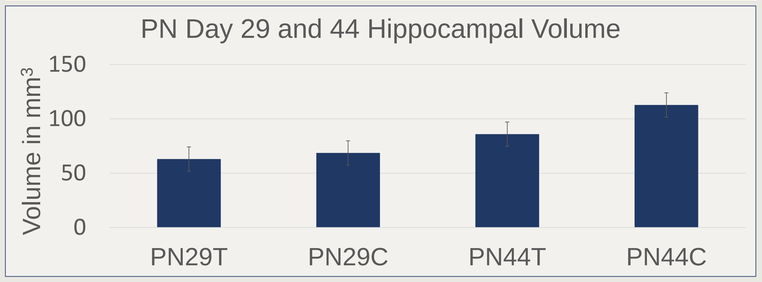


Figure 1. displays averages of 63.04mm^3 for PN29T, 68.63mm^3 for PN29C, 85.94mm^3 for PN44T, and 112.74mm^3.

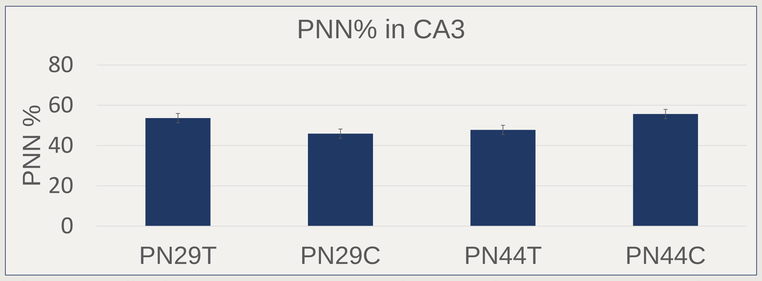


Figure 2. displays PNN averages of 53.6% for PN29T, 45.9% for PN29C, 47.75% for PN44T, and 55.63% for PN44C.

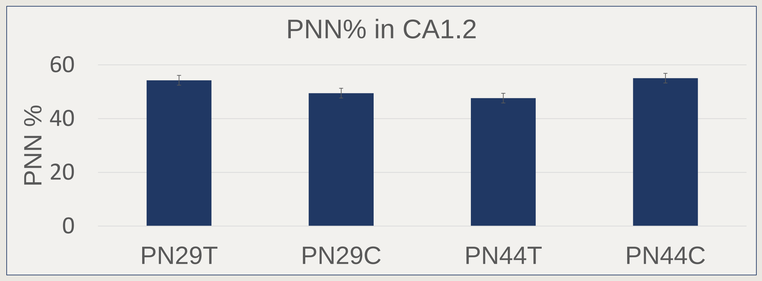


Figure 3. displays PNN averages of 54.28% for PN29T, 49.49% for PN29C, 47.64% for PN44T, and 55.06% for PN44C.

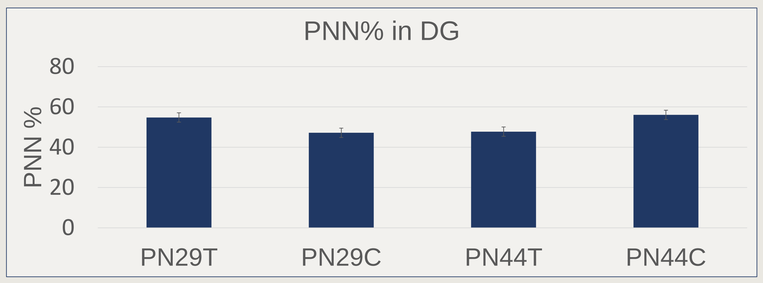


Figure 4. displays PNN averages of 54.74% for PN29T, 47.16% for PN29C, 47.72% for PN44T, and 56.07% for PN44C

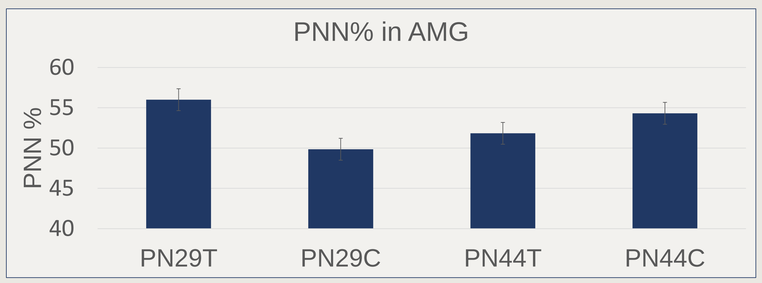


Figure 5. displays PNN averages of 56% for PN29T, 49.85% for PN29C, 51.83% for PN44T, and 54.31% for PN44C

Discussion & Conclusion

PN 29 and PN 44 Hippocampal Volume

The Cresyl Violet stain on average revealed a lower hippocampal volume of the PN29T group compared to PN29C group with a difference of 5.59mm^3. Similarly, PN44T revealed a lower hippocampal volume than PN44C by 26.8 mm^3.
These results are comparable with findings from a previous study which states that ELS has significant effects on the growth, particularly in the left hemisphere, of the hippocampus.[3]
In the future, it is worth considering measuring and averaging specific regions of the hippocampus to provide a more detailed analysis. Additionally, examining the amygdala could yield interesting and valuable results.

PN 29 and PN 44 PNN Percentages

On average, PN29T shows a higher PNN % than PN29C while PN44T shows a lower PNN % than PN44C. This shows a correlation between developmental stages and PNN formation and the effects that ELS can have on said formation.

Increased levels of PNNs during early adolescence results in overstabilization. Adolescents who experience ELS are unable to maintain high PNN levels resulting in low levels of PNNs in adulthood which can increase susceptibility to disorders such as Alzheimer's, schizophrenia, and bipolar disorder.

Lowered levels of PNNs during adulthood can produce both positive and negative results. Lowered PNN levels can promote improved learning and adaptability. However, lowered PNN levels can also result in memory issues and increased risk of neuron injury and deterioration.

Acknowledgements

I want to thank the SI Bridges Program for the opportunity and assistance in completing this project. I would also like to thank graduate students Claudia Ford and Caitlyn Richardson for their guidance and assistance. Finally, thank you to Dr. Michael Hylin for allowing me to utilize his lab and other necessary materials.

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