A neurodevelopmental perspective to improve innovation in preventive treatment of substance use disorders

Ismael Perez[1], MSc., John L. Vandeberg, PhD[2], and Mario Gil[1, 3], PhD

[1]Department of Psychological Science, The University of Texas Rio Grande Valley

2 School of Medicine South Texas Diabetes and Obesity Institute and Department of Human Genetics

[3]Department of Neuroscience and Institute for Neuroscience, School of Medicine, The University of Texas Rio Grande Valley

Background

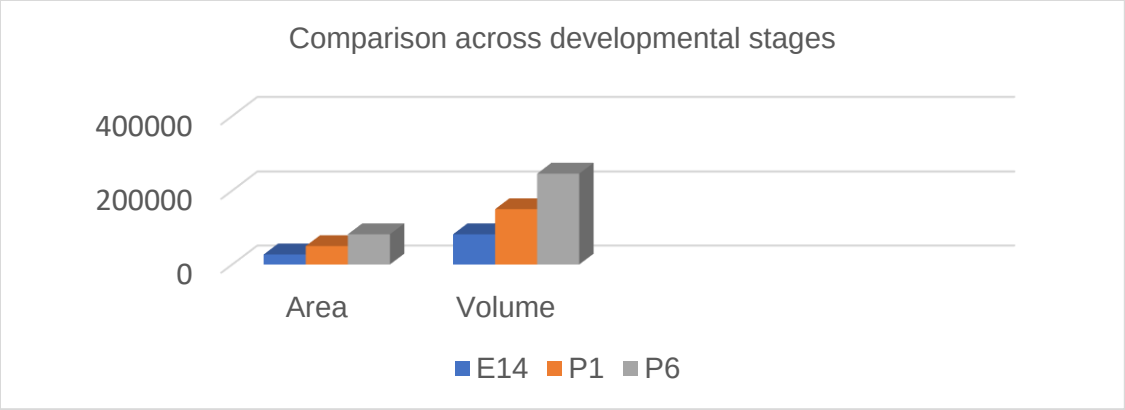
Midbrain dopaminergic neurons have been associated with substance use disorders (Blaess & Ang, 2015). Understanding their neurodevelopment during early stages of life is fundamental for innovating preventive care treatments. The animal model *Monodelphis domestica* has been proposed as an excellent candidate to study neurodevelopmental changes due to the ease of access to see changes in their embryonic development (Mate et al., 1994). The purpose of our study is to inform how brain cells, including and especially dopaminergic neurons, mature by quantifying their number during early development. Additionally, the study aims to compare different midbrain areas and track neurodevelopmental changes across early development.

Methods

Monodelphis brains were collected at different developmental times points, brains were sliced, and brain sections processed following standard immunohistochemistry and other staining protocols to visualize different protein markers. ImageJ and Zen software were used to conduct area analysis and neuronal quantification. A modified stereological approach developed by our lab was utilized for precise neuronal quantification. A descriptive analysis was utilized to compare anatomical and neuronal numerical differences across different developmental stages. Inter-rater reliability was utilized to reduce bias during the neuronal quantification process.

Results

A preliminary analysis from a previous study (Perez et al., 2021) revealed anatomical differences in area and volume across three different stages, embryonic day 14 (area= 27260.36 µm, m= 381.376, V=81781.0735 um^3), postnatal day 1 (49917.28 µm, m= 404.12, V= 149751.827 µm^3), and postnatal day 6 (81866.66 µm, m=166.016, V= 245599.9853 µm^3). Neuronal and area differences from the stages of postnatal day 21, 30, 8 weeks and 23 weeks will be included once inter-rater reliability is established.



Conclusions

A preliminary analysis revealed that the *Monodelphis domestica* is a viable model for tracking neurodevelopmental changes. We expect an increase in dopaminergic neurons per area square/microns in the midbrain as the brain matures. We are currently conducting experiments to test the hypothesis that developmental changes in the brain are associated with changes in behavior. Multiple neuropsychiatric disorders have been linked to perturbations of the brain during early stages of development, therefore, neurodevelopmental research is critical for identifying the causative mechanisms of these conditions.

References

Blaess, S., & Ang, S. L. (2015). Genetic control of midbrain dopaminergic neuron development. Wiley interdisciplinary reviews. Developmental biology, 4(2), 113–134. https://doi.org/10.1002/wdev.169

Mate, K., Robinson, E., Pedersen, R., Vandeberg, J. (1994). Timetable of in vivo embryonic development in the grey short-tailed opossum (*Monodelphis domestica*). *Molecular Reproduction & Development, 39*(4), 365-374. https://doi.org/10.1002/mrd.1080390404

Perez, I., Vandeberg, J.L., PhD, & Gil, M. (2021, February). A Preliminary Timeline of the Midbrain Development in the Monodelphis Domestica Animal Model. Poster session presented UTRGV School of Medicine Research symposium, (Virtual).