Gamma-aminobutyric acid (GABA) Neurons and Perineuronal Nets (PNN) in the Monodelphis domestica and Relevance to Psychiatric Disorders

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Gamma-aminobutyric acid (GABA) Neurons and Perineuronal Nets (PNN) in the *Monodelphis domestica* and Relevance to Psychiatric Disorders

**Keywords**

Neurological Disorders, Epilepsy, Alzheimer's, GAD$_{67}$, Lectin, GABA, PNN

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**Brief Description**

The purpose of this study is to quantify and analyze the number and size of GABA neurons and Perineuronal Nets (PNNs) in the brain of the *Monodelphis domestica* using antibodies that target GAD$_{67}$ and Lectin.

**Abstract**

**Background/ Purpose**

Gamma-aminobutyric acid (GABA) is an amino acid that serves as the central nervous system's (CNS) main inhibitory neurotransmitter. By inhibiting nerve transmission, it works to lower neuronal excitability. Altered GABA levels have been associated with a variety of psychiatric disorders, for example Epilepsies, Parkinson's Disease, and Schizophrenia. Perineuronal nets (PNN) are extracellular molecules that are released by neurons and glial cells that modulate many neuronal and glial functions by encapsulating the inhibitory cells and neurites. Altered PNN levels serve as a potential trigger to synaptic imbalance. The purpose of this study is to quantify and analyze the presence, change in number, and area difference of GAD$_{67}$ and Lectin in the brain of the *Monodelphis domestica*.
Methods

4 Monodelphis domestica were transcardially perfused with 4% paraformaldehyde and sliced at a thickness of 35 µm. Antibodies for Glutamic acid decarboxylase (GAD$_{67}$) and Lectin were used to identify GABAergic neurons and PNNs, respectively, following the ABC-DAB method of immunohistochemistry. The criteria for identifying GAD-positive neurons and PNNs include presence of a dark brown reaction within the perikaryal cytoplasm. Using Image J software and stereological methods, midbrain sections targeting the Superior Colliculus sensory and motor, Substantia Nigra, and Ventral Tegmental Area were used to compare the number of GABA cells and PNNs that were present. Moreover, a Kruskal-Wallis Test was used to determine whether there was a statistically significant difference between the medians of the brain regions in focus. In addition, the area of 10 neurons for the GAD$_{67}$ antibody and Lectin were measured and compared.

Results

GAD$_{67}$ antibody and Lectin were both used to identify GABAergic neurons and PNNs, respectively. GAD$_{67}$ neurons were smaller and had a less clearly defined cell body and nucleus than PNNs. The expression of GAD$_{67}$ neurons in the Superior Colliculus were also more dispersed but smaller in comparison to the PNNs with an average area of 0.0059 um$^2$ for GAD$_{67}$ neurons and 0.0198 um$^2$ for PNNs. Based on preliminary quantification of GAD$_{67}$ neurons, the number of GAD$_{67}$ neurons in the Superior Colliculus was significantly higher in animals under a visual stimulus while the number of GAD$_{67}$ neurons in the Substantia Nigra and Ventral Tegmental Area were significantly higher in animals with a social stimulus.

Conclusion

Our findings support the relevant literature regarding the way in which GAD$_{67}$ and PNNs are expressed. By assessing the change in number and area difference in various regions of the brain, our recent findings will contribute to the use of Monodelphis as a model for neurological illnesses. Furthermore, we plan to relate our findings between GABAergic neurons and PNNs to hypothesize a connection between neural morphometry and connectivity and establish a relationship (or lack of relationship) between them.