Miles Ingram

2015/11/2

Final Project Proposal

**Introduction**

The transport protein p11(S100A10) has been linked both to depression and addiction[[1]](#endnote-1) [[2]](#endnote-2)[[3]](#endnote-3). While its connection to depression has been suggested to be as a result of moving the 5-HT1b to the cell surface­­­­­­­­ 1, its mechanism of action in addiction is still somewhat unclear. However it has been shown that selectively eliminating p11 in D2 expressing medium spiny neurons (MSNs), but not in D1 expressing MSNs 2. Additionally prenatally stressed rats have been shown to have both higher nicotine CPP scores, but also an increase in D2 receptor mRNA[[4]](#endnote-4). Taken together this suggests that p11 may be acting upon D2 receptors in the Nac, though the exact mechanism is unclear. For this project I want to first model the expression of D2 receptors and firing of neurons in the Nac, and then model different ways p11 could be effecting D2 receptor expression and how that could effect firing rates. The ultimate goal would be to test these models against experimental data gathered at a later date.

**Methods**

I intend to run simulations in the program Neuron ([www.neuron.yale.edu](http://www.neuron.yale.edu) ). Neuron is an open source simulation environment designed specifically for simulating neurons. I will first simulate the firing and D2 expression levels of a Nac neuron, I will then introduce p11 as an element and simulate various effects p11 could be having. I will then attempt to categorize what effects on firing rates different actions of p11 are having. Hopefully I will be able to attempt to confirm one of these models at a later date.

**Expected Outcomes and Significance**

Based on the studies cited in the introduction, I suspect that p11 is likely reducing the numbers of D2 receptors at the cell surface. This project will provide me with a model to attempt to confirm in my keystone. If I can determine how p11 is working in addiction I would hope to move on to an animal model and search for pharmacological targets for the treatment of addiction.

References

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