The Affect of Wellbutrin on Dopamine Reuptake Transporters in Rodent Striatal Tissue

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Introduction

Neurotransmitter reuptake is an important process involved in keeping the body functioning properly, and disruption of reuptake can variably affect the body and brain. Dopamine (**Figure 1**), a neurotransmitter associated with movement and Parkinson's disease as well as sensations such as reward/punishment, sleep, and mood, mediates feelings of euphoria or depression depending on the heightened or lowered synaptic concentrations present, respectively. Drugs such as cocaine or bupropion (commonly known as Wellbutrin [**Figure 2**]) will produce an excess of dopamine in the synapse, by blocking reuptake transporters in the neuron thereby boosting signaling to post-synaptic cells. Wellbutrin, often used as an anti-depressant, supposedly boosts the concentration of dopamine to an average level in the synaptic gap by inhibiting the reuptake transporters. An *in vitro* study comparing reuptake velocities, in the presence and absence of bupropion, was performed in order to better understand the affects of bupropion on this transporter. A rotating disk electrode was used to measure electrochemical changes in rodent striatal tissue following sequential additions of Wellbutrin and dopamine. The changes in electrochemical signal were then converted to reuptake velocities through a sequence of data manipulations.

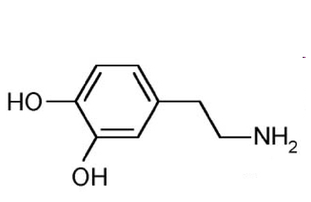

Figure 1. The structure of dopamine.

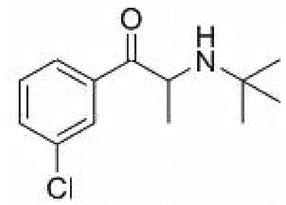

Figure 2. The structure of bupropion.

Methods

- Male Sprague-Dawley rats (300-500g) were rapidly decapitated and the brain dissected on ice
- Striata (**Figure 3**) were removed and chopped by hand with a razor blade, and washed eight times in 500 µL of fresh oxygenated buffer

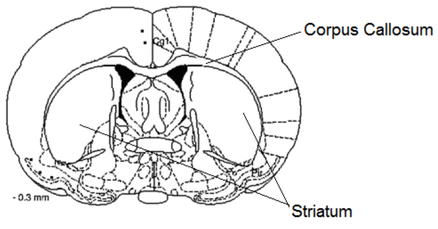

Figure 3. A coronal slice of a rodent brain, exposing the striatum, directly below the corpus callosum.

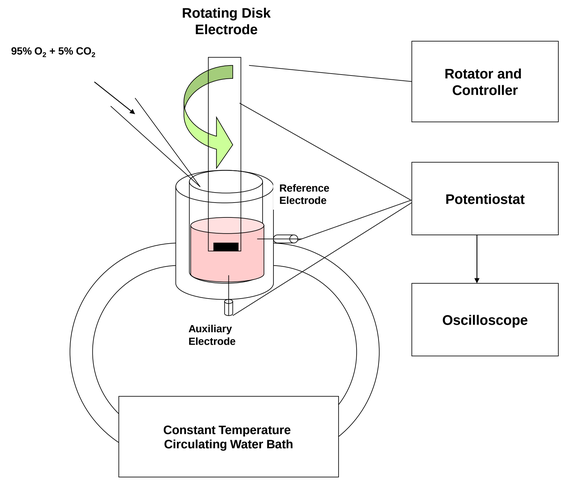

Figure 4. The setup of the rotating disk electrode with tissue in chamber.

- A glassy carbon rotating disk electrode (**Figure 4**) was then placed into the cell and rotation begun at 2,000 rpm
- The electrode was allowed to equilibrated to the tissue sample (Potentiostat set to 450 mV, and sample chamber heated to 37ºC with air flow set to 95% O_2, 5% CO_2)
- Inject dopamine or dopamine/bupropion solutions and analyze data by correcting the signal with the baseline
- Run regression statistics on concentrations to solve for initial velocity using the equation:

$$\mathrm{Re}uptakeVelocity = \frac{(TotalVolume)(Slope)}{MassofStriatum}$$

Results and Discussion

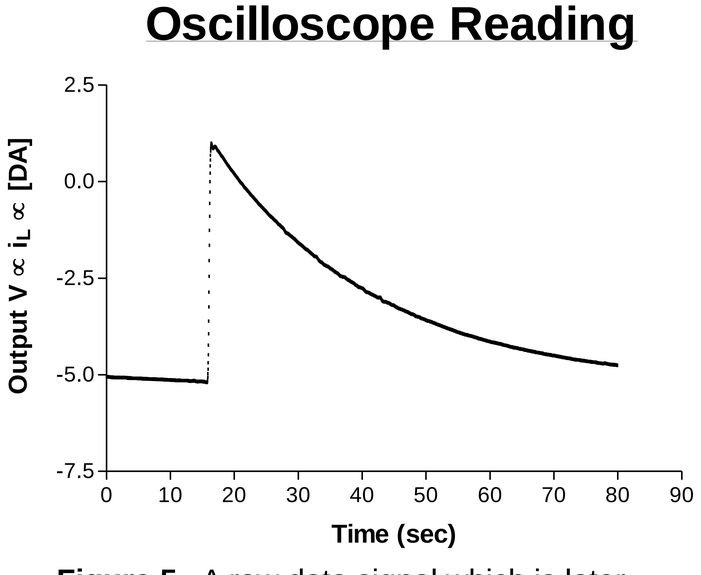

Figure 5. A raw data signal which is later converted to reuptake velocity using initial slope.

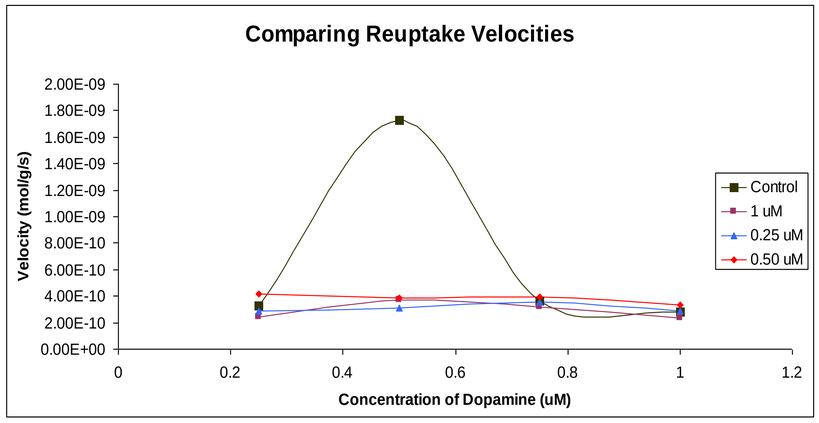

Figure 6. The plot of the concentration of dopamine added versus the calculated reuptake velocities.

- Wellbutrin showed an inhibitory affect on the striatum as hypothesized (**Figure 6**)
- The reuptake transporter showed the most inhibition from the 1 µM solution of Wellbutrin as expected
- The 0.50 µM solution of Wellbutrin showed the lowest degree of inhibition and actually expressed catalytic affects when compared to the control
- Compared to the control, the degree of inhibition provides evidence that non-competitive inhibition may be ruled out as a possibility (**Figure 7**)

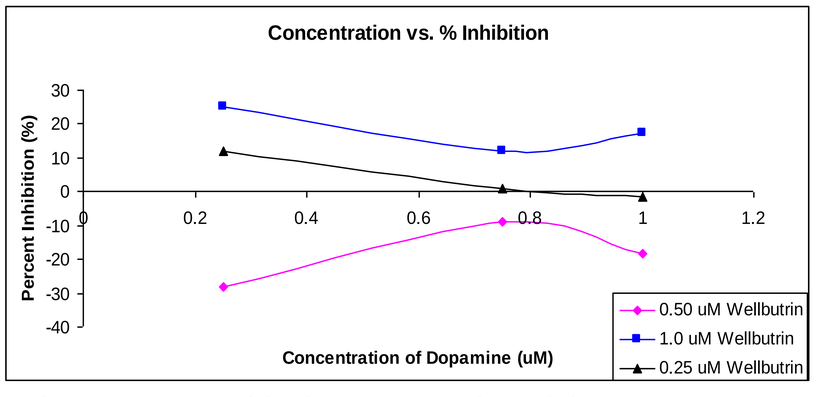

Figure 7. A graphical representation of the percent inhibition for each Wellbutrin concentration. The 0.50 µM dopamine concentration was omitted due to the presence of a constant value despite the differing concentrations.

Future Directions

- Focus research on types of inhibition excluding non-competitive to better understand the mechanism of Wellbutrin binding
- Investigate the affects of known Wellbutrin metabolites, S,S-hydroxybupropion and threo-hydroxybupropion, on the reuptake transporters in comparison to the parent drug

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