Characterization of Dopamine Release in a Penicillin Model of Seizure

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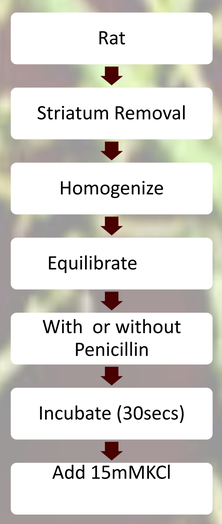
Introduction

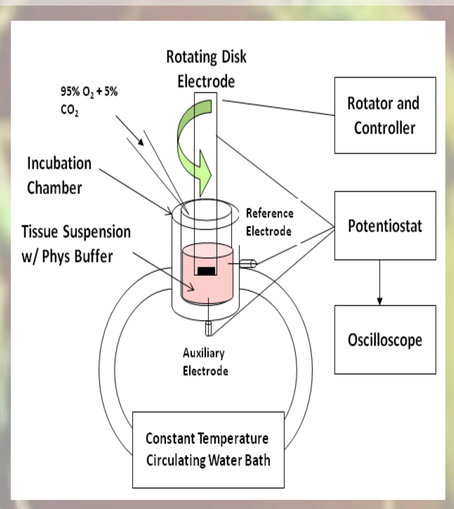
Neuronal seizures, as in epilepsy, are typified by random neuronal activity which produces interruptions in normal neuronal functioning. Effective treatments for preventing and/or recovering from a seizure require knowledge about the timing of neurotransmitter fluxes during seizures. Dopamine (DA) is a neurotransmitter that helps regulate movement and emotional responses. The work here is an attempt to characterize the neurotransmitter release in an experimental model of a seizure. This experimental model takes place in the striatum, an area of high DA density that mediates motoric activity in the brain which may be involved in physical manifestations of the seizure.

Penicillin G (PG) is a well studied seizure inducer that is known to block depressant action of Gamma Aminobutyric Acid (GABA) interneuron's and has been used in multiple studies to produce seizure activity. Although it is widely used, it has not been biochemically characterized. This study is composed of multiple in vitro PG induced seizures to monitor their DA release and reuptake readings in the striatum. Does PG cause DA release and/or affect the transporter activity? If so, is this because of the GABA and DA interactions? Also, does the RDE homogenate disrupt tissue and show direct PG and DA terminal effects?

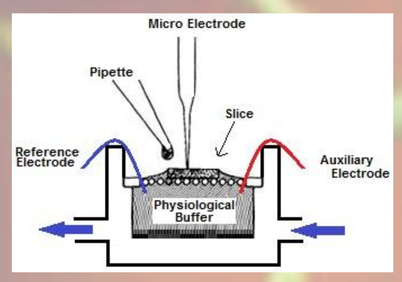
Methods

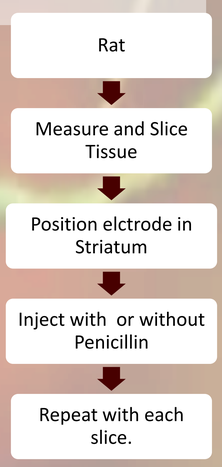
A Rotating Disk Electrode (RDE) is a measurement of hydrodynamic voltammetry of current vs. time across an electrochemical glassy carbon surface.



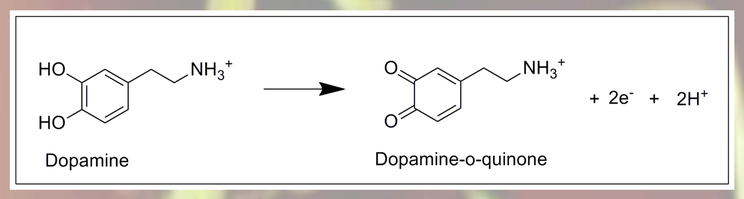


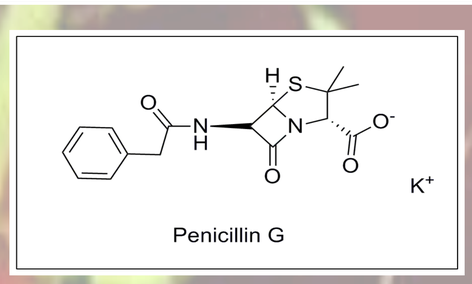
An In Vivo Electrochemistry (IVEC) measurement is a chronoamperometry measurement of current vs. time surrounding a carbon fiber. The PG was introduced in a mixture with the KCl control substance.



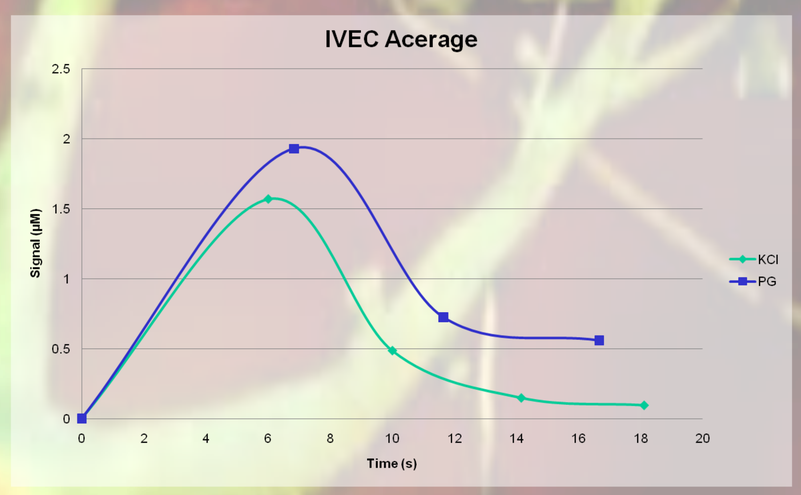


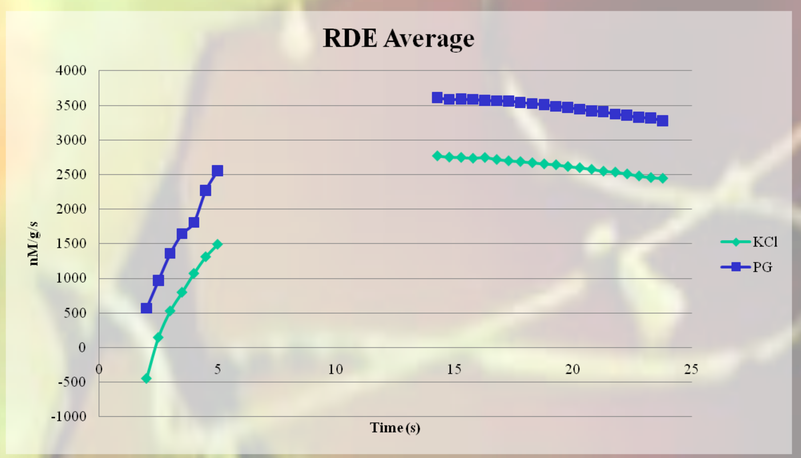
Molecules of Interest

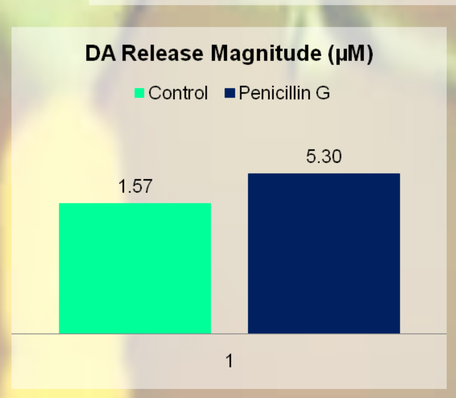


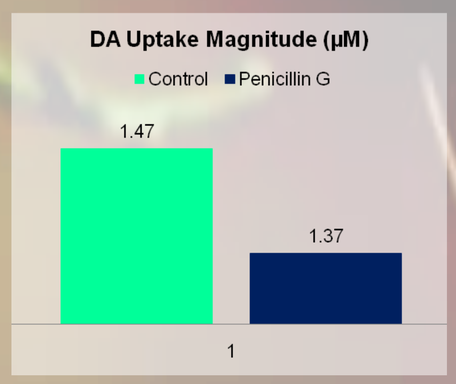


Results









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Results Summary

RDE results:
- Increases the magnitude of DA release.

IVEC results:
- Increases the magnitude of DA release.
- Decreases the magnitude of DA uptake.
- Decreases the velocity of DA release.
- Decreases the velocity of DA uptake.

In both methods, PG did interact with the DA and cause an increase in the DA release in the rat striatal tissue. In the RDE there was an increase of approximately 7/10 of a µmol/g of wet weight tissue.

Conclusions

Penicillin G does affect DA release and reuptake. Because DA controls motoric neuronal function, this explains the physical movement and actions that occur during a seizure.

Future Directions:

A wider range of Penicillin G concentrations will be used to do measures of seizure strength.

Measures will be taken for the position of each injection in the striatum.

To fully block the GABA interneurons interactivity with DA, bicuculline will be used as a antagonist to confirm the direct interaction of penicillin and DA interneurons.

Acknowledgements

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References

Adiguzel, Esat, Ilgaz Akdogan, S. Ender Duzcan, and A. Cevik Tufan. "Effect of Penicillin Induced Epilepsy Seizure on Granulare Cell Layer of Dentate Gyrus in Rat: a Stereological Study." *Neuroscience Research Communications* 31.2 (2002): 101-09. *Wiley Online Library*. Web. 7 June 2011. <http://http://onlinelibrary.wiley.com/doi/10.1002/nrc.10043/pdf>.

Canan, Sinan, Seyit Ankarali, and Cafer Marangoz. "Detailed Spectral Profile Analysis of Penicillin-induced Epileptiform Activity in Anesthetized Rats." *Epilepsy Research* 82.1 (2008): 7-14. *Science Direct*. Web. 7 June 2011. <http://http://www.sciencedirect.com/science/article/pii/S0920121108001721>.

Lockton, J., and O. Holmes. "Penicillin Epilepsy in the Rat: The Responses of Different Layers of the Cortex Cerebri." *Brain Research* 258.1 (1983): 79-89. *ScienceDirect*. Web. 6 June 2011. <http://http://www.sciencedirect.com/science/article/pii/0006899383912283>.

Stankiewicz, J. "Neurotoxicity of Penicillin: Effects of Repeated Systemic Injections on Convulsive and Nonconvulsive Epileptic Seizures in Rats." *Toxicology Letters* 78 (1995): 76. *Acta Neurobiologiae Experimentalis*. Web. 7 June 2011. <http://www.ane.pl/pdf/5532.pdf>.