Case Study 1

Question/Biological Problem

3,4-methylenedioxymethamphetamine (MDMA) — recognized by its street names: 'ecstasy,' or 'molly'— is an illegal recreational drug that is known to stimulate ecstatic emotional responses and in some cases cause hallucinations. When MDMA is consumed by a user, the empathogen breaks apart into nonpolar molecules, diffuses into the bloodstream and finally travels to the different regions of the brain. Ecstasy then binds to serotonin/dopamine transporters, which prevents the neurotransmitters from attaching to transporters that lead to the terminals. Additionally, serotonin/dopamine can actually be brought back from the terminals and into the synaptic space; this causes a large amount of these neurotransmitters to stay in the synaptic cleft and therefore alter the brain chemistry [2].

Aim: To build a model and study how repeated use of the recreational drug known as MDMA will lead to an eventual decrease in natural production of dopamine and serotonin in the neurons.

Research Model and Plan:

- iPSCs are chosen over primary neurons because iPSCs do not require invasive procedures to obtain the cells. In addition, we want to be able to study MDMA's long term effects on the neurons; therefore, primary cells are not ideal for the experiment since primary neurons have only a limited lifetime. Furthermore, primary cell cultures typically need to be extracted from the tissue of fetal and neonatal organisms and thus experiment would not achieve ideal results since our objective is to study the effects of MDMA on adult neurons [1].
- Adult somatic cells will be taken from the skin biopsy of healthy, consenting, patients with no history of MDMA use (control), and another set of cells will be taken from the skin biopsy of anonymous patients who report using MDMA regularly.
- The fibroblast cells will then be cultured *in vitro*, where pluripotency genes such as SOX2, Nanog, and Oct4 are introduced into the cells to create our neuronal iPSCs [3].
- With our patient specific neuronal iPSCs, we can now apply *in vitro* differentiation to analyze our targeted neurons (such as serotonergic neurons).
- We will then generate a small electrical impulse into the neurons and measure the amount of neurotransmitters (i.e. serotonin) that is released from the neuron and compare the data between healthy neurons and neurons derived from frequent MDMA users.
- This experiment will allow us to understand whether or not long term constant use of MDMA will decrease the amount of natural production of serotonin and dopamine in our neurons and eventually lead to more research on the drug's potential impact on neuronal survival.

Works Cited

[1] Carter, Matt, and Jennifer Shieh. “Chapter 14- Cell Culture Techniques.” *Guide to Research Techniques in Neuroscience (Second Edition)*, 2015, www-sciencedirect-com.proxy1.library.jhu.edu/science/article/pii/B9780128005118000149?via%3Dihub.

[2] NIDA. “The Neurobiology of Ecstasy.” *National Institute of Drug Abuse*, Jan. 2007, d14rmgtrwzf5a.cloudfront.net/sites/default/files/1920-the-neurobiology-of-ecstasy-mdma.pdf.

[3] Seymour, Tracy, et al. “Pluripotency Genes and Their Functions in the Normal and Aberrant Breast and Brain.” *International Journal of Molecular Sciences*, MDPI, 13 Nov. 2015, www.ncbi.nlm.nih.gov/pmc/articles/PMC4661882/.