Inquiro, the UAB undergraduate science research journal

Volume 2015 | Number 9 Article 18

2015

Experience in the Study of Dystonia

Aseel Dib

Experience in the Study of Dystonia

Aseel Dib

Department of Neurology, University of Alabama at Birmingham, Birmingham, AL, USA

In the spring of 2015, I had the wonderful opportunity to join the lab of Dr. David Standaert and participate in research involving dystonia, a mysterious movement disorder characterized by involuntary muscle contractions and tremors. My connection to the field of movement disorders stems from much more personal roots besides my interest in the underlying mechanisms of science. During my freshman year of high school, my father was diagnosed with Parkinson's Disease. I remember my confusion and personal struggle to understand the debilitating disease that had taken over my father's body. As I matured, my eagerness to be fully educated and understand the means underlying movement disorders grew along with me. My father has been participating in the Parkinson's Research study at UAB under Dr. David Standaert for a couple of years. After each appointment, my father would return with a stack of research articles explaining the latest findings of his disease that I would enjoy reading, amazed by the different terminology and techniques that I never knew existed. When time came around to find a research mentor, I had no hesitation in delving into studying movement disorders under a more fundamental level in the Standaert lab.

As it was my first time in a laboratory-based research setting, I was quite nervous and unfamiliar with many of the skills and techniques required. Nevertheless, thanks to the help of my mentor, I was trained to acquire all that I needed to know in order to be successful in the lab. Dystonia, which leads to abnormal postures or repetitive and slow movements, is one of the most common movement disorders in the US. What differentiates dystonia from Parkinson's Disease is that the combination of symptoms targets a wide range of ages, from infancy to late adulthood. Dystonia cannot be cured and may last either for a few years or throughout a lifetime. Depending upon the type of dystonia, symptoms may include foot cramps, rapid eye movements, muscle tremors, as well as some difficulty in speech. The cause for dystonia is still a mystery but it is suspected to stem from damage in the basal ganglia or other regions of the brain involved in motor control. Currently, there are no medications that can slow dystonia's progression or prevent it; however, there are a few treatments that can alleviate some of the symptoms, such as anticholinergic agents, dopaminergic agents, injections of botulinum toxin (Botox) within affected muscles, and deep brain stimulation. Dystonia is currently an active area of investigation, with new therapies continually being developed in the hope to find a better treatment.

My study focuses on DYT1 early onset torsion dystonia, which is a rare form of dominantly-inherited generalized dystonia, which affects most of the body. Specifically, I work with mice called DYT1 deltaGAG knock-in mice (DYT1 KI), which carry the same genetic anomaly as human DYT1 carriers. This mutation involves the *TOR1A* gene, which codes for torsinA. Studies in our lab and some others have found that there is an abnormality in neurotransmitter release within the striatum, a brain area involved in motor control. Specifically, dopamine release is reduced in these mice, while cholinergic function is elevated. Thus, DYT1 mice are studied to investigate whether these neurotransmitter systems can be modulated in order

to reverse the symptoms of dystonia. In the clinic, dystonia is usually treated with anticholinergic drugs. These nonselective muscarinic receptor antagonists, such as trihexyphenidyl and benztropine, function to block the receptors for the neurotransmitter acetylcholine. Anticholinergic drugs can be quite effective but come along with a number of side effects such as sleepiness.

Working in the Standaert lab, I have been able to test anticholinergic drugs, specifically trihexyphenidyl, on DYT1 KI mice in order to see how they affect both acetylcholine and dopamine levels in the brain. Our analysis focuses on the striatum because many patients with striatal defects develop dystonia and striatal direct brain stimulation is an effective therapy. The major technique we use to study neurotransmitter activity in the striatum is *in vivo* microdialysis, which involves the insertion of a probe into tissue in order to sample the extracellular cerebral fluid (ECF). This technique can be used to measure the amount of neurotransmitters in blood and tissue while infusing substances into the brain or spinal cord. Various samples at different phases through the period of *in vivo* microdialysis are taken and analyzed using high-pressure liquid chromatography (HPLC). HPLC allows us to quantify the concentrations of acetylcholine and dopamine in our ECF samples, thus providing the outcome measure for our tests of anticholinergic drugs. Although this study can be expanded, this approach gives me a starting point to achieving my future goals in finding effective treatments for dystonia.

During the last few months of my research experience, I have watched myself grow and have been astonished at the skills and information I have been able to learn. Specific skills my project has required include preparing tissue samples for analysis, performing behavioral tests, *in vivo* micro dialysis, genotyping using PCR, brain slicing, and many other "wet lab" techniques. I have also learned the importance of trial and error and how not every day in the laboratory will be a day of successful results. It is important to be patient when conducting research since there are various factors that can pose threats to the ideas we construct. For example, there have been numerous times in which the analysis of my data post microdialysis yields disappointingly low HPLC results.

Prior to experiencing what research really is, I had no idea about the amount of time and effort it really takes to conduct an experiment that can potentially be worthwhile. It has definitely been quite an exciting learning experience to acquire such advanced lab techniques and understand their use and contribution in science today. In addition, it is an honor to be surrounded by "cream of the crop" mentors and graduate students that have allowed me to feel comfortable as I work inside and outside of the lab. I am very excited to see the future growth and development of my project as I grow in the lab field in the remainder of my undergraduate career.