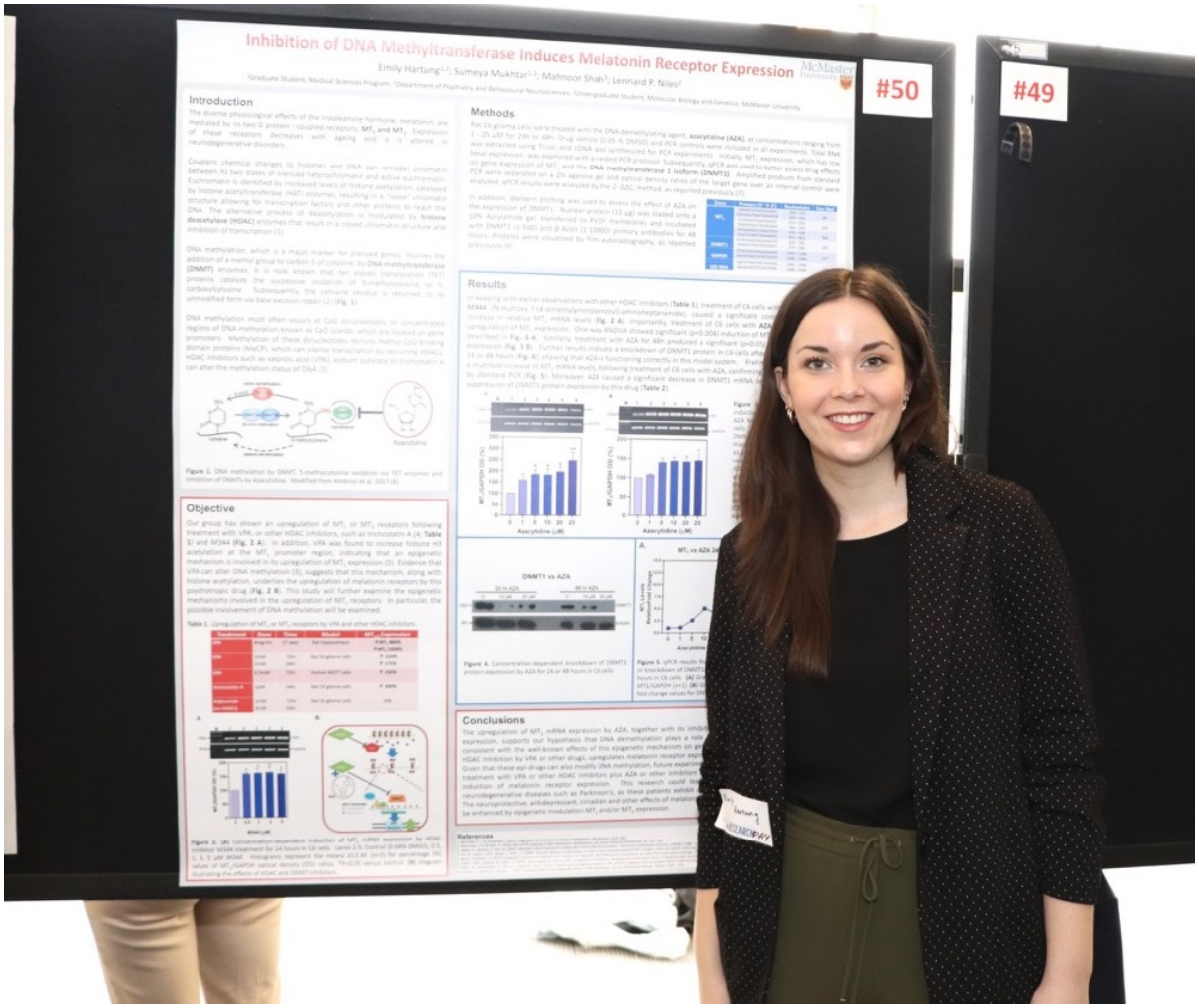
SPOTLIGHT ON RESEARCH

Research Day 2019 Top 3 Posters: Graduate – Non-Clinical



First place Research Day 2019 poster competition award winner:
Emily Hartung – Graduate (non-clinical) – supervisor: Lenard Niles

1st Place

Name: Emily Hartung

Supervisors: Dr. Lenard Niles

Education Program and Level: Medical Science MSc (2nd year)

About Emily:

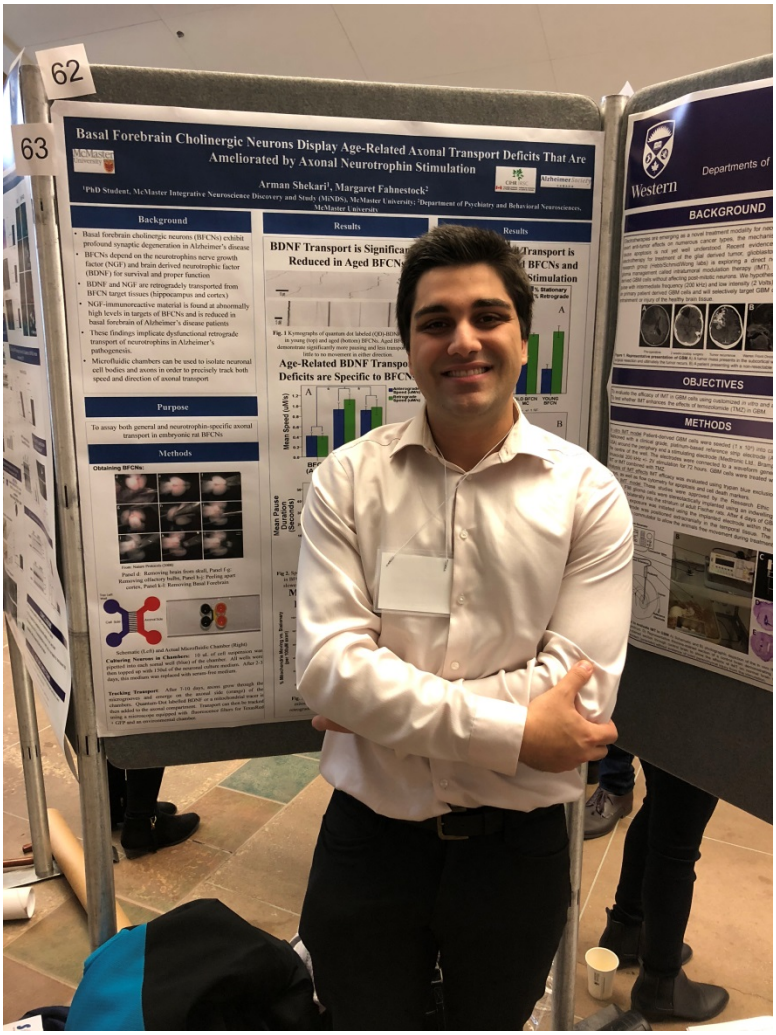
I am currently finishing my MSc thesis in Dr. Niles' Lab, and I have also completed a graduate certificate in Clinical Research. I plan on furthering my academic career by continuing my involvement in clinical research activities at McMaster, and in the future, I plan on pursuing clinical research coordination as a profession. I hope to continue to engage in opportunities to present fascinating research projects to my peers at McMaster at conferences and through publication.

Emily's Project:

The pineal gland secretes a hormone or chemical messenger called melatonin into the bloodstream. This hormone is involved in the regulation of circadian rhythms, sleep, and numerous other physiological activities. Notably, melatonin has protective effects on neurons or brain cells to help keep them alive and functioning properly. These neuroprotective effects involve the antioxidant actions of melatonin and its modulation of beneficial neurotrophic factors. The multiple physiological effects of melatonin are initiated by its binding to specific proteins called receptors.

Important to this study is the concept of epigenetics, which involves heritable changes in gene activity, without changes in the DNA sequence. These changes include the addition of chemical tags to DNA and its protein partners, termed histones, which maintain the wound-up structure of DNA, called chromatin. Active chromatin is identified by increased levels of acetyl groups or tags on histone proteins, resulting in a "loose" chromatin structure, with DNA more accessible to other proteins, which initiate gene activity or transcription. The process of making DNA accessible, is mediated by histone acetyltransferase, which transfers acetyl groups or tags to histones. Conversely, histone deacetylase proteins remove acetyl groups, and this results in a closed chromatin structure and inhibition of gene activity. Another key epigenetic mechanism of interest to this study is DNA methylation, which is a major marker for non-active or silenced genes. It involves the addition of a methyl tag to DNA by another protein called DNA methyltransferase.

Drugs or other agents, which alter the acetylation or methylation pattern of histones and/or DNA, can have profound effects on gene function and physiology. Our group has shown increased levels of melatonin receptors following treatment with such epigenetic drugs, including the anticonvulsant and mood stabilizer, valproic acid (VPA), and trichostatin A (TSA), in cultured cells and in the rat brain. Both VPA and TSA increase histone acetylation and this mechanism is thought to underlie their ability to upregulate the expression or levels of melatonin receptors. Importantly, since these drugs can also alter DNA methylation, the possible involvement of this second major epigenetic mechanism in the upregulation of melatonin receptor expression was examined. Rat brain-derived glioma cells were treated with azacytidine (AZA), which inhibits the methylation of DNA, due to suppression of DNA methyltransferase. Therefore, in addition to examining melatonin receptor levels following AZA treatment, DNA methyltransferase levels were assessed to confirm the action of AZA. Treatment of the cells with AZA caused a significant increase in melatonin receptor expression. Conversely, as expected, AZA suppressed or abolished DNA methyltransferase protein levels. These results show that DNA demethylation plays a role in the regulation of melatonin receptors, consistent with the well-known effects of this epigenetic mechanism on gene transcription. The levels of melatonin decrease with aging, while its receptors in the human brain exhibit changes in neurodegenerative and psychiatric disorders including Parkinson's, Alzheimer's and depression. Understanding the mechanisms underlying the regulation of melatonin receptors, could provide avenues for enhancing the neuroprotective and other benefits of this hormone.



2nd Place

Name: Arman Shekari

Supervisor: Dr. Margaret Fahnestock

Education Program and Level: Neuroscience Graduate Program, PhD Stream

About Arman:

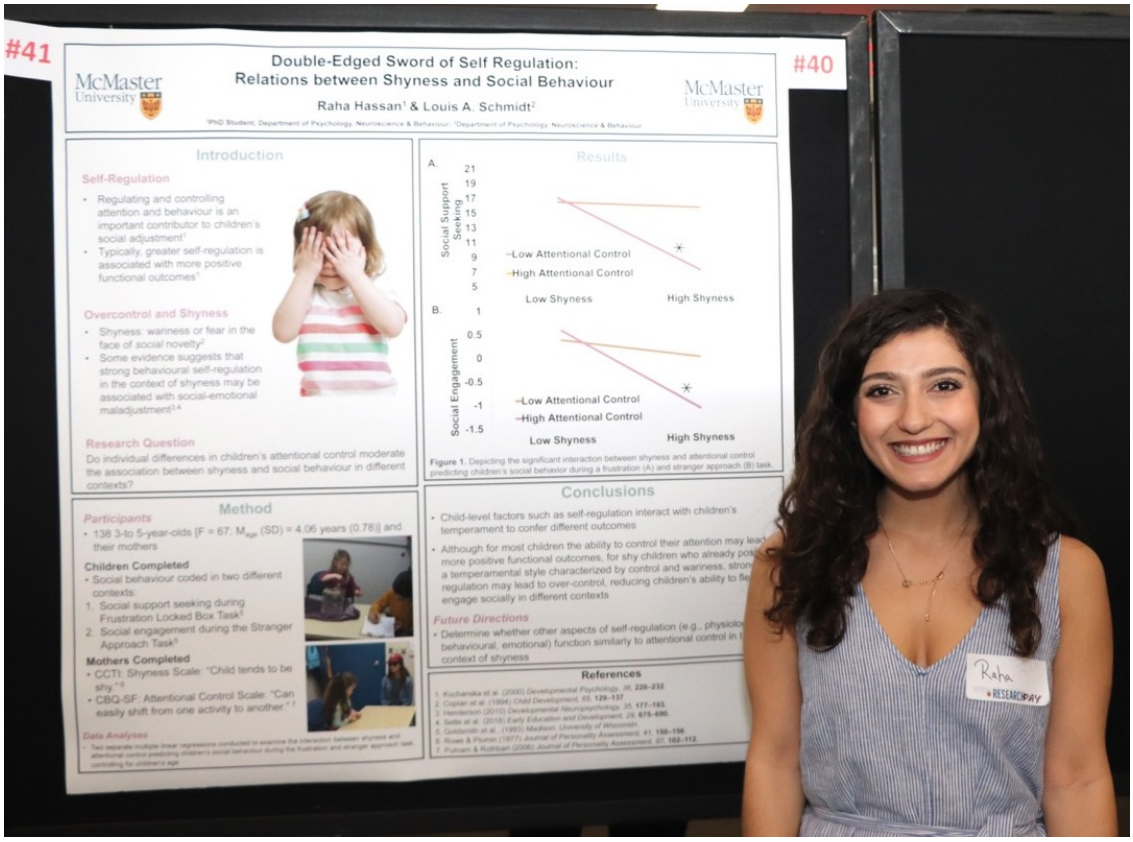
I am a PhD student heading into my 3rd year of study in the Neuroscience graduate program. My project has really made me fall in love with the research process and I hope to pursue post-doctoral studies upon my graduation in hopes of becoming a principal investigator.

Arman's Project:

I study the basal forebrain in the context of Alzheimer's Disease. The basal forebrain is a brain area critical for learning and memory and is one of the first areas affected in Alzheimer's Disease. Basal forebrain neurons are unique because they do not produce their own neurotrophic factors, proteins that neurons need to survive and thrive. To account for this, basal forebrain neurons transport neurotrophins from the other neurons they connect with via a process termed "retrograde axonal transport". The basal forebrain is like a small island that needs to import supplies from other countries. There is evidence that this transport process becomes defective in Alzheimer's Disease.

My project involves characterizing these transport problems in the basal forebrain and understanding why they happen in the first place. To do this, I grow basal rodent basal forebrain neurons in small devices designed specifically to study axonal transport called “microfluidic chambers”. These chambers act like a cellular stencil and organize axons linearly so we can track transport easily. Our lab labels neurotrophins with very bright dyes called “quantum dots” in order to track the transport of neurotrophins in these cells in real time. We can then manipulate the neurons and probe for transport disruptions.

In my poster, I’ve presented results that demonstrate that the transport of 2 neurotrophic factors, brain derived neurotrophic factor and nerve growth factor, becomes defective with age in basal forebrain neurons. Our lab focuses on age-related changes in these neurons because the single largest risk factor for developing Alzheimer ’s disease is age. Our lab is now focused on determining exactly why this transport is disrupted in an age-related manner in these neurons.



3rd Place

Name: Raha Hassan

Supervisor: Dr. Louis Schmidt

Education Program and Level: PhD 1, Psychology (RCT) McMaster

About Raha:

I am a 1st year PhD student under the supervision of Dr. Louis Schmidt. My research interests are centered around the relation between children's self-regulation (physiological and behavioral) and their temperament. With respect to my clinical work, I am currently a second year practicum student at the Anxiety Treatment and Research Centre at St. Josephs West 5th Campus, delivering supervised cognitive behavioral individual and group therapy treatments to adults with anxiety disorders. In the future I hope to marry my research and clinical interests by practicing the scientist-practitioner model, and contributing to our understanding of how dysregulation early on contributes to the development and maintenance of anxiety disorders throughout the lifespan.

Raha's Project:

The ability to regulate and control one's behaviour and attention has been regarded as an important contributor towards children's social and functional adjustment, with greater self-regulation associated with more positive adjustment. However, using behavioural and neurophysiological correlates of self-regulation, some researchers have found that shyness is associated with social-emotional maladjustment in children with strong attentional and behavioural self-regulation.

The goal of the present study was to determine whether individual differences in children's attentional focusing influenced the association between shyness and social behaviour across multiple contexts in preschool aged children.

Children's shyness and attentional control were maternally reported Children's social behaviour was coded during a frustration and stranger approach task. During the frustration task, children were precluded from playing with a desirable toy. The amount of time children spent asking the experimenter for help was operationalized as social support seeking. During a stranger approach task, a novel adult approached and attempted to engage the child. The number of times the child spoke and the inverse of expressed bodily fear was operationalized as social engagement.

There was a significant interaction between shyness and attentional control predicting children's social support seeking during a frustrating task and children's social engagement during a stranger approach task. For children with high attentional control, shyness was negatively associated with social support seeking during a frustrating task, and children's social engagement and fear during a stranger approach task. For children with low attentional control, shyness was not associated with children's social behaviour during a frustrating and stranger approach task.

These results fit within the larger body of literature suggesting that child-level factors such as self-regulation interact with children's temperament to confer different outcomes. Although for most children the ability to control their attention may lead to more positive functional outcomes, for shy children who already possess a temperamental style characterized by control and wariness, strong self-regulation may lead to over-control, and further reduce children's ability to flexibly engage socially in different contexts.