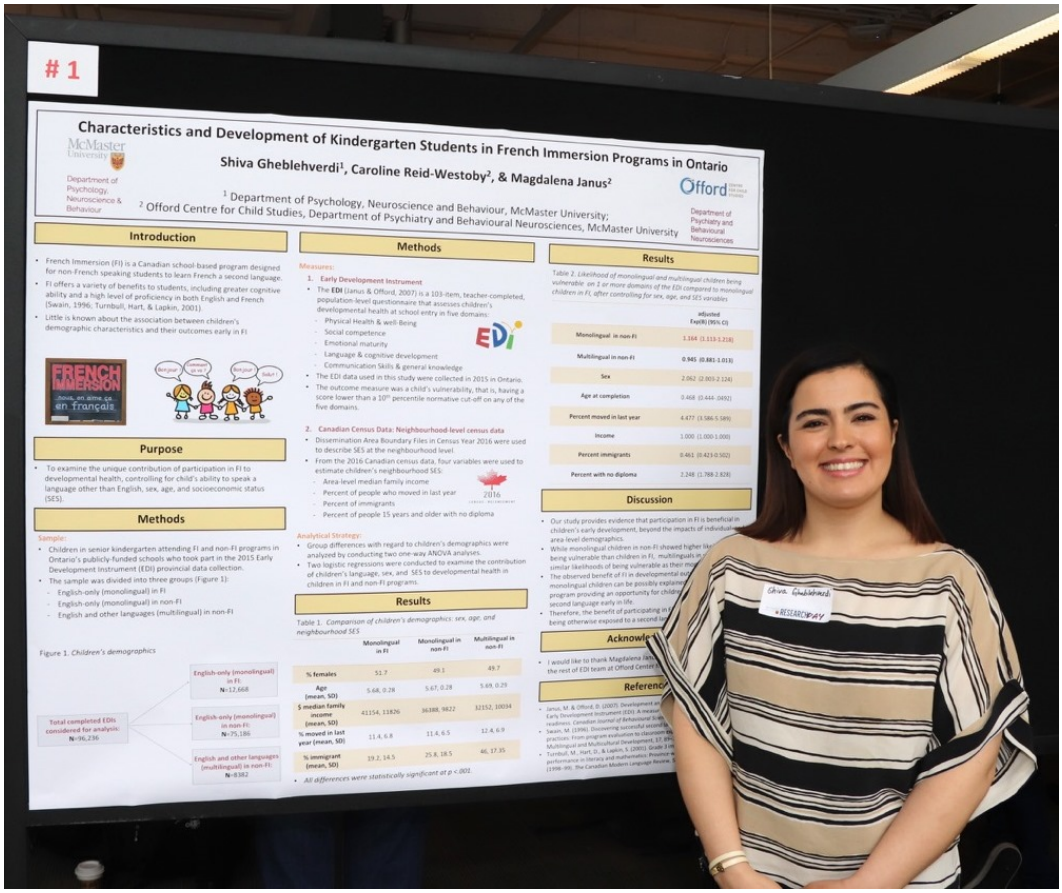
SPOTLIGHT ON RESEARCH

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



First place Research Day 2019 poster competition award winner:
Shiva Gheblehverdi – Undergraduate (non-clinical) – supervisor: Magdalena Janus

1st Place

Name: Shiva Gheblehverdi

Supervisors: Dr. Magdalena Janus

Education Program and Level: Psychology, Neuroscience, and Behaviour (PNB), Level 4

About Shiva:

I am currently completing my undergraduate studies in the Psychology, Neuroscience and Behaviour program at McMaster University. I am planning to continue my education in the domain of psychology and human development. I am particularly interested in working with children as well as conducting research focusing on inclusion, special education, and child development.

Shiva's Project:

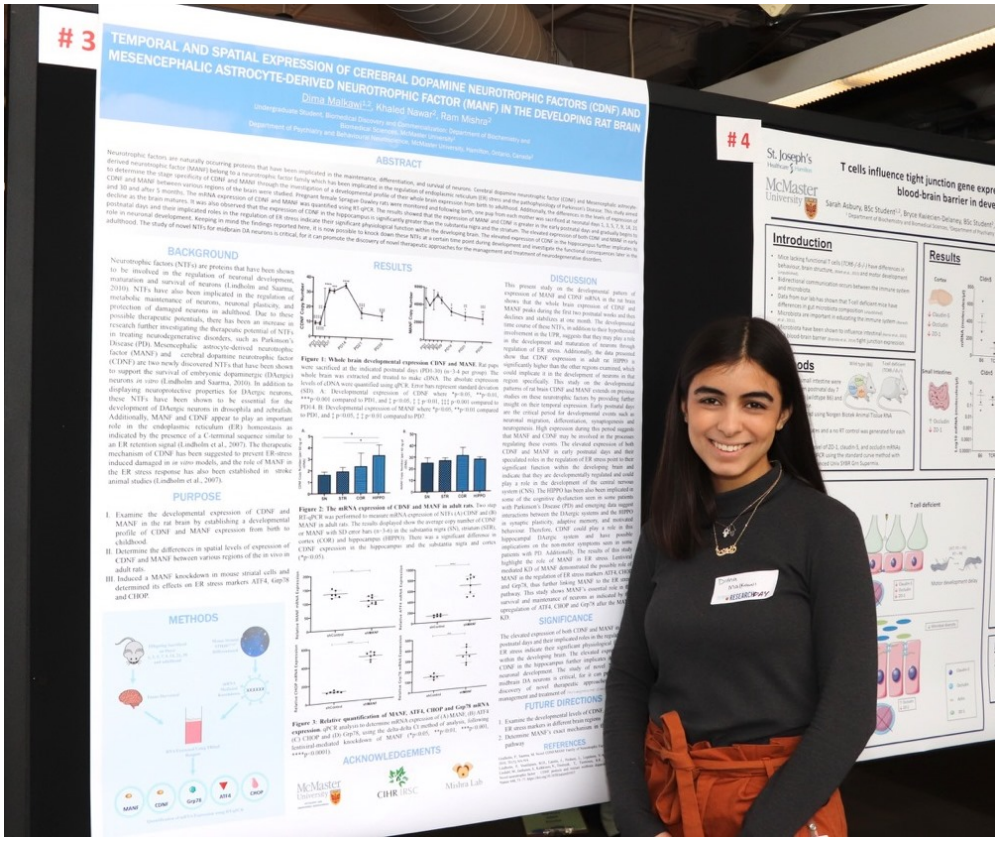
French Immersion (FI) is a program in English-language schools where children are taught in French. The program is designed for non-French speaking students to give them an opportunity to learn French as a second language. In elementary schools, at least 50 percent of the instruction in FI is in French.

A great deal of research has shown that FI programs enable students to develop various skills and that children in FI programs do better in school compared to those in non-FI programs. However, it is uncertain whether FI truly offers an advantage to children or whether child- and family-related factors (e.g. their age, sex, income) have a greater influence on their success in FI programs.

Our study explored the characteristics of kindergarten students in FI programs in Ontario by using data from the Early Development Instrument (EDI) and the 2016 Canadian Census. The EDI is a questionnaire completed by kindergarten teachers which measures children's ability to meet age-appropriate developmental expectations at school entry. The EDI measures children's behaviours and abilities in five main areas of development: physical health and well-being, social competence, emotional maturity, language and cognitive development, and communication skills and general knowledge.

In our study, we examined differences in children's development between those attending FI and non-FI programs in Senior Kindergarten. To gain a better understanding of the effects of the program, we compared the development of children in FI who only spoke English to two other groups of children: children attending non-FI programs who only spoke English and those in non-FI programs who spoke English and another language. We also took into account children's age, sex, and the socioeconomic status of the neighbourhood where they lived, as these factors can influence children's development. The way we examined children's development was by looking at whether children were vulnerable (scoring below a specified threshold) in at least one of the five areas of their development.

We found that participation in FI was associated with children's early development even when the effects of child- and family-related characteristics were taken into account. Children in FI were less likely to be vulnerable in at least one area of their development compared to children speaking English -only attending non-FI programs. Children in FI did not differ from the children who spoke more than one language attending non-FI programs. The observed benefit of FI in the early development of children speaking English-only could potentially be explained by the program's goal of providing children with the opportunity of learning a second language. In other words, the observed benefit of participating in FI appears to be due to being exposed to a second language early in life. Our findings suggest that early exposure to a second language, including participation in FI programs, could be advantageous to children's development and education.



2nd Place (tied)

Name: Dima Malkawi

Supervisor: Dr. Ram Mishra

Education Program and Level: Biomedical Discovery and Commercialization, Level 4

About Dima:

I recently graduated with an Honors Bachelor of Health Sciences from the Biomedical Discovery and Commercialization program. This fall, I will be entering medical school where I hope to continue contributing to research being done on neuropsychiatric and neurodegenerative diseases. Outside of lab and school, I am extremely passionate about volunteering and giving back to my community. Currently, I am heavily involved in helping refugees resettle in Canada through various initiatives.

Dima's Project:

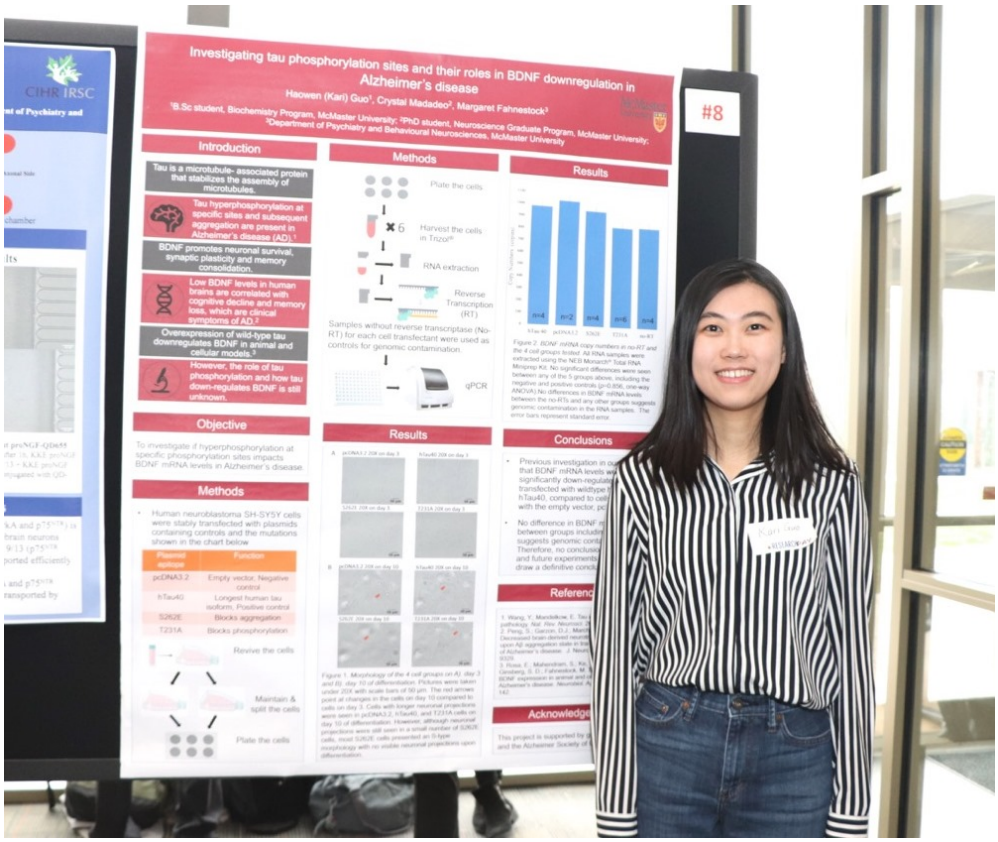
Neurotrophic factors are naturally occurring proteins that have been implicated in the maintenance, differentiation, and survival of neurons[1]. Cerebral dopamine neurotrophic factor (CDNF) and Mesencephalic astrocyte-derived neurotrophic factor (MANF) belong to a recently discovered neurotrophic factor family which has been implicated in supporting survival and protection of midbrain dopaminergic neurons. The degeneration of these neurons has been implicated in Parkinson's Disease

(PD). These neurotrophic factors have also been implicated in the regulation of endoplasmic reticulum (ER) stress. The ER is an organelle involved in the proper folding and processing of translated proteins. Prolonged ER stress can ultimately lead to cell death. A defense mechanism known as the unfolded protein response (UPR) functions to counteract the ER stress induced cell death.

The purpose of this study is to determine the stage specificity of these neurotrophic factors through the investigation of a developmental profile of the whole brain expression of CDNF and MANF from birth to adulthood, as well as to investigate the differences in the levels of expression of CDNF and MANF between various regions of the brain were studied. Additionally, the study aimed to consider the effect of a MANF knockdown on ER stress in a cell model in order to further elucidate the role of MANF in its mechanism.

The results showed that the expression of MANF and CDNF is greater in the early postnatal days and gradually begin to decline as the brain matures. It was also observed that the expression of CDNF in the hippocampus is significantly greater than the substantia nigra and the striatum. A knockdown of MANF demonstrated its possible role in the regulation of ER stress markers ATF4, CHOP and Grp78, thus further linking it to the ER stress pathway.

The elevated expression of both CDNF and MANF in early postnatal days and their implicated roles in the regulation of ER stress indicate their significant physiological function within the developing brain. The elevated expression of CDNF in the hippocampus further implicates its role in neuronal development. Keeping in mind the findings reported here, it is now possible to knock down these NTFs at a certain time point during development and investigate the functional consequences later in the adulthood. CDNF and MANF knockdown studies can reveal their functions early in development and moreover, it can help elucidate their mechanism of action. The study of novel NTFs for midbrain DA neurons is critical, for it can promote the discovery of novel therapeutic approaches for the management and treatment of neurodegenerative disorders. This study also demonstrated MANF's essential role in the survival and maintenance of neurons as indicated by the upregulation of ATF4, CHOP and Grp78 after the MANF knockdown.



2nd Place (tied)

Name: Haowen (Kari) Guo

Supervisor: Dr. Margaret Fahnestock

Education Program and Level: Honours Biochemistry, Level III

About Haowen:

I am a third-year biochemistry student who is currently working in Fahnestock lab to study the impact of phosphorylation of tau on BDNF levels in Alzheimer's disease. In the lab, I primarily work with cells and use qRT-PCR to quantify BDNF mRNA levels. I started my journey in research in the summer of second year by getting accepted to an internship at Fudan University. I then joined Dr. Fahnestock's lab and worked closely with the lab team members to further develop my research skills and advance my knowledge in neurobiology. I am excited to continue my work in the Fahnestock lab next school year to complete my undergraduate thesis. Beyond undergraduate studies, I wish to enroll in a MD or MD/PhD program and pursue a career in medicine and neurobiology.

Haowen's Project:

Alzheimer's disease (AD) and other forms of dementia affect millions of people around the globe. Clinically, AD is characterized by memory loss and cognitive decline. The neuropathology of AD includes the presence of neurofibrillary tangles consisting of abnormally hyperphosphorylated and aggregated tau proteins. Tau proteins are microtubule-associated proteins that stabilizes the assembly of

microtubules which are important in the regulation of cell division, stability, transport and shape of neurons.

Brain-derived neurotrophic factor (BDNF) is a neurotrophin that promotes neuronal survival, synaptic plasticity, learning and memory consolidation. Low BDNF levels in human brains are shown to be correlated with cognitive decline and memory loss. Additionally, previous research has found that over-expression of tau proteins down-regulates BDNF messenger RNA. However, whether hyperphosphorylated or aggregated tau leads to neurotrophin dysregulation still remains unclear.

Therefore, in this project, we investigated whether abnormal hyperphosphorylation of tau at specific phosphorylation sites implicated in AD, Serine 262 (S262) and Threonine 231 (T231), is responsible for BDNF down-regulation *in vitro.* Mutation at S262 to glutamate prevents tau aggregation, while mutation at T231 to alanine hinders hyperphosphorylation. We hypothesize that hyperphosphorylation and aggregation at S262 and/or T231 lead to BDNF down-regulation and blocking abnormal phosphorylation at these sites can prevent BDNF down-regulation.

In this project, SH-SY5Y human neuroblastoma cells were stably transfected with plasmids containing S262E and T231A mutations. SH-SY5Ycells stably transfected with the empty vector, pcDNA3.2 and with plasmids overexpressing unmutated human tau, were used as controls. Cells were revived, maintained and then differentiated with retinoic acid. RNA was then extracted from the cells and reverse transcribed. Real-time PCR was used to quantify BDNF mRNA levels. However, due to genomic DNA contamination seen in the RNA samples, future experiments must be conducted to draw a definitive conclusion. If hyperphosphorylation and aggregation of tau at these sites indeed lead to BDNF down-regulation, drugs can be developed to arrest hyperphosphorylation and aggregation at these sites and prevent BDNF down-regulation. Therefore, if the hypothesis is not rejected, this project can provide an insight to improve cognitive functions and prevent further memory loss in AD patients.