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2025 NeuGeneration Case Competition: Psychoneuroimmunology

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Abstract
The NeuGeneration Case Competition is an annual research case competition organized by students in the NeuGeneration Club at Queen's University. Held during our 10th annual neuroscience conference on January 25th and 26th, 2025, at Queen's Biosciences Complex, the competition aims to provide undergraduate students with valuable research experience and networking opportunities in the field of neuroscience. Undergraduate students in teams of 2-5 were given a month to prepare an abstract and an oral presentation on a novel research question within the theme of Psychoneuroimmunology. This booklet showcases the abstracts of the top 7 teams. We hope you enjoy exploring the proposals and we encourage you to be on the lookout for next year's case competition through our Instagram (@q_neugeneration).

Keywords: neugeneration case competition; neuroscience; psychoneuroimmunology; immunology; psychology; neuroinflammation; case competition; neugeneration

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Conference Abstracts
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NeuGeneration Abstracts

Anti-NMDA Receptor Autoimmune Encephalitis: Exploring PROTACs as a Novel Treatment Approach

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Anti-N-methyl-d-aspartate receptor (Anti-NMDAR) encephalitis is a progressive autoimmune disorder characterized by the antibody-mediated internalization and reduction of NMDA receptor density, resulting in symptoms that range from headache to psychosis. Anti-NMDAR encephalitis is the most common form of autoimmune encephalitis, often triggered by ovarian teratomas and viral infections. Current treatments, including tumour resection and immunosuppression, lack specificity, highlighting the need for targeted approaches. Previous studies have identified the role of proteolysis targeting chimeras (PROTACs) in degrading pathogenic proteins. Anti-NMDAR encephalitis is titer-dependent and reversible through the degradation of antibodies in the cerebrospinal fluid (CSF). This study will evaluate the potential of PROTACs to degrade anti-NMDAR antibodies and restore NMDA receptor density as a therapeutic approach for anti-NMDAR encephalitis. Anti-NMDAR encephalitis will be induced in Wistar rats (n=30) through intraventricular injection of human anti-NMDAR IgG1 antibodies and confirmed by indirect immunofluorescence of CSF until antibody titers reach 10%. PROTACs will be designed with a specific antibody-binding domain linked to an E3 ubiquitin ligase recruitment moiety. Rats will be randomized into three groups: intravenous PROTAC, intraventricular PROTAC, and intravenous saline (control). Dosing will occur following baseline measurements of CSF antibody levels via immunofluorescence and receptor density via positron emission tomography (PET) scan. Tests will be repeated 6, 24, and 48 hours post PROTAC administration. PROTAC-treated rats are anticipated to exhibit anti-NMDAR antibody CSF levels of <10% and increased NMDA receptor density compared to the control. The utilization of PROTACs to reduce anti-NMDAR antibody levels would revolutionize treatment for antibody-mediated autoimmune disease.

Investigating the Effects of Microaggressions on the Gut Microbiome in University Students of Colour

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Microaggressions, subtle actions or comments reflecting prejudice against marginalized groups, are a recognized source of chronic stress. Studies have shown heightened stress levels adversely affect the gut microbiota by increasing gut permeability, promoting harmful bacteria growth due to inflammation, and reducing microbial diversity. Specifically, decreased Prevotella bacteria levels have been linked to lower T-cell activity and short-chain fatty acid production, both involved in combating stress-induced inflammation. While previous research has examined microaggressions' effects on mental health, their impact on human gut microbiomes remains underexplored. Our study seeks to investigate this relationship by recruiting 50-60 self-identified minority students from 10-20 Canadian universities. Participants will complete a pre-screening questionnaire covering lifestyle habits, socioeconomic status, gender, and age, alongside an initial stool sample to establish baseline gut microbiome composition. Respondents with extreme dietary patterns, recent antibiotic/supplement use, and diagnosed gastrointestinal or autoimmune diseases will be excluded. Over 12-17 weeks, participants will submit bi-weekly stool samples for RNA sequencing and Prevotella level analysis using qPCR. Daily questionnaires via a mobile app, based on the Racial Microaggressions Scale (RMAS), will track microaggressions' frequency and impact. A matched-pair study design and linear mixed-effects model will control for lifestyle and demographic variables for accurate result analysis. We anticipate that frequent exposure to microaggressions will correlate with decreased Prevotella levels. These findings could illuminate the impact of racism on the gut health of minorities, inspiring healthcare providers to offer more personalized and supportive care.

Regulatory T Cells in Modulating GABA Signaling and Neuroinflammation: Therapeutic Insights for Stiff Person Syndrome

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Stiff Person Syndrome (SPS) is an autoimmune disorder that causes autoimmune attacks on the enzyme glutamic acid decarboxylase (GAD), reducing the inhibitory neurotransmitter Gamma- Aminobutyric Acid (GABA) levels, leading to neuronal excitability and hence muscle spasms. Research shows that regulatory T cells (Tregs) suppress immune responses, however the potential to modulate GABAergic pathways remains unexplored. This study investigates the role of Tregs in stabilizing GABAergic signaling, hypothesizing that Tregs reduce inflammation and microglial activation, thus reinforcing the GABAergic pathway. We will conduct 3 trials using 16 mice models of autoimmune neuroinflammation (EAE) per trial, with 8 mice receiving the Treg-enhancing agent IL-2 via intraperitoneal injections to increase Treg levels, and 8 mice staying as is (control). The mice's neuronal tissues will be analyzed with transmission electron microscopy after 12 hours of IL-2 injection and compared to the control groups for microglial activation markers. Neuronal excitability will be assessed via patch-clamp electrophysiology. We anticipate that the Treg enhancement will reduce microglial activation and upregulate GABA receptor expression, restoring neuronal function and reducing neuroinflammation in the experimental group, indicating that Treg enhancement can decrease neuronal excitability in SPS patients via IL-2 injections. By linking Tregs, microglial activity, and GABAergic pathways, our findings may discover novel therapies for SPS to ultimately decrease muscle spasms in patients. However, further research with larger sample sizes is required to evaluate the potential of Treg-based therapies for restoring GABAergic signaling in SPS and other similar autoimmune disorders.

Proinflammatory Cytokine Responses in Contamination-Based OCD: A Virtual Reality Study

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Contamination-based obsessive-compulsive disorder (OCD) involves fears of coming into contact with germs or disease, and using cleaning behaviours to decrease perceived threats. The immune system responds to visual exposure of disease-related cues through increased production of proinflammatory cytokines (IL-6 and IL-1β), even in the absence of actual pathogens. A relationship has been found between heightened proinflammatory cytokines and OCD, yet no studies have compared immune responses in contamination-based OCD with other OCD subtypes. The present study will examine whether visual exposure to contamination cues elicit stronger proinflammatory cytokine responses in those with contamination-based OCD compared to other OCD subtypes. The study will also investigate whether individuals with contamination- based OCD exhibit heightened proinflammatory cytokine responses to contamination cues compared to other fear-inducing stimuli. Participants with contamination-based OCD (n=100) and other OCD subtypes (n=100) will be randomly assigned to a virtual reality condition. Condition one involves an environment with contaminated stimuli, and condition two contains general fear-inducing stimuli. Saliva samples will be collected through swabs, prior to and after task engagement, to measure how IL-6 and IL-1β levels change in response to threats. It is anticipated that individuals with contamination-based OCD will have higher increases in IL-6 and IL-1β towards contamination cues than other OCD subtypes. Inflammatory responses to contamination triggers are also predicted to be greater than responses to fear-inducing stimuli for individuals with contamination-based OCD. This research will provide insight into the physiological mechanisms underlying contamination-based OCD and whether this subtype has a greater risk of developing autoimmune disorders.

The Replacement of Nanoparticles by Plant-Derived Extracellular Vesicles in Trifluoperazine to Reduce Neurotoxicity

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Nanoparticles have emerged as promising vehicles for targeted drug delivery, offering advantages such as enhanced bioavailability, controlled release, and reduced side effects. However, concerns about their neurotoxic effects have driven interest in alternate drug delivery methods. Plant-derived extracellular vesicles (PDEVs) are naturally occurring nanoparticles with the ability to encapsulate and transport bioactive compounds. The biocompatibility and sustainability of these vesicles

present opportunities to address the drawbacks of conventional nanoparticles. Although the exploration of PDEVs in medicine is ongoing, their use in the transport of pharmaceutical agents offers a promising pathway for improving therapeutic efficacy and reducing neurotoxicity. Our study hypothesizes that PDEVs can replace synthetic nanoparticles in the delivery of Trifluoperazine, in order to reduce neurotoxic effects while maintaining efficacy. 20 mice of the C57BL/6 strain will be randomly assigned to treatment and control groups. The treatment group will receive Trifluoperazine encapsulated in PDEVs, while the control group will receive Trifluoperazine via traditional nanoparticles. A Functional Observational Battery behavioral screening procedure will be conducted over a four-week period to assess neurotoxicity; focusing on motor and sensory functions. Additionally, biochemical analyses will be performed to assess biomarkers such as oxidative stress and glial activation. All procedures will adhere to CCAC guidelines. We anticipate that drugs with a PDEV-based delivery system will demonstrate reduced levels of neurotoxicity compared to those with a nanoparticle-based system. Upon further testing, these findings would support the feasibility of PDEVs as a safer alternative for drug delivery, with broader implications for reducing toxicity among pharmaceutical treatments.

Exploring the Therapeutic Potential of Transcutaneous Vagus Nerve Stimulation in ALS - Related Inflammation and Depression

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by progressive motor neuron loss and muscle control impairment. Chronic inflammation, driven by elevated cytokines, exacerbates ALS symptoms, while stress and depression amplify this inflammatory response, creating a self-perpetuating cycle. Transcutaneous vagus nerve stimulation (tVNS) is a non-invasive method shown to reduce inflammation in other conditions, but remains unexplored in ALS and comorbid depression. This study investigates tVNS's therapeutic potential in mitigating the positive feedback loop between ALS, depression, and inflammation. Fifty adults (18+), diagnosed with ALS and comorbid depression, will be randomly allocated to the treatment or control group in a double-blind study. tVNS will be delivered via Ag/AgCl electrodes on the left ear twice daily for thirty minutes, five days per week, for twelve weeks, starting at 1 mA, with current adjusted based on participant tolerability. Treatment groups will receive stimulation at the left inner tragus, targeting vagal afferents, while control groups will receive stimulation at the left posterior earlobe, a site with minimal vagal innervation. Cytokine levels (IL-1β, TNF-α, IL-6) will be quantified through RT-qPCR. Depression and ALS symptoms will be measured at baseline, post-treatment, and six months post-intervention, using the ALS Functional Rating Scale-Revised and American Psychological Association's Severity Measure for Depression. Data will be analyzed using a two-way mixed ANOVA. We anticipate reduced cytokine levels and improved ALS & depression symptoms in the treatment group compared to controls. These findings have potential to holistically enhance quality of life for ALS patients, alleviating physical and psychological burdens.

Development of a Public-Access Database of Salivary Inflammatory Biomarkers in Populations with mTBI

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Mild traumatic brain injury (mTBI) significantly impacts Canadian public health, with 1.6% of individuals over 12yrs reporting concussions in 2019, and 33% experiencing multiple incidents; mTBI is associated with various physical/cognitive consequences. The lack of standardized diagnostic criteria and objective testing methods limits accurate clinical assessment. While research has identified potential salivary biomarkers, including S100B and UCHL-1, their diagnostic utility is constrained by insufficient disease-specificity and an incomplete understanding of mTBI's inflammatory cascade. This longitudinal, multicentre study aims to collect a representative sample of salivary inflammatory biomarker data from multiple phases post-mTBI. We anticipate identifying significant differences between mTBI patients and controls. Participants will include individuals with mTBI, and orthopaedic (OC) and healthy (HC) controls, with admission on a rolling basis from participating trauma/sports medicine centres (target: n=1000). Salivary samples will be collected at three phases following trauma (acute (within 24h), sub-acute (1wk), chronic (2mon.)) alongside cognitive screenings (PHQ-9, GAD-7, ACE). Samples will be analysed via mass-spectroscopy for the presence of inflammatory/neural injury biomarkers (interleukins, TNF-α, S100B, etc.,) to identify distinct trends amongst cohorts and injury phases. As an exploratory secondary outcome, correlations between overall well-being and inflammatory status will be investigated. Unique biomarker signatures are expected to be identified at each temporal phase of mTBI. More narrowly-focused studies have reported distinct serum/saliva

concentrations of select biomarkers between controls and mTBI. This database will provide a comprehensive understanding of the unique inflammatory environment of mTBI, supporting the creation of more specific, non-invasive mTBI diagnostic and prognostication tools.

Conflicts of Interest

The authors declare that they have no conflicts of interests.

Authors' Contributions

ED: Led organization of the 2025 NeuGeneration Case Competition, served on the planning committee for the 2025 NeuGeneration Conference, assisted authors with their abstract submissions, reviewed the abstract submissions and ensured that they adhered to correct formatting standards, drafted the conference abstract booklet, and gave final approval of the version to be published.
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Case Competition
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