2020
Rotman Research
Institute Conference

Aging &
Brain Health

Mental Health and Well-being

Featuring the 2nd Annual What's Next Canada Innovation Day

# ABSTRACTS

# Virtual Conference Talks

# Virtual Session 1: Lifelong and Intergenerational Impacts of Trauma

## Hosted by Dr. Brian Levine

### KEYNOTE: Transgenerational impact of genocide – what do we know? Mental health of genocide survivors' offspring

Dr. Jutta Lindert
University of Applied Sciences Emden Leer, Germany, and Brandeis University, USA

The health of those who survived genocides in the 20th century, and especially the Holocaust, has stimulated a wealth of research on psychopathology that has documented a wide variety of immediate or late-onset psychopathological symptoms and disorders. The psychopathological disorders include post-traumatic stress disorder, depression and anxiety, but the potential health impact is not restricted to these disorders. Controversies still exist regarding the transgenerational impact of genocides on survivors, perpetrators and bystanders offspring mental health and mental disorders. However, despite important scientific advances in understanding the transgenerational impact of genocides on mental health and psychopathologies, this impact is still understudied. We recognize that, tragically, there have been many atrocities and crimes against humanity committed in the 20th and 21st centuries. However, genocide is a crime against humanity characterized by the intent to annihilate a group defined by presumed group characteristics, such as ethnicity, religion or class. We choose genocide as the trauma exposure as it differs from other crimes against humanity in that it is both a crime against a group, defined on the basis of group identity and against its individual members. Following the official genocide definition of 1948, the killing of Armenians by Turkey (1915-1917), the Holocaust (1939-1945), and the mass atrocities committed in Cambodia (1975-1979), former Yugoslavia (1992-1995), and Rwanda (1994) were defined as genocides. Each of these genocides has particular characteristics that may have a transgenerational impact on the health of survivors' offspring.

The aim of this talk is to provide a guide to some of the most important studies and systematically review and evaluate findings from the studies on the mental consequences of genocides. Therefore, I will provide a review on qualitative and quantitative studies investigating the transgenerational impact of genocide on mental health. First, I will give an overview of the results of qualitative studies on the impact of genocide. Second, for the assessment of quantitative studies, I will systematically review studies from electronic databases that used an observational quantitative study design and included: (i) exposure to genocide; (ii) mental health outcomes; (iii) validated instruments; and (iv) statistical tests of associations. Third, the quality of the selected studies will be investigated using a quality assessment tool for genocide studies. The results vary widely across studies. Data from the high quality studies with random sampling methods suggest that there are few statistically significant differences in the psychopathology of survivors offspring compared to non-survivors. These differences may reflect various factors, including the particular characteristics of the genocides and the subsequent experiences of those studied, related both to the genocide and to demographic, socioeconomic and other factors such as life events and relationships. Life events and relationships after the genocide may be important to consider to fully understand the transgenerational impact of genocides on survivors, perpetrators and bystanders offspring. There is an urgent need to study genocide survivors' offspring assessing and evaluation the transgenerational impact in different groups.

**Lindert, J.**, et al. (2019) The long-term health consequences of genocide: developing GESQUQ - a genocide studies checklist. *Conflict and Health, 13*, 14.

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**Lindert J**, Knobler HY, Kawachi I, Bain PA, Abramowitz MZ, McKee C, Reinharz S, McKee M. (2017). Psychopathology of children of genocide survivors: a systematic review on the impact of genocide on their children`s psychopathology from five countries. International Journal of Epidemiology, 46, 246-257.

## Full catastrophe aging: the impact of perceived stress on cognitive aging and the importance of stress management

Dr. Alexandra J. Fiocco
Ryerson University, Canada

Perceived stress is an insidious phenomenon which may be experienced across the lifespan, including later adulthood. Contrary to the coveted post-retirement golden years, older adults may be faced with a number of challenging experiences including role transitions, financial strain, loss of loved ones, and medical illness. Over four decades of research have progressively elucidated the harmful effects that persistent perceived stress may have on brain health and the aging process. While activation of stress-sensitive systems, including the sympathetic-adrenal-medullary (SAM) axis and the hypothalamic-pituitary-adrenal (HPA) axis, is adaptive in the short run, prolonged activation of stress sensitive systems may have maladaptive health outcomes. According to the allostatic load model, chronic activation of SAM and HPA axes may result in secondary outcomes, including dysregulation of cardiovascular, metabolic, and immune function, which then lead to tertiary outcomes, including cognitive impairment. Dr. Fiocco will present an overview of the research outlining mechanisms by which perceived stress and stress hormone exposure may influence neural structures that are implicated in executive functioning, learning, and memory. Individual difference factors, including personality and genetic polymorphism, will also be highlighted in accordance with the stress-diathesis model. Finally, Dr. Fiocco will present on lifestyle behaviors that may modulate the impact of stress on healthy aging.

## The threatful self: disrupted functional connectivity between the periaqueductal gray and the default mode network in posttraumatic stress disorder

Dr. Ruth Lanius
Western University, London, Canada

Trauma can have a profound impact on the sense of self, frequently leaving a lasting imprint on both the cognitive and somatic domains of the sense of self. Cognitively, traumatized individuals often remain tortured by thoughts that reflect intensely negative core beliefs about themselves. Such thoughts can include “I will never be able to feel normal emotions again,” “I feel like an object, not like a person,” “I don’t know myself anymore,” and “I have permanently changed for the worse.” Traumatized individuals also frequently report somatically based alterations in self-experience, including feelings of disembodiment and related identity disturbance, demonstrated by reports like “I feel dead inside,” “I feel as if I am outside my body,” or “I feel like my body does not belong to me.” Recent provocative neurobiological findings in PTSD are beginning to shed light on self-disturbance in traumatized individuals both during resting state and under conditions of threat. Results are demonstrating that the brain network that underlies self-experience, the default mode network (DMN), is most intact under states of threat. Specifically, the periaqueductal grey (PAG), a brain region critical to autonomic

regulation and defensive responses, appears to directly influence the function of large-scale neurocognitive networks, in particular the DMN, under conditions of threat. These findings are consistent with reports suggesting that individuals with PTSD frequently report that their trauma has become a part of their identity, which may be mediated, in part, by DMN-related alterations. Clinically, these results may underlie disturbances in self-related processes, including symptoms of disrupted social cognition, autobiographical memory, depersonalization/derealization, and deficits in making self-/other- distinctions frequently observed in individuals with PTSD.

**Indigenous Mental Health: Historical Trauma as AlterNative Psy-ence**

Dr. Joseph P. Gone
Harvard University, USA

In the early part of my career, I explored depression and problem drinking among my own people on the Fort Belknap Indian reservation in Montana, USA. There I met a middle-aged cultural traditionalist named Traveling Thunder who explained to me why many community members struggled with substance abuse and associated distress. In his view, the primary problem was that, "We never was happy living like a Whiteman." As it turned out, this straightforward observation captured an entire explanatory rationale about reservation mental health that reappears everywhere I go in "Indian Country." Specifically, Traveling Thunder highlighted history and spirituality in his account of the emergence of reservation mental health problems, overtly attributing these forms of disabling distress to processes of Euro-American colonization. This problem frame overtly recasts "mental disorders" as (post)colonial pathologies under the designation *historical trauma*. Importantly, historical trauma anchors an entire alternate and parallel indigenous discourse concerning "mental health." This alter-Native psy-ence not only invokes coloniality as the etiology for indigenous dis-order, but also posits distinctive approaches to treatment, outcome, and evaluation. In this presentation, I will unpack this alter-Native indigenous psy-ence and trace the implications for mental health research, policy, and practice.

**Gone, J. P.** (2016). Alternative knowledges and the future of community psychology: Provocations from an American Indian healing tradition. *American Journal of Community Psychology*, *58*, 314-321.

**Gone, J. P.**, & Calf Looking, P. E. (2015). The Blackfeet Indian culture camp: Auditioning an alternative indigenous treatment for substance use disorders. *Psychological Services*, *12*, 83-91.

**Gone, J. P.** (2013). Redressing First Nations historical trauma: Theorizing mechanisms for indigenous culture as mental health treatment. *Transcultural Psychiatry*, *50*, 683-706.

**Gone, J. P.** (2012). Indigenous traditional knowledge and substance abuse treatment outcomes: The problem of efficacy evaluation. *American Journal of Drug and Alcohol Abuse*, *38*, 493-497.

**Gone, J. P.**, & Trimble, J. E. (2012). American Indian and Alaska Native mental health: Diverse perspectives on enduring disparities. *Annual Review of Clinical Psychology*, *8*, 131-160.

**Gone, J. P.** (2009). A community-based treatment for Native American historical trauma: Prospects for evidence-based practice. *Journal of Consulting and Clinical Psychology*, *77*, 751-762.

**Gone, J. P.** (2007). "We never was happy living like a Whiteman": Mental health disparities and the postcolonial predicament in American Indian communities. *American Journal of Community Psychology*, *40*, 290-300

## Virtual Session 2: Mood and Cognition as Transdiagnostic Markers of Brain Health

### Hosted by Dr. Brian Levine

**KEYNOTE: Metabolism and inflammation in mood disorders, and novel treatment options informed by new literature**

Dr. Roger S. McIntyre
University of Toronto, Mood Disorders Psychopharmacology Unit, Brain and Cognition Discovery Foundation (BCDF), Toronto, Canada

Mood disorders are the most common and disabling conditions across Canada and globally. The disease models regarding mood disorders have been substantially refined and it's now recognized that alterations in brain metabolism and neuroinflammatory processes are playing a critical role in the disease pathogenesis. Alterations in metabolism and inflammation are particularly relevant to disturbances in general cognitive systems, as well as reward-based systems which represent key symptoms/domain dimensions in adults with mood disorders. This presentation will review extant evidence regarding cognitive impairment and reward disturbances and synthesize the new literature from our lab regarding disturbances in metabolism and inflammation. The presentation will also discuss how this novel information is changing or informing novel treatments for adults with mood disturbances.

**Prevalence of neuropsychiatric symptoms across the cognitive spectrum and their impact on future cognitive decline**

Dr. Linda Mah
Rotman Research Institute, Baycrest, Division of Geriatric Psychiatry, University of Toronto, Canada

What is the clinical significance of neuropsychiatric symptoms (NPS) such as depression and apathy in older adults with cognitive impairment? Older adults with memory and other cognitive complaints frequently present with comorbid NPS that range from alterations in sleep, appetite, mood, and motor behaviour, to development of agitation and psychosis in more cognitively impaired individuals. The 2018 National Institute on Aging and Alzheimer's Association (NIA-AA)'s Research Framework conceptualizes NPS as "commonly coexisting and may be a prominent part of the presentation" of Alzheimer's disease (AD). However, there is growing evidence that NPS are core features of neurodegenerative cognitive syndromes that may serve as prognostic indicators of outcome. This talk will provide an up-to-date review of the clinical relevance of NPS in the context of cognitive impairment by reviewing the prevalence of NPS across the cognitive spectrum, from subjective cognitive decline (SCD) and mild cognitive impairment (MCI) to AD, discussing emerging evidence linking specific NPS with biomarkers of AD and their impact on future cognitive decline and disease progression, and finally, highlighting the efficacy of pharmacologic, non-pharmacologic, and neuromodulatory interventions on specific NPS, with emphasis on recent findings.

**Impact of early-life adversity on brain development and suicide risk**

Dr. Gustavo Turecki
Department of Psychiatry, McGill University, Douglas Institute, CIUSSS ODIM, Montreal, QC Canada

Suicide is a complex behaviour that frequently associates with a history of early-life adversity. Dr. Turecki will discuss how adversity during childhood may differentially regulate molecular processes in the brain and increase lifetime risk of suicide. He will present data from his laboratory suggesting that specific biological pathways are regulated by the early-life environment through diverse epigenetic processes, which may contribute to suicide risk by differentially adjusting behavioural trait and emotional development, as well as influencing cognitive function. A conceptual framework to understand suicide risk among individuals exposed to early-life adversity will be presented.

## Virtual Session 3: Living Well in Older Age

### Hosted by Dr. Cheryl Grady

**KEYNOTE: "Living well" with dementia: well-being among people with dementia and family carers**

Dr. Linda Clare
University of Exeter, UK

There are currently over half a million Canadians living with dementia, and in 10 years' time the figure will be nearer one million. Worldwide, around 50 million people currently have dementia, and by 2030 the figure will reach 75 million. Alongside research into risk reduction and disease-modifying treatments, therefore, research on how to optimize well-being for people living with and affected by the condition is an urgent priority. In this presentation I will focus on the well-being of people with mild- to moderate dementia living in the community, and the family members and friends who provide vital unpaid support (here termed "family carers").

Experiencing an optimal level of well-being, encapsulated in the concept of "living well" with a long-term condition such as dementia, reflects a subjective sense of "comfort, function, and contentment with life." Well-being can be defined as a state of equilibrium or balance of positive and negative emotions. Other indices of "living well" are life satisfaction – individuals' global evaluations of satisfaction with their current life – and quality of life – individuals' perceptions of their position in life in the context of the relevant culture and value systems, and in relation to their goals, expectations, standards and concerns. All these aspects of subjective experience are affected by life events, stressors and challenges, of which developing and living with dementia is a prime example. As with other long-term, progressive conditions, it is helpful to think of this challenge in terms of living with and managing disability, where key rehabilitative goals are optimizing functioning and well-being at any given stage.

I will present a theoretically derived framework as a basis for examining influences on "living well" for people affected by dementia. In this framework the potential for living well with dementia is influenced by, and reflects the balance between, the unique set of resources that each person brings to the situation and the particular challenges faced. Using this framework, I will explore evidence about psychological, social and environmental factors associated with well-being for people with dementia and carers, and emerging evidence about reciprocal influences on well-being within caregiving dyads (person with dementia + carer). Recent evidence will be drawn in particular from the Improving the experience of Dementia and Enhancing Active Life (IDEAL) program, a longitudinal cohort study of people with dementia and carers throughout Great Britain.

The value of better understanding factors associated with well-being lies in the potential for using this information to identify ways of enhancing the ability to "live well" for those affected by dementia. Building on concepts of rehabilitation, this can be tackled from two directions. A community perspective focuses on dismantling barriers to inclusion and social participation, while a personal perspective focuses on supporting functioning and participation in daily life. I will describe examples of initiatives and interventions from each of these perspectives that are aligned with evidence about factors associated with well-being, making reference where possible to recommendations on psychosocial interventions in CCCDTD5 and the English NICE Guideline, and consider future directions for research and practice.

Clare, L., et al. (2014). Improving the experience of dementia and enhancing active life – living well with dementia: study protocol for the IDEAL study. *Health and Quality of Life Outcomes.* 12:164. DOI: 10.1186/s12955- 014-0164-6

Clare, L. (2017). Rehabilitation for people living with dementia: a practical framework of positive support. *PLOS Medicine, 14*, e1002245

Martyr, A., et al. (2018). Living well with dementia: a systematic review and correlational meta-analysis of factors associated with quality of life, well-being and life satisfaction in people with dementia. *Psychological Medicine, 48,* 2130-2139.

Clare, L., et al., on behalf of the IDEAL study team. (2019). A comprehensive model of factors associated with subjective perceptions of living well with dementia: findings from the IDEAL study. *Alzheimer Disease and Associated Disorders, 33,* 36-41.

Clare, L., et al., on behalf of the IDEAL study team. (2019). A comprehensive model of factors associated with capability to 'live well' for family caregivers of people living with mild-to-moderate dementia: findings from the IDEAL study. *Alzheimer Disease and Associated Disorders, 33,* 29-35.

Clare, L., et al. (2019). Individual goal-oriented cognitive rehabilitation to improve everyday functioning for people with early- stage dementia: a multi-centre randomised controlled trial (the GREAT trial). *International Journal of Geriatric Psychiatry, 34,* 709-721.

**The arousal hub region in the aging brain**

Dr. Mara Mather
Leonard Davis School of Gerontology, University of Southern California, USA

Current evidence suggests that, during the course of aging, the sympathetic arousal system becomes more tonically active. In the brain, a small nucleus in the brainstem called the locus coeruleus plays a key role in inducing and maintaining sympathetic arousal. When activated, locus coeruleus neurons release norepinephrine in cortical and subcortical regions throughout much of the brain to modulate physiology and cognition. Its neurons have extensive projections and tend to release norepinephrine at varicosities along their axons rather than at a synapse. This broad and non-specific brain coverage makes it ideal to serve as a broadcast system that alerts the brain when something critical is happening and additional resources may be needed. However, this brain region has also been identified as the site of early Alzheimer's tau pathology that emerges in most people by their 20's and spreads from there to medial temporal brain regions. In my talk, I will discuss the importance of this brain region's structural integrity for maintaining cognitive function during aging and how compensatory mechanisms dealing with diminished function may lead to hyperactive sympathetic activity among older adults. In particular, the cognitive consequences may be increased distractibility, especially during arousing situations.

**The self in dementia**

Dr. Donna Rose Addis
Rotman Research Institute, Baycrest, Canada

The self is dynamic; an individual's sense of identity develops and changes immensely over a lifetime. Nevertheless, most individuals have a deep sense that they remain the same person despite these changes and that their self persists over time – a fundamental belief known as diachronic unity. In this talk, I will present a model of how different forms of autobiographical memory support diachronic unity. I will draw on findings from our recent study of the self in Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI) showing a complex relationship between autobiographical memory and diachronic unity, as well as a dissociation between strong subjective beliefs of self-persistence and explanations about one's persistence over time.

**Precarity in late life: rethinking dementia as a "frailed" old age**

Dr. Amanda Grenier
Rotman Research Institute, Baycrest, University of Toronto, Canada

This paper analyses the extent to which frailty and dementia are better understood in the context of new forms of insecurity affecting the life course. Approaches to ageing that are organized around productivity, success and active late life have contributed to views of dementia as an unsuccessful, failed or "frailed" old age. Operating through dominant frameworks, socio-cultural constructs and organizational practices, the "frailties" of the body and mind are often used to mark the boundaries of health and illness in late life, and shape responses accordingly. Our concern is that whether taken for granted or "imagined," ideas that couple dementia and frailty can marginalize persons who occupy the locations of dementia and disablement. In this paper, we draw on the concept of "precarity" to reconsider debates, and shift interpretations of the "fourth age" away from age- or stage-based thinking into a recognition of the shared vulnerability and responsibilities for care. We conclude with a call to acknowledge the fragility and limitations which affect human lives, and argue that this recognition be grounded in an inclusive form of citizenship.

## Virtual Session 4: Biomedical Interventions - Beyond Medication

### Hosted by Dr. Howard Chertkow

**KEYNOTE: Towards a brain health indicator to assess and promote brain health across the lifespan**

Dr. Alvaro Pascual-Leone
Harvard Medical School, USA

Mental and brain diseases are the main cause of lifelong disability worldwide, affecting one in four people, but also their families and friends, and the magnitude of this threat continues to grow. Unless we develop interventions to minimize the impact of brain illnesses, society will face an insurmountable crisis.

Despite enormous efforts and substantial investments from the public and private sectors, progress in addressing the challenge of neurological and mental disorders has been small. A transformative approach may be needed: instead of trying to treat diseases, one focused on promoting brain health and mental well-being to minimize the risk of developing mental and brain diseases; and in patients who already have a brain disease, promoting resilience to minimize disability and optimize function. Success in this endeavor will directly impact a large number of patients and will also deliver substantial indirect social benefits and economic impacts.

In order to achieve this transformative goal, the first step is to identify and characterize the complex interaction between the multidimensional factors that help a given individual sustain brain health and mental well-being across their lifespan, or in the case of patients with brain and mental diseases, sustain function and avoid disability.
Ultimately, we need a “Brain Health Indicator,” a new “vital sign” that will quantify an individual’s risk of brain-related disability and can guide the development, evaluation, and optimization of interventions to promote better brain health and mental well-being, and enable lifelong, true precision medicine for the brain, minimize the impact of neurological and psychiatric illnesses, and extend the human health-span.

Constructing such an index poses a complex challenge that will demand integrating genetic, developmental, cognitive, behavioral, physical, emotional, environmental, and lifestyle factors with brain structural and physiological measures. Perturbation biomarkers levering the integration of noninvasive brain stimulation approaches with imaging and neurophysiologic methods, methods to characterize the mechanisms of brain plasticity, and digital biomarkers that capture cognitive performance and behavior across the lifespan can enable deep insights into the individual state of brain health, and allow for true precision health for the brain.

**Revisiting the theoretical foundations of therapeutic brain stimulation**

Dr. Jed Meltzer
Rotman Research Institute, Baycrest, Departments of Psychology and Speech-Language Pathology, University of Toronto, Canada

Noninvasive brain stimulation techniques such as TMS and TDCS have now been used as therapeutic interventions for several decades, achieving mainstream clinical use in the area of depression but remaining experimental for other psychiatric and neurological disorders. Despite an ever-growing

number of clinical trials and exploratory studies, the status quo of TMS for depression with no other approved uses seems firmly entrenched. This presentation will review the theoretical basis on which the currently approved protocols for TMS treatment were originally proposed two decades ago, the accumulated evidence for and against the original hypothesis for its mechanism of action, and the prospects for further refinement of brain stimulation as a more effective treatment for a wider range of disorders.

Various TMS and TDCS protocols have been shown to either increase or decrease cortical excitability, which is quantified as the amplitude of response in a peripheral muscle to a given intensity single pulse of TMS to the motor cortex (motor-evoked potential). Based on findings that depression is linked to reduced metabolism in the left prefrontal cortex, early treatment studies applied excitatory high-frequency repetitive TMS to that area and demonstrated improved mood outcomes, a finding since replicated several times, forming the basis of FDA-approved treatment protocols. Other excitatory protocols have shown similar effects, including theta-burst stimulation and anodal TDCS. Based on the idea that the left hemisphere subserves more positive emotions whereas the right hemisphere subserves negative ones, other studies have applied inhibitory stimulation to the right hemisphere, also demonstrating clinical efficacy, and still other studies have combined both approaches. The success of these techniques fuels the idea that hemispheric imbalances of neural activity underlie disorders, and can be corrected through repeated brain stimulation.

The hemispheric imbalance idea has been highly influential in research seeking to improve motor and language abilities in stroke survivors. Exciting the damaged hemisphere and inhibiting the healthy one are seen as competing approaches, with variable success across individuals. Despite this progress, clinical outcomes from TMS are highly variable, with the common assumption that there is still room for improvement. The original treatment parameters developed in the mid-1990s have largely remained unchanged, as comparing outcomes between different parameters requires expensive and time-consuming clinical trials that risk assigning large numbers of patients to a less effective treatment option. Thus, there is much interest in developing fast and inexpensive biomarkers of neural dysfunction, to assess the short-term and long-term physiological effects of brain stimulation within individuals.

My laboratory has conducted a series of studies of brain electrical activity in patients with language disorders caused by both stroke and neurodegenerative disease, characterizing focal abnormalities within tissue that is structurally intact but functionally compromised. Such abnormalities may index neural dysfunction that underlies behavioural symptoms but is potentially responsive to interventions. The latter portion of the presentation will review the evidence establishing focal electrical abnormalities as a potential biomarker for treatment effectiveness in noninvasive brain stimulation, and will present more recent findings showing that they do in fact normalize in response to treatment.

## Breaking barriers with sound: from depression to Alzheimer's disease

Dr. Nir Lipsman
Sunnybrook Health Sciences Centre, Division of Neurosurgery, University of Toronto, Canada

Focused ultrasound (FUS) is an emerging disruptive technology with the ability to non-invasively and precisely intervene in key circuits driving common and challenging brain conditions. FUS can be used to permanently ablate tissue as well as temporarily open the blood-brain barrier (BBB), permitting enhanced delivery of therapeutics. Emerging applications are investigating FUS mediated modulation of deep and superficial brain targets, a potential alternative to more invasive, and riskier, neuromodulatory approaches. The last 5 years have seen a dramatic expansion of global attention to experience with

human FUS applications, with a resultant exponential increase in academic and public interest. This spans clinical FUS applications in psychiatric, neurologic and neurodegenerative conditions, with insights from pre-clinical models to human trials. Our group has published the first human applications of FUS BBB opening in brain tumours, Alzheimer's and ALS, with other groups globally actively pursuing FUS applications. This presentation will provide a brief background on therapeutic ultrasound, as well as its current and emerging indications. It will examine the current and potential impact of FUS on the landscape of brain therapies and the challenges facing further advancement and broader adoption

Meng Y, et al. (2019). Safety and efficacy of focused ultrasound induced blood-brain barrier opening, an integrative review of animal and human studies. *Journal of Controlled Release*, *309,* 25-36.

Lipsman N, et al. (2018). Blood-brain barrier opening in Alzheimer's disease using MR-guided focused ultrasound. *Nature Communications, 9,* 2336.

Meng Y. et al. (2017) Focused ultrasound as a novel strategy for Alzheimer disease therapeutics. *Annals of Neurology, 81*, 611-617.

## The future of neuromodulation for the treatment of depression

Dr. Jeff Daskalakis
Centre for Addiction & Mental Health, Canada

Background: Little is known about the neurophysiological pathology of depression and how Magnetic Seizure Therapy and repetitive transcranial magnetic stimulation (rTMS) may affect neurophysiological markers in depression.

Methods: The TMS-Evoked Potential (TEP) waveform was assessed in subjects with major depressive disorder (MDD) undergoing treatment trials with both rTMS and MST.

Results: Patients receiving MST demonstrated significant changes in neurophysiology related to LTP-like plasticity. By contrast, patients who received active rTMS demonstrated significant changes in neurophysiology related to LTD-like plasticity. Additional neurophysiologic data demonstrated that both MST and rTMS resulted in suppression in neurophysiological activity from the subgenual cingulate through region of interest analysis.

Conclusions: Our results highlight that TMS-EEG measures of plasticity and inhibition are related to brain stimulation therapy in TRD. The most noteworthy changes occurred in the DLPFC. Our results also demonstrate that while magnetic stimulation treatment was applied to the DLPFC, neurophysiological changes in the subgenual cingulate were also observed and related to treatment response.

## FACULTY

*(listed in order above)*

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**Dr. Ruth Lanius**
Harris-Woodman Chair, Professor of Psychiatry, Western University, London, Canada

**Dr. Joseph P. Gone**
Faculty Director, Harvard University Native American Program; Professor of Anthropology, Faculty of Arts and Sciences; Professor of Global Health and Social Medicine, Faculty of Medicine, Harvard University, Boston, USA

**Dr. Roger S. McIntyre**
Professor of Psychiatry and Pharmacology, University of Toronto; Chairman and Executive Director, Brain and Cognition Discovery Foundation (BCDF), Toronto, Canada; Director, Depression and Bipolar Support Alliance (DBSA), Chicago, USA

**Dr. Linda Mah**
Clinician Scientist, Rotman Research Institute, Baycrest; Assistant Professor, Department of Psychiatry, Division of Geriatric Psychiatry, Faculty of Medicine, University of Toronto, Canada

**Dr. Gustavo Turecki**
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**Dr. Linda Clare**
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**Dr. Donna Rose Addis**
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**Dr. Amanda Grenier**
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**Dr. Nir Lipsman**
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## SESSION CHAIRS

Drs. Brian Levine, Cheryl Grady, Howard Chertkow
Rotman Research Institute, Baycrest

## LEARNING OBJECTIVES

After active participation in this virtual conference, participants will be able to:

- Describe and predict many health consequences of exposure to mental trauma
- Identify adaptational styles and their influence on the transmission of trauma
- Diagnose and address stress management and its practice with older adults
- Analyze and include the centrality of cultural differences in shaping responses to trauma
- Explain the neurobiological underpinning of different variants of posttraumatic stress disorder
- Identify and address the impact of mood, early life adversity and neurobiological processes, such as inflammation, on cognitive impairment and neuropsychiatric disorders
- Compare and evaluate the interactive contributions of biological, psychological and social factors in determining well-being in old age and dementia
- Describe and use (or refer for) different forms of invasive and non-invasive neurostimulation approaches for the treatment of neuropsychiatric disorders

## CONFERENCE PLANNING COMMITTEE

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**Alain Fournier,** IT Design Engineer, Rotman Research Institute, Baycrest

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