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Place of employment and host institution: Centre for Addiction and Mental Health, Canada and Faculty of Health and Medical Sciences – Department of Clinical Medicine, University of Copenhagen,

Host principal investigator: Associate Professor Bjørn H. Ebdrup, University of Copenhagen, Mental Health Centre Glostrup

Title of project: Establishing real-world interdisciplinary care and research approaches for cardiometabolic care in schizophrenia spectrum disorder (SSD)s

ABSTRACT

Abstract: Schizophrenia spectrum disorders, as compared to the general population are associated with exceedingly high rates of obesity(2x) and type 2 diabetes (3-5x). As a consequence, people living with this devastating mental illness die prematurely from cardiovascular (CV) disease (by 15-20 years). Metabolic comorbidity, particularly insulin resistance and Type 2 diabetes (T2D), also has detrimental outcomes on quality of life, cognitive function (with possible associated brain structural changes, in areas important to cognition such as the hippocampus), and psychopathology. The mechanisms underlying high cardiometabolic comorbidity are however complex, including biological illness associated factors, lifestyle factors, disparities in medical care, and antipsychotic medications.

Moreover, patients even when diagnosed with modifiable risk factors for CV disease, remain vastly under treated, contributing to poor physical and mental health outcomes and premature CV mortality. The present visiting professorship has three aims, which build on an existing collaboration with Danish researchers:

Aim 1: Establishment of integrated metabolic clinic in Denmark.

In Toronto, at the Centre for Addiction and Mental Health (CAMH), we have established a world-first Mental Health and Metabolism Clinic (MHMC), which integrates mental and metabolic care for patients with severe mental illness. The clinic comprises an integrated care pathway (ICP), which collects measures related to metabolic outcomes (anthropometrics, vitals, fasting metabolic bloodwork, HbA1c, renal/liver function), as well as questionnaires related to quality of life, psychopathology, and cognitive functioning. The data is collected as part of clinical care, and informs sequential metabolic interventions, providing data as to real-world effectiveness of metabolic interventions. The ICP provides an extraordinary opportunity to: 1) collect pilot data for larger, multi-site intervention randomized clinical trials (RCT)s; 2) build a one-of-a-kind clinical and biomarker database which can be leveraged for collaborative grant applications. We propose to align, optimize and implement, the existing CAMH metabolic ICPs to psychiatric care at Mental Health Centre Glostrup (Prof. B. Ebdrup).

Aim 2: Concrete data analyses - Role of dysglycemia on brain structural changes in schizophrenia-spectrum disorders with comorbid obesity.

We will investigate the role of dysglycemia and T2D on brain structural changes in schizophrenia-spectrum disorders. To this end, we have acquired structural magnetic resonance imaging (MRI) data from two independent RCTs (Danish and Canadian), examining metformin and exenatide across our centers. The visiting professorship will allow us to analyze and compare brain scans of people with obesity to those of people with T2D and obesity, with the potential to provide insight into pathophysiology and possible interventions for brain structural alterations in schizophrenia. The goal is to produce a manuscript by the end of the 4 month award period, with future plans to also combine our data to examine effects of improvements in insulin sensitivity on brain structure and function.

Aim 3: Training in clamping techniques: From Copenhagen to Toronto.

Dr. Hahn was recently awarded a research chair, which will allow CAMH to purchase equipment to conduct euglycemic and hyperglycemic clamp studies in humans. As Prof. Knop (Director of Center for Clinical Metabolic Research, Gentofte Hospital), has world renown expertise in human clamping procedures, Dr. Hahn will have the opportunity to learn these techniques, which will allow future cross-centre grant

applications and collaborations to investigate questions related to glucose metabolism in schizophrenia spectrum disorders.