Title Slide

My name is Jonelle and I am a PhD candidate in the Epigenetics of Severe Mental Disorders Group with Stéphanie in Bergen. Thank you for selecting my proposal for this meeting. I will share my vision for moving research forward by incorporating the ketogenic diet in the treatment of severe mental disorders. This vision incorporates the role of epigenetics and mitochondrial function in psychiatric disorders.

Slide 1:

Close geographical proximity between the nucleus and mitochondria – and their genomes.

Slide 2:

Environmental factors that influence the epigenome also influence mitochondrial function. And many of these factors have already been studied in psychiatric disorders.

This project looks at using diet as an intervention.

WHAT - Ketogenic diet?

A ketogenic diet is a very low-carbohydrate diet which helps to keep blood glucose levels low. The body looks for another source of energy and will burn fat instead which produces ketones.

The goal is for the brain to burn ketones instead of glucose and thereby give the

Simply put, a ketogenic diet typically derives about 70-80% or more of total calories from healthful fats. The remaining 20% of calories are derived from carbohydrates and proteins. Eating like this puts your body in a state of ketosis, where it primarily burns fat for energy.

To get into and stay in ketosis, you must restrict carbs and sugar – less than 50 grams per day. This initiates your body to burn the remaining carbohydrates present, after which it moves on to stored glucose (glycogen), and finally it taps into ketones. Ketones are produced by the liver and readily used by the body *for* potent energy production and critical brain-related functions.

WHAT SYMPTOMS OF METABOLIC DISEASE are shared with SMI (look up Pillinger)

* Weight gain
* Dyslipedemia
* Cardiovascular disease
* Cognitive impairment
* Sleep disturbances
* Loss

Studies – Keto diet

* Epilepsy. Rho PMID: 35361967 (anti-seizure meds)

So the term “diet” is somewhat understated, hopefully you can see now that it is actually a “metabolic intervention.”

* Used to treat intractable epilepsy (in children, with good affect in adolescents and adults), however in the 1930’s anti-seizure medication became available and offered a more practical solution.
* Used to treat diabetes in the 1800’s
* Used to help alcoholics detox – in the lab of Nora Volkow, the director of the National Institute of Drug Addiction, subjects adhering to the ketogenic diet during detox used few benzodiazepines than controls, and their MRI scans showed reduced inflammation.
* Has been used to *alleviate* symptoms of anxiety, depression, BPD and SCZ.

Metabolism - Brain Energy – Mitochondria

Metabolism is much more than burning calories – it affects the structure and function of all cells in the human body. Metabolism is regulated by hormones, neurotransmitters, inflammation and epigenetics. And mitochondria are master regulators of metabolism.

Mitochondrial dysfunction or dysregulation can cause many of the symptoms of mental disorders through 5 distinct mechanisms:

1. Cell activity can be overactive
2. Cell activity can be underactive
3. Some cells can develop abnormally
4. Cells can shrink and die (4 and 5 lead to absent brain functions)
5. Cells can have problems maintaining themselves.

Not all of these mechanisms respond adequately to medication – but protocols that support a healthy metabolism also support healthy mitochondrial function.

One such protocol is the ketogenic diet.

There is some evidence to suggest that a ketogenic diet may help improve mitochondrial function in certain circumstances, although more research is needed to fully understand the mechanisms at play.

Mitochondria are the cellular organelles responsible for producing energy in the form of ATP through the process of oxidative phosphorylation. Dysfunction in the mitochondria can contribute to a range of health issues, including neurological disorders, metabolic disorders, and aging.

One proposed mechanism by which a ketogenic diet may improve mitochondrial function is through the production of ketone bodies. When the body is in a state of ketosis, it relies on ketone bodies as an alternative source of energy to glucose. Some research has suggested that ketone bodies may be a more efficient fuel source for the mitochondria than glucose, leading to improved mitochondrial function.

In addition, a ketogenic diet may also increase the production of mitochondria through a process called mitochondrial biogenesis. Some studies have found that a ketogenic diet can increase the expression of genes involved in mitochondrial biogenesis, leading to an increase in the number of mitochondria in cells.

However, the research on the effects of a ketogenic diet on mitochondrial function is still in its early stages, and more research is needed to fully understand the mechanisms at play and the potential benefits and risks of a ketogenic diet for mitochondrial function.

EPIGNETICS

Currently there are no clinical tests for many of the subcellular pathologies – however we could use an epigenetic approach to identify changes in differential methylation – or even a candidate approach for metabolic genes.

Aims –

For patients:

To foster and support patient engagement in their own recovery

For clinicians:

To shift the focus from symptom-based treatment to system-based recovery.