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 as an intervention in the treatment of severe mental disorders. This vision incorporates the role of epigenetics and mitochondrial function in psychiatric disorders.

Slide 1: The Environment

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

Slide 2: Mitochondrial epigenetics (maybe remove the points and just talk)

Epigenetic nuclear mechanisms have evolved to couple gene expression to the metabolic state of the cell.

There are many signaling interactions between the nuclear and mitochondrial genomes including metabolites from xxx and non-coding RNAs. The mitochondria also regulate the production of S-adenosyl methionine (SAM) which is the universal methyl donor for both nuclear and mitochondrial methylation. (through synthesis of ATP and folate). Most co-substrates required for histone modifications are generated through mitochondria. (41-32) phosphorylation, acetylation and deacetylation

Slide 3: Mitochondrial dysfunction

Reduced energy production in the form of ATP, increased Reactive Oxygen Species leading to inflammation, increased mtDNA mutations, altered gene expression and impaired signaling to nuclear DNA.

Notice that the inner membrane folds are diminished.

Slide 4: What is the classic ketogenic diet?

A ketogenic diet is a very low-carbohydrate diet which shifts metabolism from burning glucose to burning fat. Ketone bodies are produced as an alternative fuel source to glucose, which is believed to be a more efficient fuel source for the mitochondria.

KD shown to have beneficial effects on metabolic health – counteracting the effects of metabolic abnormalities seen with psychotropic medication use.

ie improving blood glucose, body weight, insulin resistance, triglycerides, and cholesterol. . AD and mood stabilizing effects in BP (murphy et al., 2004)

Slide 5: Reported therapeutic effects

The diet is an evidence-based treatment for Intractable epilepsy and has been used for 100 years. Anti-seizure medications are used in psychiatry as mood-stabilizers.

Detox for alcohol abuse. A study of alcohol detoxification at the National Institute of Drug Abuse showed that individuals on a KD used fewer benzodiazepines while detoxing and less cerebral inflammation when scanned with MRI.

In a study with subjects whose symptoms were poorly controlled with medication, the KD diet reported significant improvements in the Hamilton Depression Rating Scale, the Montogomery-Åsberg Depression Rating Scale and PANSS for SCZ. In SCZ, subjects first report an antidepressant effect, followed by reduction of auditory hallucinations, and finally delusions.

Slide 6: Astrocytes also generate ketones

It has been shown that ketone bodies are a more efficient energy source than glucose for astrocytes and neurons (Zhane et al, 2013). But in a diet high in bad fats, astrocytes in the hypothalamus produce an excess of ketone bodies that can override the neuron´s sensitivity to hormones such as leptin, insulin, and ghrelin.

This area of the influence of ketone bodies on metabolic hormones warrants more research in psychiatry.

Slide 7: Project title - Mental Health is Metabolic HealtH

Research aims - To identify:

- Epigenetic / gene expression changes associated with the KD

- Mechanisms associated with symptom reduction/positive outcome

Slide 8: Mental Health is Metabolic Health

Clinical aims - To foster and support:

Recovery through a low-risk metabolic intervention (KD)

Patient engagement in their own recovery

Slide 9: Acknowledgements