

Treating Mental Health Disorders with a Ketogenic Diet

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Christopher Palmer, M.D., David Puder M.D. have no conflicts of interest to report.

In today's episode of the podcast, we interview Dr. Chris Palmer, a psychiatrist, researcher, and expert in using the keto diet as a medical treatment for some treatment-resistant patients. Dr. Palmer is currently the director of the Department of Postgraduate and Continuing Education at McLean Hospital and is an assistant professor of psychiatry at Harvard Medical School. He also runs his private practice specializing in treatment-resistant mental health patients.

In his upcoming book, [Brain Energy](#), Dr. Palmer theorizes that there is a direct connection between metabolic health and mental health. In short, he believes there is sufficient evidence to support that all mental health disorders stem from metabolic disorders in the brain. He asserts that understanding mitochondrial function and health at a cellular level will fundamentally change how we interpret and treat patients with psychiatric conditions and result in more effective treatment plans.

The Connection Origins

We have long understood that metabolic dysfunction and mental illness have some degree of relationship. As early as the 1800s, it was known that those suffering from psychiatric conditions were significantly more likely to develop diabetes (and vice versa); it was observed that these two disorders ran in the same families. (At the time, psychiatric conditions were generically labeled as insanity and would now fall under diagnoses such as bipolar disorder, psychotic depression, or schizophrenia.)

The connection between these two systems was made before medicines existed to treat these conditions. Some believe that diabetes and obesity, along with other conditions, are side effects of modern-day medications, and certainly they may add to the proclivity, but these connections were well-known before the introduction of medications.

A Growing Body of Research

In the 1940s, the basic research evidence of the metabolic-mental health connection began accumulating. Studies researched the differences in lactate levels in people with bipolar disorders and chronic depression, finding that levels were elevated in these populations.

By the 1990s, the body of research had grown enormously. Neuroimaging studies employed a variety of imaging techniques such as CT scans, fMRI, PET scans, etc. Dr. Palmer points out that the core of each of these imaging techniques is measuring brain metabolism.

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By 2000, researchers and neuroscientists began to focus on formulating data based on the earlier research, further concluding there is significant evidence that mental illness can be attributed to metabolic defects in neurons.

The root of any metabolic problem is at the mitochondrial level because they control metabolism. As a result, research began on the mitochondrial level of metabolic function. Research on these metabolic defects has led to what Dr. Palmer refers to as the “mitochondrial theory of mental disorders,” including autism, bipolar, schizophrenia, depression and other disorders.

The Metabolic-Mental Health Connection Theory

Dr. Palmer argues that the theory of metabolic dysfunction being a causal root for mental illness unites the biological, psychological, and social theories between mental and physical health. He points out that there is significant overlap between what we believe can cause mental illness and what can cause mitochondrial dysfunction, such as vitamin deficiencies, trauma, genetics, epigenetics, adverse childhood events, poor sleep schedule, diet, etc.

Based on his research, treatment should always be approached from a metabolic perspective no matter the trauma or diagnosis. Every intersection of factors that lead to metabolic dysfunction (trauma, vitamin deficiency, hormonal dysfunction, etc.) meet at a mitochondrial level and should be treated with metabolically-related methods (diet, exercise, sleep, eliminating toxic substance abuse, etc.).

Dr. Palmer believes that if mental health professionals conceptualize mental illness at the cellular level, treatment will become more practical and less ambiguous. Therefore, this theory suggests the need for a paradigm shift in the understanding of mental illness, and, more importantly, how professionals go about treating it. Dr. Palmer states, “We can develop much more effective and lasting treatments if we target mitochondria and metabolism as opposed to shooting in the dark, trying one pill after another and seeing if anything works.”

Dr. Palmer makes clear that the theory of metabolic/mitochondrial dysfunction does not replace other effectively-known treatments. It exists to better our understanding of the causes of mental illness and provide additional treatment methods to help restore long-term health.

How Does Psychotherapy Fit Into a Metabolically-Minded Treatment Plan?

The role of psychotherapy depends on how we are using it and what the intervention is. Psychotherapy is well known to improve metabolic dysfunction and mental illness. Dr. Palmer

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argues that cognitive psychotherapy may work effectively by reducing stress and, therefore, alleviating metabolic dysfunction and improving mitochondrial function leading to improved mental health. In terms of behavioral therapy, Dr. Palmer suggests that the modification or reduction of certain behaviors can also improve metabolic function.

Examples of Metabolic Interventions

Exercise

There is a strong link between improving muscular metabolic and mitochondrial function and improved brain mitochondrial and metabolic function. The evidence in both human and animal studies is robust.

Exercise is known to improve brain health and, when taken down to the cellular level, that means increased BDNF (brain-derived neurotrophic factor). BDNF increases mitochondria count and health which leads to higher plasticity and more neurogenesis. Consequently, the brain can grow and thrive and adapt, leading to a decrease in mental health disorders, even neurodegenerative disorders. It all comes down to mitochondrial function and health, which exercise is known to improve.

But exercise isn't a stand-alone treatment. Treatment plans are multifaceted. However, understanding this cellular-level impact provides insight that is helpful in developing more effective treatment plans.

The Ketogenic Diet

What is it?

The ketogenic diet is a low-carbohydrate, high-protein, high-fat diet with the ultimate goal of putting the body in a state of ketosis (when your body begins to burn fat instead of glycogen and produces ketones for energy).

What does it do in the body?

The ketogenic diet causes changes in many systems of the body. In the brain, the ketogenic diet influences multiple neurotransmitter systems such as GABA, glutamate, and ATP. It also assists in regulating calcium channels and decreasing inflammation. The ketogenic diet changes the gut biome and improves insulin signaling to the brain, as well. Dr. Palmer believes the ketogenic diet's two most important impacts (in regards to the metabolic theory) are that it improves

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mitophagy and mitochondrial biogenesis. There is evidence that shows the ketogenic diet improves mitochondrial count and more importantly, mitochondrial health.

Keto and Mental Health

The ketogenic diet has been prescribed for treatment-resistant epilepsy for over 100 years. Both human and animal models provide significant evidence that the ketogenic diet is an effective treatment for various psychiatric conditions, the effectiveness being attributed to the improvement of metabolic and mitochondrial dysfunction.

One of the key advantages of the ketogenic diet as a treatment, as compared to other diet regimens, is that it can be objectively measured via blood ketone levels.

What is the evidence?

There is emerging research on the ketogenic diet as a treatment for mental illness and there will be much more to come. The Baszucki Brain Research Fund has invested over 60 million dollars towards research on the ketogenic diet and mental illness.

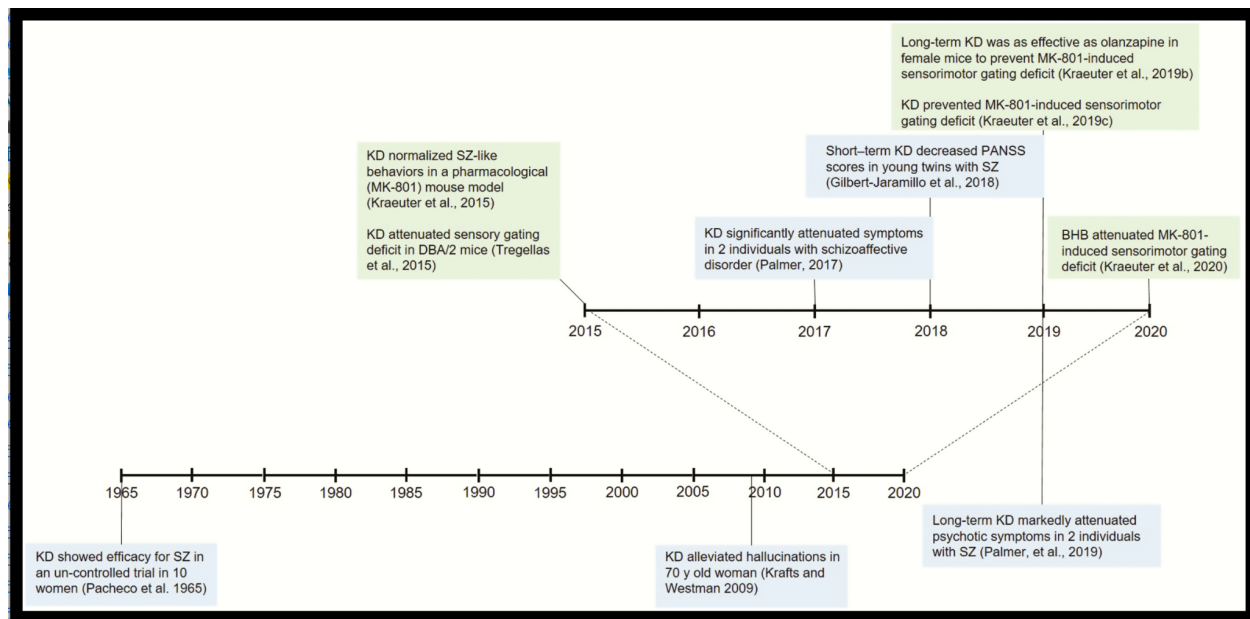
Some examples and summaries of Dr. Palmer's work on the ketogenic diet are listed below.

- Sarnyai, Z., C.M. Palmer. Ketogenic Therapy in Serious Mental Illness: Emerging Evidence. *International Journal of Neuropsychopharmacology*. 2020; 23(7), 434–439, <https://doi.org/10.1093/ijnp/pyaa036>.
 - This is a meta-analysis of studies regarding the variety of ways in which the ketogenic diet has marked implications for the treatment of mental illness and schizophrenia. A few key takeaways are:
 - Pharmacological inhibition of NMDA-type glutamate receptors in rodents results in the expression of typical schizophrenic behaviors (hyperactivity, stereotyped behaviors, decreased sociabilities, and working memory deficits). A ketogenic diet was introduced over the course of 3 weeks. Ketosis was measured by observing elevated beta-hydroxybutyrate levels, decreased glucose levels, and weight loss. Rodents who received the ketogenic diet intervention displayed significant decreases in schizophrenia-like abnormal behaviors (Kraeuter et al., 2015) (Sarnyai, Z., 2015).

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- Impaired P50 gating is one biological marker of schizophrenia in animal and human models. DBA/2 mice exhibit schizophrenia-like symptoms. Hippocampal P20/N40 gating in DBA/2 mice is a translational endophenotype that manifests similarly to impaired P50 sensory gating in people who suffer from schizophrenia. Following a ketogenic diet, animals with the highest blood ketone levels showed the lowest P20/N40 gating ratios, which implies that the ketogenic diet may alleviate impaired sensory gating (Tregelles et al., 2015).
- The ketogenic diet has been studied for its antipsychotic effects for over 50 years. In clinical settings, there have been some recorded cases of patients with treatment-resistant schizophrenia/schizoaffective disorder reporting alleviation, and in some cases remission of symptoms after beginning a ketogenic diet. The paper analyzes multiple studies and cases in which this has occurred.



- Palmer, C.M., J. Gilbert-Jaramillo, E.C. Westman. "The Ketogenic Diet and Remission of Psychotic Symptoms in Schizophrenia: Two Case Studies." *Schizophrenia Research*. 2019 June; 208: 439-440, ISSN 0920-9964. <https://doi.org/10.1016/j.schres.2019.03.019>
 - An 82-year-old woman suffered from treatment-resistant schizophrenia for 65 years. This patient was prescribed 15 different mood stabilizing and antipsychotic

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medications throughout her treatment. In 2008, she was taking six medications when she began a ketogenic diet in order to lose weight (she weighed 330 pounds). Within two weeks of beginning her ketogenic diet, she reported marked decreases in schizophrenia symptoms and (by her own volition) stopped taking her medication. Her hallucinations, paranoia, and suicidal thoughts were completely remitted and she lost 150 pounds. She is now able to live an independent life, with no legal guardian, for the first time in her life.

- A 39-year-old woman had a history of depression, anxiety, and paranoia. When she finally told her healthcare provider about her hallucinations, she was diagnosed with schizophrenia. Over the course of her treatment, she was prescribed 14 different mood-stabilizing/antipsychotic medications. She began the ketogenic diet in 2013 after reporting a series of gastrointestinal issues. Shortly after, she stopped taking all 14 medications and became severely psychotic, resulting in hospitalization. After her hospitalization, she was prescribed haldol-decanoate (a medication she had already tried) and continued her ketogenic diet. In the following months, she tapered off of haldol-decanoate and she experienced full remission from her psychotic symptoms for the first time since 1993.
- Norwitz, N., G.A. Dalai, S. Sethi; C. Palmer. “Ketogenic diet as a metabolic treatment for mental illness.” *Current Opinion in Endocrinology & Diabetes and Obesity*: 2020 Oct: 27(5): 269-274. doi: 10.1097/MED.0000000000000564
 - This is a literature review. The researchers propose that schizophrenia, depression, bipolar disorder, and binge eating disorder all share mechanistic pathologies. Examples are glucose hypometabolism, neurotransmitter imbalances, oxidative stress, and inflammation. The ketogenic diet may be an effective treatment for these 4 diseases and their symptoms thereof.
- Campbell, I., & H. Campbell. “Mechanisms of insulin resistance, mitochondrial dysfunction and the action of the ketogenic diet in bipolar disorder. Focus on the PI3K/AKT/HIF1a pathway.” *Medical Hypotheses*. 2020 Dec; 145:110299. <https://doi.org/10.1016/j.mehy.2020.110299>
 - Campbell and colleagues discuss possible mechanisms by which the pathogenesis of bipolar disorder may take place. The researchers note that glucose metabolism and mitochondrial dysfunction are key diathesis for bipolar disorder. Further, many individuals who suffer from bipolar disorder are insulin resistant. The researchers propose that hyperinsulinemia resistance triggers

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mitochondrial dysfunction through a complex insulin-signaling pathway, and a ketogenic diet acts directly on these pathways to alleviate mitochondrial dysfunction.

- Danan, A., E.C. Westman, L.R. Saslow, & G. Ede. "The Ketogenic Diet for Refractory Mental Illness: a Retrospective Analysis of 31 Inpatients. *Frontiers in psychiatry*. 2022 Jul; 13:951376. <https://doi.org/10.3389/fpsyt.2022.951376>
 - This study was done retrospectively on 31 inpatients suffering from MDD, bipolar disorder, and schizoaffective disorder. Participants were put on a strict ketogenic diet, limited to 20 grams of carbohydrates per day. Mean scores and standard deviations for all three diagnoses improved after 14 days, with the most marked improvement for those with schizoaffective disorder. This study provides some evidence that the ketogenic diet is a viable treatment for psychiatric disorders. However, more controlled studies in which researchers ensure ketosis is taking place and diets are more individualized are needed in the future.

What are the risks?

The ketogenic diet causes major shifts in fluid and electrolyte levels in the body. In the early stages before ketosis is achieved, the body burns a lot of glycogen which can lead to muscular dehydration. This also causes the loss of electrolytes. Dr. Palmer advises that, for this reason, those on the ketogenic diet should use more light salt (half sodium, half potassium chloride).

There are other options in terms of supplements as well, but Dr. Palmer continuously stresses the importance of following the instructions of dietitians who specialize in the ketogenic diet. He also warns about the importance of monitoring L-carnitine and selenium levels. L-carnitine aids in moving fat into the cell, and if levels are low, mitochondria may not be able to burn ketones efficiently. The ketogenic diet can result in selenium deficiency, which can be fatal. Dr. Palmer ensures that these cases are incredibly rare, but that selenium levels should be monitored.

Additionally, there is a version of the ketogenic diet used for weight loss, but the version used as a psychiatric intervention is very different and should be administered and closely supervised by a licensed medical professional or ketogenic physician. Professionals who wish to use this diet in their treatment plans need to be well-trained in the medical version of this diet and committed to consistently monitoring specific patient biomarkers, such as cholesterol, triglycerides, insulin, and glucose.

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Incorporating the Ketogenic Diet Into Your Practice

The first step in implementing the ketogenic diet as a treatment is determining whether or not it is appropriate for a specific patient. In his practice, Dr. Palmer begins with a standard mental health assessment and evaluation. After assessment, he determines what medications a patient is on that enhance metabolism and what medications impair metabolism. If a patient has tried multiple medications at different doses and has seen no significant decrease in symptoms, off-label treatments can be considered.

However, using the ketogenic diet should only be suggested if the patient is not experiencing significant metabolic dysfunction due to extraneous factors in other areas of their life, such as lack of exercise, substance use, abuse, sleep patterns, stress levels, etc. If a patient is willing to try a ketogenic diet, it may be implemented. Patients should remain on their medications while starting the diet and be evaluated during the stages of ketosis to assess any clinically significant change in symptoms.

Dr. Palmer suggests trying the ketogenic diet with a patient for three months. If the diet seems to be working after that three-month period (Dr. Palmer says it is typically working profoundly at this point), the clinician should begin to create a plan with the patient to slowly taper off other medications. Common psychoactive medications work against the ketogenic diet by increasing insulin and blood glucose levels. In terms of atypical antipsychotic medications, however, tapering off these should be done very slowly and carefully. The rate at which this tapering can be implemented depends on the amount of time the patient has been using the medication, the severity of symptoms, the overall danger to the patient, etc.

The risk of adverse effects due to the absence of medication is only half of the issue. If a medication is being taken less or not taken at all, the patient is now more reliant on the ketogenic diet to keep symptoms under control. This can pose issues because compliance to the ketogenic diet can be rather fickle. As Dr. Palmer says, there are no “cheat days” in the ketogenic diet. It typically takes about 2-5 days to achieve ketosis, and if a patient reverts from ketosis, symptoms can dramatically reappear. Therefore, mental health professionals that are interested in using the ketogenic diet as a treatment must be adequately informed on the scientific details of the ketogenic diet and metabolic functioning as a whole. Perhaps before utilizing the ketogenic diet in practice, one should adhere to Dr. Palmer's two first steps:

1. Find a licensed ketogenic dietician and partner with them.
2. Read the book “[Ketogenic Therapies](#)” by Eric Kossoff.

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While Dr. Palmer did not mention this, it would probably help to read his book, [Brain Energy](#), which comes out on November 15th, 2022.

Conclusions:

One issue regarding the ketogenic diet is that a patient must be willing to make the sacrifices and follow through. Dr. Puder had one patient dive into it 100% for three weeks, but could not maintain the diet because she missed fruit and complex carbs.

When asked his opinion on how mitochondrial issues are central to mental illness, Dr. Michael Cummings stated, "I agree with the author that the likely role of mitochondrial abnormalities in neurological and neuropsychiatric diseases has likely been underappreciated. It seems to me, however, that ascribing the cause of all or most brain disease to mitochondrial abnormalities is an example of overly simplistic reductionism. While there are diseases in which a single abnormality or single class of abnormality accounts for the entire etiology of the disease (e.g., sickle cell anemia), such diseases are the exception rather than the rule, especially in organ systems that are complex. Instead, it seems to me that neurological and psychiatric diseases most often arise as emergent properties arising from a cascade of interrelated abnormalities, which are likely to include genetic, epigenetic, histological, endocrine, and inflammatory elements."

In conclusion, there is no doubt that exercise and diet make a huge impact on mental health. Hopefully, more patients will become open to trying the ketogenic diet as an off-label way of treating schizophrenia and bipolar, but they must be well enough to have 100% follow through. We will also look forward to well done randomized controlled trials in the future.

Acknowledgments:

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