Dietary Interventions in Schizophrenia and Psychosis: A Review

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Background

- Schizophrenia spectrum disorders (SSD) have incompletely understood etiology with heterogeneity between patients
- Treatment options are insufficient for adequately addressing negative symptoms and cognition
- Individuals with SSD suffer from increased morbidity and mortality from cardiometabolic disease than the general population[1]
- Dietary interventions may offer low-risk treatment options with minimal side effects[1]
- Personalized nutrition may help address biological heterogeneity

Methods

We searched PubMed.gov with combinations of the keywords “schizophrenia” and “psychosis” with “nutrition,” “metabolic psychiatry,” “ketogenic diet,” “gluten-free diet,” “Mediterranean diet,” “gut-brain axis,” “supplementation,” “dietary intervention,” “omega-3,” “vitamins,” and “probiotics.” We then summarized these papers into the following categories: gluten-free diet, ketogenic diet, Mediterranean diet, probiotic supplementation, and nutritional supplementation, which was further categorized into vitamin D, B vitamins, and omega-3 fatty acids.

Other Considerations

- Supplement sales in the USA do not require pre-market approval, necessitating careful brand selection to ensure quality[2]
- Access to fresh produce, specialized diets, and supplements may be limited due to distance from grocery stores or high cost of specialized items
- Adherence to specialized diets may be poor but can be improved with patient education and increased access to nutritious food[3]

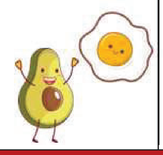
Potential Diets for Treating Schizophrenia

Medical Ketogenic Diet

What it is:
- Originally developed as a treatment for epilepsy[4]
- Focuses on macronutrient ratios of high fat to low carbohydrates with moderate protein
- Forces body to metabolize fat and produce ketone bodies

Potential clinical benefits:
- Reduction of positive and negative symptoms[5,6]
- Potential benefit to metabolic and gastrointestinal health[5,6]

Potential mechanisms:
- Reduced oxidative stress and inflammation[7]
- Compensation for impaired cerebral glucose metabolism[7]



Gluten-Free Diet

What it is:
- Prescribed to treat celiac disease, non-celiac gluten sensitivity, and wheat allergy
- Strict avoidance of grains containing gluten, which is composed of glutenins and gliadins

Potential clinical benefits:
- Reduction of negative symptoms[8]
- Possible of other inflammation-related symptoms, such as gastrointestinal issues[8]

Potential mechanisms:
- Decreased inflammation related to anti-gliadin antibodies[9]
- Decreased potential auto-reactivity caused by structural resemblance between gliadin peptides and GRIN1, an NMDA receptor subunit[10]

Mediterranean Diet

What it is:
- Inspired by the dietary habits of countries bordering the Mediterranean Sea, including Greece, Italy, and Spain
- Emphasizes consumption of plant-based foods, olive oil, fish, and other seafood with limited red meat

Potential clinical benefits:
- Improvement in immune function and cardiovascular disease co-occurring with schizophrenia[11]
- Negatively correlated with negative symptom severity and increased BMI in SSD[12]

Potential mechanisms:
- Increased consumption of omega-3 fatty acids
- Increased production of short-chain fatty acids[11]

Potential Nutritional Supplementation for Treating Schizophrenia

Omega-3 Fatty Acids

What they are:
A group of polyunsaturated fatty acids that are important in membrane function[13]

Where they’re found:
Fatty fish (salmon, mackerel, sardines) flax and chia seeds, walnuts

Potential clinical benefits:
Reduction of positive and negative symptoms[14] and improvements in cognition[15]

Potential mechanisms:
Support proper neurodevelopment and neural functioning, especially cell membranes[16]; reduced inflammation[16]

Vitamin D

What it is:
Fat-soluble vitamin that is involved in calcium absorption, neuromuscular function, and the immune system[13]

Where it’s found:
Sunlight exposure, fatty fish, egg yolks, and fortified foods

Potential clinical benefits:
Reduction of positive and negative symptoms[17]

Potential mechanisms:
Modulate GABA/glutamate balance[18], maintain proper calcium homeostasis[18]

B Vitamins

What they are:
Eight water-soluble vitamins that play diverse roles in bodily functions, including metabolism and energy production[13]

Where they’re found:
Depending on the specific B vitamin—animal products, leafy greens and legumes, fortified foods

Potential clinical benefits:
Prevention of cognitive decline[19], improvements in cognition[19]

Potential mechanisms:
Support proper neurodevelopment[20], support neurotransmitter formation[20]

Probiotics

What they are:
Live microorganisms that are broadly considered beneficial when consumed in adequate amounts

Where they’re found:
Yogurt, kombucha, kimchi, and other fermented foods

Potential clinical benefits:
Reduction of positive and negative symptoms[21], improvements in cognition[22], reduction of gastrointestinal symptoms[23]

Potential mechanisms:
Increase microbiome diversity, increase short-chain fatty acid production[21]

Conclusion

Nutritional and dietary interventions offer low-risk options that could expand the existing treatment toolbox. Many of these interventions show improvements in negative symptoms and cognition, which can be challenging to treat with existing medications. Further work into understanding the mechanisms underlying these improvements and increasing patient access to foods and supplements aligned with these interventions are necessary to increase treatment knowledge and efficacy.

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