

# Food for Thought: The Cognitive Effects of Mediterranean, High-fat Low-carbohydrate, and Traditional American Diets – Study Design

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## *Background*

Dietary patterns have long been associated with a range of health outcomes. Findings from cross-sectional studies suggest that dietary patterns can affect cognitive function.

Mediterranean diets, rich in fruits, vegetables, olive oil, and fish, have been associated with improved cognitive function and reduced risk of cognitive decline. Conversely, the standard American diet, rich in saturated fats and sugars, has been linked with adverse cognitive outcomes. Findings regarding the effects of low-carb diets are mixed. However, some studies have reported potential cognitive benefits.

## *Hypothesis*

A two-week consumption of high-fat diets, such as the standard American diet and high-fat, low-carbohydrate diets, will lead to inferior cognitive outcomes when compared with a Mediterranean diet over the same period.

## *Specific Aims*

1. To determine the short-term effects of the Mediterranean, high-fat low-carbohydrate, and traditional American diets on measures of cognition.
2. To integrate data with findings from the Nutrition for Precision Health (NPH) study, facilitating the exploration of cognitive change mechanisms, with a focus on alterations in the gut microbiome.

## *Methods*

This research serves as a supplementary investigation within the broader scope of the NPH study. The NPH study is a nationwide, NIH-funded project to develop algorithms that predict individual responses to food and dietary patterns. The second phase of the study includes three separate controlled-feeding dietary intervention trials conducted in a free-living setting. These interventions are designed to reflect the typical dietary patterns found in the Mediterranean, high-fat low-carb, and standard American diets.

The Mediterranean diet is characterized by high consumption of fruits, vegetables, whole grains, and beans, moderate consumption of dairy, meat, eggs, fish, nuts, seeds, and vegetable oils, and minimal consumption of sugar-sweetened beverages and desserts. Conversely, the standard American diet is characterized by high consumption of refined grains, meat, eggs, sugar-sweetened beverages, sweets, snacks, desserts, and processed foods, moderate consumption of dairy, and low consumption of fruits, vegetables, whole grains, and fish. The low-carb high-fat diet is characterized by moderate to high consumption of vegetables, meat, eggs, fish, nuts, seeds, fats, and oils, with minimal fruit and dairy consumption, and extremely limited grain and sugar consumption.

Participants will participate in each diet intervention for two weeks, with a two-week washout period between diets. Researchers will be blinded to the dietary intervention assigned during each diet period. Efforts have been made to keep participants as blind to the dietary intervention as feasibly possible. To achieve this, dietary interventions have been assigned the neutral color labels “orange,” “purple,” and “blue.”

To evaluate changes in aspects of cognition, such as response inhibition, attentional inhibition, attention, and processing speed, two game-like tasks named “Left or Right” and

“City or Mountain” from the *All of Us* Research Program will be administered in 23 adult participants before and after each dietary intervention.

The study will be conducted at the NPH clinical research site located at the Louisiana State University Health Sciences Center, New Orleans. Approval from the Institutional Review Board is currently pending.

#### *Data analysis*

Data will be analyzed using mixed model ANOVA to discern the effects before and after each dietary intervention, as well as the comparative effects between the diets. This will allow for a comprehensive assessment of the relationships between diet and cognition.

#### *Future directions*

The proposed research is a feasibility study. As such, the findings from this research will be instrumental in ascertaining the effects of diet on cognition and measuring the magnitude of any potential effects, as well as in securing funding for a large-scale study. The findings will provide the effect sizes to guide the sample size calculations. Moreover, this study will begin to unravel the complexities of the diet-cognition relationship by examining the direction and strength of associations between varied diets and different cognitive domains. These insights will allow us to formulate hypotheses about the underlying mechanisms that mediate these effects.