Dietary Flavanols and Dentate Gyrus Function

Statistical Analysis Plan

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Trial Registration
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Statistical Analysis Plan

Demographics, baseline cognitive, and imagining measures were summarized by randomized treatment groups and differences tested using ANOVA and chi-square tests. Based on recommendation not to focus on statistical tests of baseline differences we also calculated standardized absolute mean differences as the average absolute difference between all 6 comparisons of treatment groups (four choose 2) divided by the overall standard deviation. Values > 0.25 are considered to be non-trivial imbalance due to chance. Pearson correlation coefficients were used to examine the association between baseline healthy eating, gVLM, and cognitive and imaging measures.

The flavanol effect on the change in each outcome from baseline to 12 weeks was tested using linear mixed effects models controlling for the respective baseline measures, four categories of treatment, sex, age, and education. Regression adjusted mean within-group tests of change were estimated and tested for statistical significance from the model. The primary test used for assessing the treatment effect was the linear trend contrast from the model across: placebo, low, medium and high dose. The model for cognitive measures incorporated additional outcome measurement times at 4 weeks and 20 weeks and included categorical time (4, 12, 20 weeks) as a predictor as well as a treatment (4 category) by time interaction, and a random intercept to control for repeated measures within individuals (results for 4 and 20 weeks not presented). Additional regression models tested for treatment effect modification by baseline healthy eating and gVLM. Specifically, the baseline values of the aHEI or the gVLM were included in the mixed effects model along with its interaction with the 4 categories of with treatment. To

provide a more flexible relationship to be tested than simply linear associations, the aHEI and gVLM measures were trichotomized into low, medium, and high values based on tertiles. Post hoc tests of the treatment effect within each tertile of aHEI and gVLMB were performed when the interaction test was found to be significant at 0.10.

Analyses were carried out using SAS 9.4. Cohen's d effect sizes were calculated for all treatment effect to allow direct comparison of magnitude using the baseline standard deviation of each variable across all groups.