Effects of a high fat diet in young and middle-aged rats: Microbes and Microglia

*Saxena, J.[1], *Pesaresi, T.[1], Desphande, N.[1], Carrell, C.[2], Hill, B.[3], Ashby, G.[2], Liao, M-K.[4], Freeman, L.[5]

[1]Undergraduate Student, Neuroscience, Furman University; [2]Undergraduate Student, Department of Biology, Furman University, [3]Undergraduate Student, Department of Biology, Converse College, [4]Professor, Department of Biology, Furman University, [5]Assistant Professor, Neuroscience and Department of Biology, Furman University
linnea.freeman@furman.edu

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Abstract: Epidemiological data has implicated consumption of high fat diets in the development of dementia and other degenerative disorders. A potential mechanism for diet-induced cognitive impairment is inflammation. We investigated the effects of a high saturated fat diet on a spatial memory task, gut microbe levels, tight junction, and inflammatory protein expression, and microglial activation in both young and middle-aged Sprague Dawley rats. We hypothesized that a high saturated fat diet would impair cognition via gut microbe-induced neuroinflammation. After eight weeks on the diet, rats were subjected to the 12-day water radial arm maze. Fecal samples were collected to determine how the treatment affected the ratio of two major phyla of gut microbes: Firmicutes and Bacteroidetes. Western Blot and immunohistochemistry methods were used to assess protein expression and to visualize microglia in the hypothalamus and hippocampus, respectively. A significant increase in body weight was found for the middle-aged high fat group compared to all other groups ($p<0.05$). The middle-aged high fat group revealed increased Firmicutes and decreased Bacteroidetes relative to the middle-aged low fat group, whereas there was no difference between the young low fat and young high fat groups. Errors on the water radial arm maze were analyzed with a two-way ANOVA and determined no significant differences between groups. There was no significant difference in occludin or ox-6 expression between low fat and high fat groups. There was no significant difference in SMI-71 expression between low fat and high fat groups ($p>0.05$). These findings suggest that the dietary treatment length was sufficient to induce peripheral (gut) changes, but not inflammation in the central nervous system. However, microglial activation will be further analyzed to evaluate the effect of the high saturated fat diet on neuroinflammation.