Menopause is one of the most drastic hormonal changes that a woman goes through in her lifetime. Some women experience noticeable changes in memory and other cognitive measures while other women remain unaffected. There are many factors that could contribute to this differential symptom onset in postmenopausal women. This study examined primary fatty acid intake as one of these factors. The saturated fat, palmitic acid (PA), and the monounsaturated fat, oleic acid (OA), are the most common fatty acids in the American diet and were the two fatty acids involved in this study. Western diets typically consist of low OA and high PA (HPA), while Mediterranean diets consist of low PA and high OA (HOA). In a highly controlled, randomized, cross-over design, pre and postmenopausal women were given either a high PA (HPA) or high OA (HOA) diet for three weeks. Women underwent functional magnetic resonance imaging (fMRI) at the end of each dietary period to assess brain activation in tasks that measured working memory. Premenopausal women showed greater activation in the anterior cingulate cortex, caudate, and putamen in the HPA diet compared to the HOA diet, suggesting less efficient thinking patterns in the HPA diet. Postmenopausal women showed greater activation in the anterior cingulate cortex after the HOA diet compared to the HPA diet. These results suggest that hormonal changes involved in menopause may affect fatty acid metabolism that also affects brain activation in working memory tasks.