Deposited research article

Unraveling lipid metabolism with microarrays: Effects of arachidonate and docosahexaenoate acid on murine hepatic and hippocampal gene expression

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INTRODUCTION

The functions, actions, and regulation of polyunsaturated fatty acids (PUFAs) are just now beginning to be unraveled, in large due to modern molecular techniques. In the present work, mice were fed diets rich in either arachidonic acid (AA, *n*6), docosahexaenoic acid (DHA, *n*3), or the combination (AA+DHA). Both liver and hippocampus tissue were then analyzed through a combined gene expression-, lipid-, and behavioral- profiling strategy in order to annotate the molecular functions and targets of dietary PUFA.

RESULTS

Using Affymetrix technology, 329 and 356 differentially regulated transcripts were identified in the liver and hippocampus, respectively. Selected genes were grouped by expression patterns through a combined *k*-means/hierarchical clustering approach, and annotated using gene ontology classifications. Transcription profiles in both organs demonstrate that differences in gene expression arise with AA, DHA, and the combination. Many hepatic genes were known to be transcriptionally regulated by PPARα, HNFα, and SREBP-1; transcription factors implicated in lipid metabolism. The pattern of differentially regulated genes suggested that PUFA-feeding increased hepatic β-oxidation and gluconeogenesis while decreasing fatty acid synthesis. Lipid profiling and behavioral assessments were linked to hippocampal transcriptional profiles. Furthermore, novel hippocampal PUFA-molecular targets suggest that PUFA transcriptionally regulated genes with roles in appetite and learning.

CONCLUSIONS

Examining the global transcriptional effects of PUFAs has provided both confirmation of previously identified PUFA-mediated gene expression changes and provided novel gene targets for future study. Transcriptional-, lipid-, and behavioral- data were linked to further elucidate the importance of dietary PUFA. Furthermore, additional focused studies will identify population subsets that would specifically benefit from AA, DHA, or the combination.