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Commentary

Integrated Metabolic Regulations in Mice

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DESCRIPTION

Calorie Restriction (CR) is defined as 20%-40% reduction in calorie intake sufficient to maintain health without causing malnutrition. CR may inhibit disease progression and has been shown to protect against aging-related diseases, including cardiovascular and neurodegenerative diseases and cancer. However, the metabolic changes caused by CR responsible for these effects are poorly understood. Gas Chromatography-Mass Spectrometry (GC-MS), liquid chromatography or capillary electrophoresis in combination with MS and Nuclear Magnetic Resonance (NMR) are tools for high-throughput biomarker screening and profiling of metabolites that are increasingly used in medical diagnostics. The metabolomic analysis using these methods allows evaluating the changes in the relative abundance of low molecular weight metabolites such as Amino Acids (AA), Fatty Acids (FA), amines, organic acids and nucleosides in physiological and pathological contexts [1,2].

Among these methods, GC-MS can detect and quantify metabolites with a molecular weight of less than 650. And there is a crucial procedure in GC-MS metabolomics analysis, which requires derivatization of the metabolite extracts into volatile and thermally derivatives. GC-MS is a highly sensitive, high-throughput analytical platform and is widely used for non-targeted analyses of primary metabolism. In this study, we investigated CR-induced metabolic changes from the GC-MS-based high-throughput metabolomic profile of mouse biopsy samples. We analysed the levels of metabolites in tissues known to be affected by CR, including serum, heart, liver, kidney, cortex, hippocampus, lung, muscle, and white fat. Our findings provide new insights into the physiological effects of CR that could support future research efforts to identify potential dietary therapy for the disease. Metabolomic approaches are used to detect and analyse changes in the abundance of low molecular weight metabolites in biological samples [3].

CR diets will inevitably lead to significant changes in nutrient intake and metabolism. The whole body Transmitted Electron (TE) metabolism is involved in a question of dynamic balance. When food intake is decreased, nutrition comes primarily from fat and muscle tissue to meet the body's nutritional demand. As expected, we observed significant correlations between circulating metabolites and CR at baseline and after the intervention. Here, we used GC-MS and multivariate statistical analysis to examine the metabolic profile of mice after CR with the aim of identifying metabolites associated with the protective effects of CR and uncovering the underlying physiological mechanisms. CR improved markers of general health and body weight, and reduced plasma lipids, fasting glucose, and urea. Previous studies have reported that CR reduced epididymal fat mass by 26% in mice compared to controls, showing that CR can lead to rapid weight loss [4].

However, plasma creatinine levels were not significantly affected by the CR diet. Consistent with these results, functional pathways of KEGG enriched under CR included alanine, aspartate, glutamate metabolism, phenylalanine, tyrosine, tryptophan biosynthesis, and arginine biosynthesis. In this study, amino acids are the primary change in metabolites, implying that dietary protein may be the key determinant of CR on metabolism. We found that the concentration of most AAs in our study was reduced in the CR group. A high-protein CR diet cannot extend lifespan; Mice fed a low-protein diet lived longer than those fed a high-protein diet. Those who follow a high-protein diet are more likely to develop diabetes and cardiovascular mortality than those who follow a low-protein diet. Randomized controlled trials have shown that people fed a low-protein diet can improve metabolic health, reduce cancer incidence and mortality in people. CR retards aging by protein restriction and interferes with cell signaling pathways [5].

CONCLUSION

We have established GC-MS and multivariate statistical analysis for metabolomic analysis of tissue samples to study metabolic changes induced by CR. We found that CR altered the levels of various metabolites in several tissues, particularly with changes in AA and FA metabolism. Long-term CR could benefit the body; especially protein reduction has the effect of extending lifespan. However, the effect of short-term CR on metabolism

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could not rule out stress and other factors. Additionally, we will design this study at multiple time points rather than a single time point, which will help to understand metabolite changes. Moreover, further studies are needed to elucidate the specific molecular mechanisms associated with these effects and to determine whether these findings are applicable to humans. Nevertheless, our results provide a basis for future investigations of how CR can be used to extend lifespan and improve health.

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