Abstract 32

Metabolic Pathway Perturbation of Patients With Chronic Heart Failure and Comorbid Major Depressive Disorder

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Background: Metabolomics* is the systematic and theoretically comprehensive study of the small molecules that comprise a biological sample, eg, sera or plasma and enables detection and quantification of small molecules involved in metabolic and signaling pathways. Metabolic signatures for a disease may provide valuable biomarkers and insights about mechanisms of the disease and indication of future therapeutic search. Previous study using metabolomics indicated that depression and ischemic heart disease may be associated with alterations in the metabolism of lipids and neurotransmitters. In this study, we evaluate whether metabolomics differentiate depressed heart failure (HF) patients from their nondepressed counterparts.

Methods: We performed a metabolomic analysis of blood plasma from 80 patients who have chronic heart failure with a New York Heart Association class II or greater and left ventricular ejection fraction 45% or less. Of these, 40 had a diagnosis of major depressive disorder (MDD) and the other 40 had never experienced depression. Approximately 400 metabolites were analyzed, with comparisons made between the two groups. Two parameters were evaluated when considering statistical significance, namely the P value and the q-value.

Results: Several systems of metabolites were identified to be significantly altered in currently depressed HF patients compared with HF patients who had no depression, including elevation of several excitatory amino acids that are activators of glutamatergic receptors, reduction of 3-hydroxybutyrate level, increase in dicarboxylic acid (DCA) formation with fatty acids metabolism, reduction of inositol metabolism, elevation of phenylalanine, and elevation of muscle protein catabolism.

Conclusion: These observations suggest that among patients with significant HF, metabolomics is able to differentiate metabolic profiles for the depressed from the nondepressed, which may enhance understanding of underlying pathology of depressed population. Whether treatment of depression may modify those alterations needs to be examined.

* Metabolomics: A global biochemical approach to the study of neuropsychiatric diseases. Metabolomics, the omics science of biochemistry, is a global approach to understanding regulation of metabolic pathways and metabolic networks of a biological system. Metabolomics complements data derived from genomics, transcriptomics, and proteomics to assist in providing a systems approach to the study of human health and disease. The metabolome defines a metabolic state as regulated by a net of interactions between genes and environment and provides useful information to bridge the gap between genotype and phenotype. Metabolomics became part of the NIH Roadmap vision in 2003 and is a rapidly expanding field.