Metabolomics Investigation of Opiate Addiction: Golestan Cohort Study

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Opiate addiction is a major health crisis, with numerous potential adverse health outcomes, such as cancer, infectious diseases, and psychological disorders. In the 1960s, Dole and Nyswander conducted clinical trials that lead to the theory that addiction is initiated through a disruption in metabolism that results in persistent neurochemical disturbances. Investigators have also shown that opiate exposure can modulate expression of genes involved in neuroplasticity, which could also result in long-term metabolic disruptions. Metabolomics can be used to reveal perturbations in metabolism that results from exposure, and holds promise for determining markers of addiction, withdrawal, and relapse. We conducted a pilot study to test the feasibility of metabolomics approach to reveal biomarkers of opiate exposure using urine samples obtained from 13 opium users and 3 subjects (run in triplicate) who have never used opiate. NMR metabolomics revealed four metabolites (creatinine, phenylalanine, N- phenylacetylglycine and dimethylxanthine) that contribute to the differentiation of the case and control groups. A subsequent study includes the NMR and LC-MS metabolomics analysis of urine samples from the Golestan cohort with stratification by opiate and tobacco use. The metabolomics profiles of samples from 300 current daily and 120 non-daily opiate users (stratified by sex, oral and inhalation route of exposure, and tobacco use) will be compared with profiles obtained for 90 non user controls (stratified by tobacco use). This study can lead to the identification of metabolites that can improve our knowledge of underling etiology and molecular pathways of opiate addiction.