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DNA Methylation of Candidate Genes (ACE II, IFN-γ, AGTR 1, CKG, ADD1, SCNN1B and TLR2) Implication in Substance Use Disorders (SUD) in Essential Hypertension

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Background: Physical, chemical, substance use disorder (SUD) adversely affect molecular process, resulting in cell signal transduction and transcription factor dysregulation, hence impaired gene expression and abnormal protein synthesis.

Rationale/Significance: With CVDs as the leading cause of mortality in the US and blacks/African Americans being disproportionate affected with hypertension (HTN), understanding aberrant epigenomic modulations due to SUD, is relevant in narrowing black-white mortality risk differences**.**

Hypothesis/Method: A quantitative evidence synthesis (QES) was utilized in this modeling, indicative of null correlation between SUD and HTN. Data were extracted from studies on: (a) Epigenomic modulations in HTN (SUD-nonSUD) based on ACE II (b) TLR2, (c) IFN-γ gene, (d) CAPG, ADD1, TIMP3, MEST loci, and mDNA. The random-effect QES was used for a pooled estimate as common effect size (CES), while z statistic and I^2 were used for the homogeneity of CES and between studies on heterogeneity respectively.

Results: Of the 642 studies identified, five examined hypermethylation while seven studies assessed hypomethylation in association with SUD and HTN. The hypermethylation of ACE II, SCNN1B, CKG, IFN-γ gene, and miR-510 promoter were associated with hypertension, the CES = 6.0%, 95% CI, −0.002–11.26. In addition, the hypomethylation of TLR2, IFN-γ gene, ADD1, AGTR1, and GCK correlated with hypertension, the CES = 2.3%, 95% CI, −2.51–7.07.

Conclusion: The aberrant epigenomic modulation of ACE II, TLR2, IFN-γ, AGTR1, and GCK correlated with essential HTN. Transforming SUD due to epigenomic lesions will facilitate early intervention mapping in reducing HTN in the US population, mainly socially disadvantaged individuals.