Heterogeneous Mediation Analysis on Epigenomic PTSD and Traumatic Stress in a Predominantly African American Cohort

Abstract

DNA methylation (DNAm) has been suggested to play a critical role in post-traumatic stress disorder (PTSD), through mediating the relationship between trauma and PTSD. However, this underlying mechanism of PTSD for African Americans still remains unknown. To fill this gap, in this paper, we investigate how DNAm mediates the effects of traumatic experiences on PTSD symptoms in the Detroit Neighborhood Health Study (DNHS) (2008–2013) which involves primarily African Americans adults. To achieve this, we develop a new mediation analysis approach for high-dimensional potential DNAm mediators. A key novelty of our method is that we consider heterogeneity in mediation effects across sub-populations. Specifically, mediators in different sub-populations could have opposite effects on the outcome, and thus could be difficult to identify under a traditional homogeneous model framework. In contrast, the proposed method can estimate heterogeneous mediation effects and identifies sub-populations in which individuals share similar effects. Simulation studies demonstrate that the proposed method outperforms existing methods for both homogeneous and heterogeneous data. We also present our mediation analysis results of a dataset with 125 participants and more than 450, 000 CpG sites from the DNHS study. The proposed method finds three sub-groups of subjects and identifies DNAm mediators corresponding to genes such as HSP90AA1 and NFATC1 which have been linked to PTSD symptoms in literature. Our finding could be useful in future finer-grained investigation of PTSD mechanism and in the development of new treatments for PTSD.