

Integrating Genome-Wide Association Study, Chromosomal Enhancer Maps and Element-gene Interaction Networks Detected Brain Regions Related Associations between Elements and ADHD/IQ

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Abstract

OBJECTIVE:

To explore the associations between chemical elements and attention deficit hyperactivity disorder (ADHD)/intelligence quotient (IQ).

METHODS:

We applied elements related gene set enrichment analysis (ERGSEA) to explore the relationships between elements and ADHD/IQ. The GWAS dataset of ADHD was derived from the Psychiatric Genomics Consortium, involving 55,374 individuals. The GWAS dataset of IQ was derived from UK Biobank web-based measure ($n = 17,862$), UK Biobank touchscreen measure ($n = 36,257$), CHIC consortium ($n = 12,441$) and five additional cohorts ($n = 11,748$). Enhancer-gene datasets of eight brain tissues consist of 935 individuals. Utilizing the published GWAS summary and eight brain region-related chromosomal enhancer maps to obtain the SNP association testing signals. The element-gene interaction datasets of 21 elements were downloaded from the comparative toxicogenomics database (CTD).

RESULTS:

ERGSEA observed significant associations between 4 elements and ADHD, such as Al at Hippocampus Middle (P value = 0.040), As at Angular Gyrus (P value = 0.007) and Na at Hippocampus Middle (P value = 0.026). Additionally, ERGSEA identified that 5 elements were associated with IQ, mainly including Al at Dorsolateral Prefrontal Cortex (P value = 0.017), As at Dorsolateral Prefrontal Cortex (P value = 0.004) and Pb at Germinal Matrix (P value = 0.045).

CONCLUSION:

Our study results provide novel clues for understanding the associations between elements and ADHD/IQ. This study also illustrated the good performance of ERGSEA approach for complex diseases.