To explore the association of Molecular, Genetic, and Environmental markers in Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder and Cerebral Palsy: A Cross-Sectional Study





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INTRODUCTION

- Over the last few decades, there has been increasing evidence of industrial chemicals, heavy metals in particular, as contributors to neurodevelopmental disorders(NDD) [1].
- It has been proposed that 25 % of the NDDs are the result of an interaction between environmental factors and inherited susceptibilities [2]

OBJECTIVE

To analyze the levels of heavy metals and essential micronutrients, along with molecular analysis, in blood, urine, hair and nail of children with Autism spectrum disorder (ASD), Attention deficit Hyperactivity disorder (ADHD) and Cerebral Palsy (CP) and their comparison with neurotypical controls.

MATERIALS AND METHODS

- Ongoing cross-sectional study at All India Institute of Medical Sciences, New Delhi, funded by the Department of Health research, Indian Council of **Medical Research**
- Inclusion Criteria: Children with ASD: 18 months to 18 years, fulfilling DSM 5 criteria, ADHD:6-18 years fulfilling DSM 5 criteria, Cerebral Palsy: 2-18 years, and controls: 18 months-18 years with IQ>70 on Malin's Intelligence scale for Indian children without any motor impairment or behavior issues were included.
- Those who were on special diet, health supplements, chelating agents, chronic systemic diseases and pre-existing micronutrient deficiencies were excluded.
- Blood, Urine, Hair and Nail samples underwent analysis for 21 heavy metals and trace elements.
- Additionally, an OMICs- based approach examined the molecular drivers of ASD, CP and ADHD through SNP, and methylation analysis.

CONTACT DETAILS

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RESULTS

- N=781, 320 (ASD), CP (293), ADHD (80), CN (88)
- Mean age: 5.75 ± 3.14(ASD), 6.57 ± 3.58(CP), 9.77 ± 2.44(ADHD), 7.31 ± 4.23(control)
- Sex ratio (Male: Female): 2.7:1(ASD), 1.3:1 (CP), 2:1(ADHD), 0.6:1(control)
- Molecular analysis revealed differential methylation of genes associated with neuronal developmental pathways(SGCE, ZDHHC3, HMGA1, SYT2, PRCC2). In ADHD, 412 genomic loci were differentially hypomethylated while 1218 loci were hypermethylated. In CP, 226 loci were hypomethylated and 890 were hypermethylated while in ASD 12 loci were hypomethylated and 120 were hypermethylated. (Figure 1)
- In comparison to control group, the average levels (micg/l) of following heavy metals were found significantly in higher proportion (P<0.05) in children with various neurodevelopmental disorders (Table 1; Figure 2)
- 52% children with ASD,55% with ADHD and 38% with CP, showed lead levels of >5mcg/L in blood.
- Iron and Zinc were the common micronutrients which were found deficient in blood.

comparison to control group				
Disorder	Blood	Urine	Hair	Nail
ASD	Lead (P=0.03) Chromium (P=0.02) Beryllium (P=0.006) Cobalt (P=0.0005) Mercury	Cobalt (P=0.0007) Cadmium Arsenic Thallium Antimony	Lead (P=0.02), Chromium (P=0.001) Cobalt (P=0.01), Magnesium, Selenium Columbium, Vanadium Manganese, Nickel, Arsenic, Cadmium	Lithium Vanadium Cadmium
ADHD	Lead (P=0.03) Chromium (P=0.009) Cobalt (P=0.02)	Cadmium Arsenic Antimony Thallium	Vanadium Nickel	Cobalt (P=0.01) Cadmium Arsenic
Cerebral Palsy	Lead (P=0.001) Chromium (P=0.009) Beryllium Cobalt (P=0.0001) Mercury	Lead (P=0.01) Selenium, Aluminium Cobalt (P=0.04), Arsenic Cadmium, Antimony Thallium	Chromium (P=0.001), Magnesium Lithium, Vanadium Manganese, Nickel Arsenic, Cadmium	Chromium (P=0.001), Cobalt (P=0.01), Magnesium, Lithium, Aluminium, Titanium, Vanadium, Manganese, Nickel ,Zinc, Arsenic Cadmium, Thallium
CONCLUSION				

- Landrigan, P. J., Lambertini, L., & Birnbaum, L. S. (2012). A research strategy to discover Amongst all heavy metals, Lead, chromium and cobalt were the most common the environmental causes of autism and neurodevelopmental disabilities. Environmental heavy metals found in higher levels in all the three neurodevelopmental disorders. health perspectives, 120(7), a258-a260.
- Children with ASD showed higher levels of Lead, Chromium and Cobalt in blood 2. Heng, Y. Y., Asad, I., Coleman, B., Menard, L., Benki-Nugent, S., Hussein Were, F., ... & and hair. Children with cerebral palsy showed contamination with higher number McHenry, M. S. (2022). Heavy metals and neurodevelopment of children in low and of heavy metals than other groups. middle-income countries: A systematic review. PLoS One, 17(3), e0265536.



Figure 1: Methylation Array

Methylation Array

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Figure 2: Box plot showing the distribution of heavy metals in neurodevelopmental disorders and neurotypical controls

REFERENCES

