Neonatal aluminium and cadmium co-exposures induce behavioural deficits and oxido-inflammatory imbalance in the mice brain.

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Background

Aluminium (Al) and cadmium (Cd) are known to be ubiquitously available in the environment with high risk of food-chain mediated co-exposures (1, 2). They are known to possess several neurotoxic effects and is implicated in the development of several neurodevelopmental and neurodegenerative diseases (3). With the increasing rate of industrial pollution and changes in lifestyle and consumption patterns, understanding the neurotoxic responses and mechanism of co-exposures of cadmium and aluminum mediated effects on neurodevelopmental pathologic indices becomes very imperative.

Methods

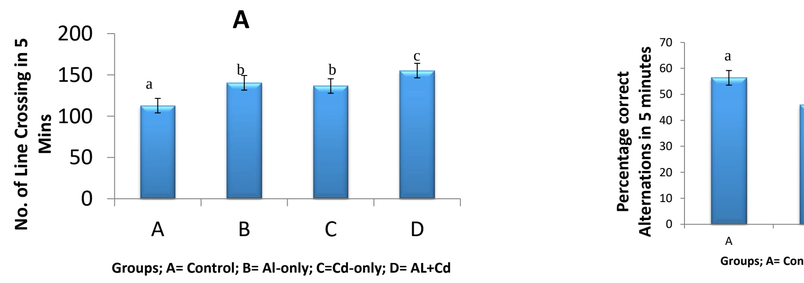
On the confirmation of pregnancy after a programmed mating, swiss mice were monitored to delivery before distribution into five different treatment groups at day 7 after delivery known as postnatal day 7 (PSD 7). Group A served as control, group B was administered 2.5mg/Kg body weight of aluminium chloride ($AlCl_3$), C was administered 0.5mg/kg body weight of cadmium chloride ($CdCl_2$) while group D was co-administered same doses of Al and Cd as in groups B and C. Intraperitoneal administration of metals was done once a week from postnatal day 7(PD7) to postnatal day 35 (PD35). Behavioural tests for hyper locomotion, spatial and non spatial working memory were carried out using Open field, Y-maze and novel object recognition test (NORT) on PD 55-57. Mice were sacrificed on postnatal day 58 while the brains were harvested and the prefrontal cortex (PFC), stratum (ST) and hippocampus (HP) were processed for oxido-inflammatory indices as previously reported (4).

Statistical analysis

Data was expressed as Mean ± SD p,0.05was considered as statistically significant using a one way anova $p < 0.05$ analyzed using the one way analysis of variance followed by Bonferonni mutiple comparison test.

Results and Discussion

The results showed that aluminium and cadmium singly administered increased hyper locomotive activities (lines crossed), reduced percentage alternations and increased novel object discrimination index (DI) compared to control. When compared together, these effects were more prominent in Cd-only group relative to Al-only group. These effects were further increased in the co-exposed group compared to control and the singly treated groups (B and C).



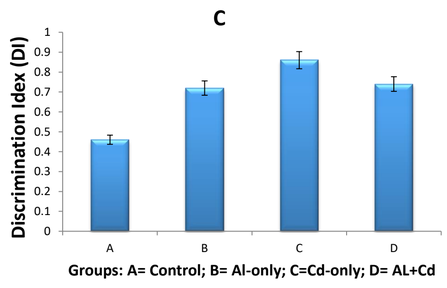
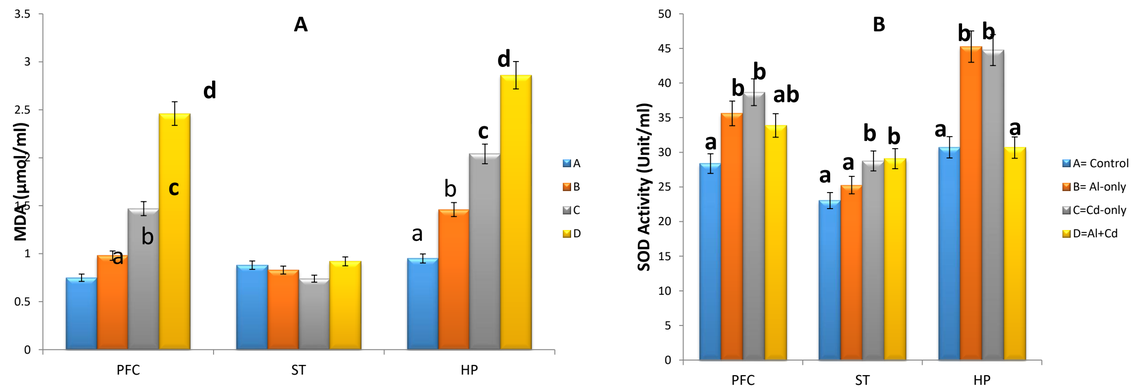


Fig. 1: Neonatal Al and Cd Co-exposure induces behavioural deficits
A: Number of line crossings in OFT; B: Percentage correct alternations in YMT, C: Discrimination index in NORT. Figure represents Mean+SD of 5 determinations. Bars with different alphabet superscripts indicates a significant difference ($p<0.05$) when compared across groups.

Oxidative stress indices showed increase on levels of malondialdhyde (MDA) in the PFC and HP. Activities of catalase, superoxide dismutase (SOD) and acetylcholinesterase significantly increased in the PFC, HP and ST while levels of reduced glutathione ws observed



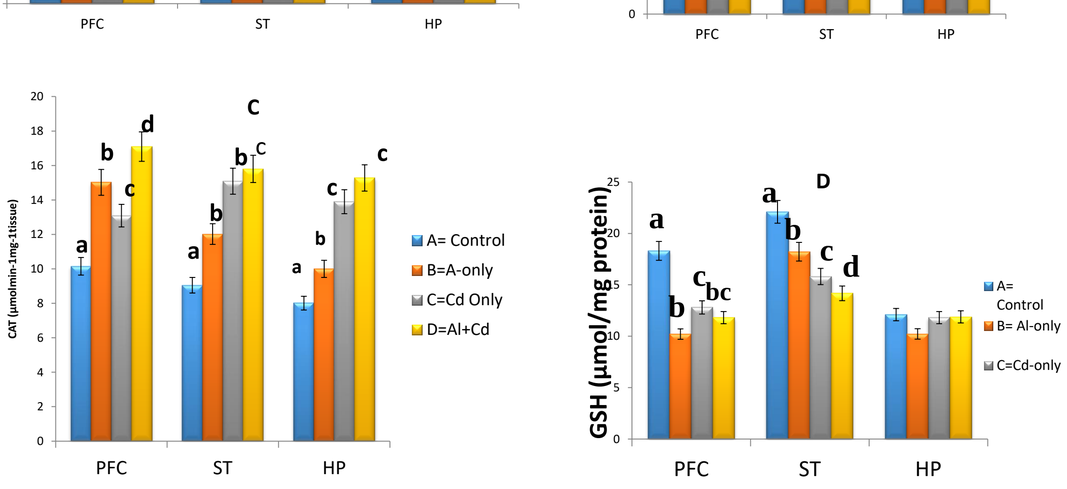


Fig. 2: Effect of neonatal Al and Cd Co-exposure on selected Oxidative stress indices
A: Malondialdehyde (MDA); B:Superoxide Dismutase (SOD) activity; C: Catalase (CAT) activity; D: Reduced glutathione (GSH). Figure represents Mean+SD of 5 determinations. Bars with different alphabet superscripts indicates a significant difference ($p<0.05$) when compared across groups.

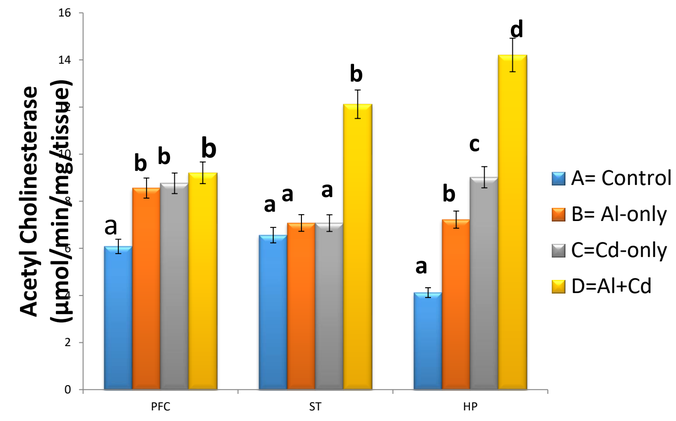


Fig. 3: Effect of neonatal Al and Cd Co-exposure on Acetyl cholinesterase activity
Figure represents Mean+SD of 4 determinations. Bars with different alphabet superscripts indicates a significant difference ($p<0.05$) when compared across groups

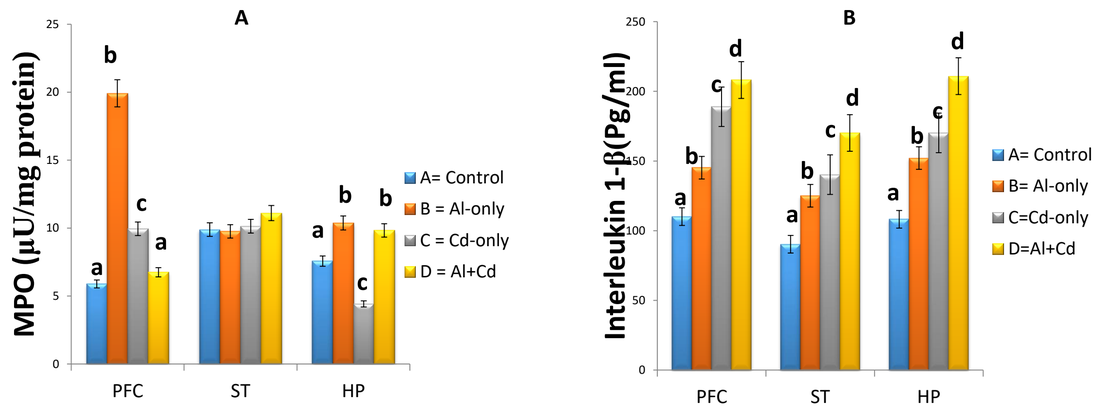


Fig. 4: Effect of neonatal Al and Cd Co-exposure on Inflammatory imbalance
A: Activity of the inflammatory enzyme (MPO) B: Levels of inflammatory cytokine (IL-1-β) in PFC, ST and HP. Figures represents Mean+SD of 4 determinations. Bars with different alphabet superscripts indicates a significant difference ($p<0.05$) when compared across groups.

Conclusions

Our findings suggests that neonatal co-exposures of aluminium and cadmium induced behavioural modifications relative to hyper locomotion and memory deficits found in several neurodevelopmental pathologies. These behavioural modifications may have ocured in response to altered oxido-inflammatory balance in the mice brain.

References

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