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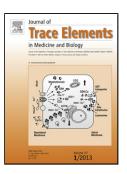
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### ACCEPTED MANUSCRIPT

# Trace element levels are associated with neuroinflammatory markers in children with autistic spectrum disorder

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#### **Highlights:**

- The association between serum trace elements and neuroinflammation was assessed
- Serum Fe, Cu, Mn, Cd levels are interrelated with neuroinflammation in autism
- High serum Mg levels were associated with lower rate of inflammation
- Modulation of trace element status may be used for reduction of neuroinflammation

#### Abstract

The objective of the present study was to estimate the association between brain inflammatory markers and serum trace element levels as assessed by inductively coupled plasma mass spectrometry at NexION 300D. Leukocyte elastase (LE),  $\alpha$ 1-proteinase inhibitor ( $\alpha$ 1-PI) activity, anti-nerve growth factor-antibodies (anti-NGF-Ab), and antimyelin basic protein-antibodies (anti-MBP-Ab) levels were assessed as inflammatory markers. The obtained data demonstrate that the increase in LE and  $\alpha$ 1-PI activity is associated with higher serum Cr and Cu levels, respectively. The increase in Anti-NGF-Ab levels was associated with a nearly significant 16% increase in serum Mn levels. Autistic children with high MBP-Ab levels were characterized by 28% higher serum Mn and lower Mg concentration. The results of correlation analysis were generally in agreement with the outcome of group comparisons. Regression analysis demonstrated that serum Mg was significantly negatively associated with LE activity, whereas both serum Fe and V concentrations were characterized by a positive influence on the parameter. In turn, serum Cu was a significant predictor of  $\alpha$ 1-PI, as well as Cr levels. At the same time, the serum concentrations of Cd and Fe were found to be inversely associated with al-PI levels. Serum Cd and Mn levels were significant positive predictors of anti-MBP-Ab levels, whereas Mg levels had a negative impact on anti-MBP-Ab values. Generally, the obtained data demonstrate the interrelationship between trace element homeostasis and neuroinflammation in autism. Hypothetically, modulation of trace element status may be used for reduction of neuroinflammatory response, although further studies are required to reveal the underlying mechanisms of the observed associations.

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