

Original Article

Toxicity biomarkers in autism spectrum disorder: A blinded study of urinary porphyrins

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Abstract ***Background:*** Recent studies suggest that children diagnosed with an autism spectrum disorder (ASD) have significantly increased levels of urinary porphyrins associated with mercury (Hg) toxicity, including pentacarboxyporphyrin (5cxP), precoproporphyrin (prcP), and coproporphyrin (cP), compared to typically developing controls. However, these initial studies were criticized because the controls were not age- and gender-matched to the children diagnosed with an ASD. ***Methods:*** Urinary porphyrin biomarkers in a group of children (2–13 years of age) diagnosed with an ASD ($n = 20$) were compared to matched (age, gender, race, location, and year tested) group of typically developing controls ($n = 20$). ***Results:*** Participants diagnosed with an ASD had significantly increased levels of 5cxP, prcP, and cP in comparison to controls. No significant differences were found in non-Hg associated urinary porphyrins (uroporphyrins, hexacarboxyporphyrin, and heptacarboxyporphyrin). There was a significantly increased odds ratio for an ASD diagnosis relative to controls among study participants with precoproporphyrin (odds ratio = 15.5, $P < 0.01$) and coproporphyrin (odds ratio = 15.5, $P < 0.01$) levels in the second through fourth quartiles in comparison to the first quartile. ***Conclusion:*** These results suggest that the levels of Hg-toxicity-associated porphyrins are higher in children with an ASD diagnosis than controls. Although the pattern seen (increased 5cxP, prcP, and cP) is characteristic of Hg toxicity, the influence of other factors, such as genetics and other metals cannot be completely ruled out.

Key words autism, autism spectrum disorder, heavy metal, mercury, porphyrins, toxicity.

Introduction

An autism spectrum disorder (ASD) is a neurological disorder that limits a person's ability to function normally. Behavioral abnormalities, social limitations, sensory processing abnormalities, and impaired ability to communicate are the main issues in these multifaceted disorders, which range in clinical symptoms, from severe to mild among individuals diagnosed with autistic disorder (autism), pervasive developmental delay not otherwise defined (PDD-NOS), to Asperger's disorder.^{1,2}

Although the role of mercury (Hg) in the pathology of autism is still being debated, many studies suggest that Hg levels are higher in children with autism than in typically developing children (controls), e.g. studies that examine Hg levels in hair, blood, urine, and teeth.³ A more recent approach is to use urinary porphyrins as measure of Hg body-burden. Previous studies have shown that urinary porphyrins (heme precursors formed in the

heme synthesis pathway, Fig. 1) can afford a measure of xenobiotic exposure, particularly Hg.^{5–7} Specific patterns of urinary porphyrins suggest the presence of Hg. Hg toxicity has been demonstrated to be associated with elevations in urinary coproporphyrin (cP), pentacarboxyporphyrin (5cxP), and by the expression of an atypical porphyrin–precoproporphyrin (prcP) (also known as keto-isocoproporphyrin) not found in the urine of unexposed controls. Woods⁵ noted that these distinct changes in urinary porphyrin concentrations were observed as early as 1–2 weeks after initiation of Hg exposure, and that they increased in a dose- and time-related fashion with the concentration of Hg in the kidney, a principal target organ of Hg compounds. In addition, urinary porphyrin profiles were also shown to correlate significantly with Hg body-burden and with specific neurobehavioral deficits associated with low level Hg exposure. Woods⁵ concluded that urinary porphyrin profiles are a useful biomarker for Hg exposure and its potential adverse health effects in human subjects.

Recent evidence suggests that the levels of Hg-associated porphyrins are different in children having a diagnosis of an ASD as compared to those levels in controls. Studies revealed that children with an ASD diagnosis had significantly increased levels

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