An Investigation of Porphyrinuria in Australian Children with Autism

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Two recent studies, from France (Nataf et al., 2006) and the United States (Geier & Geier, 2007), identified atypical urinary porphyrin profiles in children with an autism spectrum disorder (ASD). These profiles serve as an indirect measure of environmental toxicity generally, and mercury (Hg) toxicity specifically, with the latter being a variable proposed as a causal mechanism of ASD (Bernard et al., 2001; Mutter et al., 2005). To examine whether this phenomenon occurred in a sample of Australian children with ASD, an analysis of urinary porphyrin profiles was conducted. A consistent trend in abnormal porphyrin levels was evidenced when data was compared with those previously reported in the literature. The results are suggestive of environmental toxic exposure impinging upon heme synthesis. Three independent studies from three continents have now demonstrated that porphyrinuria is concomitant with ASD, and that Hg may be a likely xenobiotic to produce porphyrin profiles of this nature.

Autism is a neurodevelopmental disorder presenting in childhood that affects up to 1 in 150 children in the United States (Centers for Disease Control, 2006) and 1 in 160 in Australia (Wray & Williams, 2007). Autism is characterized by severe impairments in socialization, communication, and behavior (American Psychiatric Association, 1994). The prevalence of autism is increasing at epidemic rates (Yazbak, 2003) that cannot be accounted for by changing diagnostic criteria or improved diagnostic systems (Blaxill et al., 2003; Croen et al., 2002).

Mercury (Hg) toxicity has been proposed as a causal mechanism whereby a small subset of children are uniquely sensitive to Hg and, in such individuals, exposure triggers a cascade of events leading to autism (Bernard et al., 2001; Mutter et al., 2005; Kern & Jones, 2006). Urinary porphyrins provide a convenient and non-invasive measure of xenobiotic exposure generally (Brewster, 1988) and of Hg specifically (Woods et al., 2005; Heyer et al., 2006).

Excess urinary porphyrin excretion (porphyrinuria) results from the inhibition of enzymatic steps in conditions including genetic deficiencies in heme production enzymes, hepatitis, renal disease, and erythroid disease (Gross et al., 2000), as well as by heavy metal inhibition (Bowers et al., 1992; Woods, 1996). The causal relationship between Hg and porphyrinuria has been demonstrated both in rats (Pingree et al., 2001) and in humans (Woods et al., 1993).

The steps in the heme pathway most vulnerable to heavy metal inhibition are those that involve uroporphyrin decarboxylase (Woods & Kardish, 1983) and coproporphyrinogen oxidase (Woods et al., 2005). The result of these inhibitions is specific elevations of urinary coproporphyrin and pentacarboxyporphyrin levels. Although nonmetal agents targeting the heme pathway also elevate urinary porphyrin levels (Daniell et al., 1997), precoproporphyrin (also known as keto-isocoproporphyrin) is produced by in vivo conversion of pentacarboxyporphyrin in the presence of heavy metal, providing a specific porphyrin marker for Hg exposure (Woods et al., 2005; Heyer et al., 2006).

Two previous studies reported porphyrinuria among autistic subjects consistent with elevated body burden of Hg (Nataf et al., 2006; Geier & Geier, 2007). The pattern is one of generalized porphyrinuria with marked elevation of coproporphyrin and of precoproporphyrin and of the ratio of coproporphyrin/urophorphyrin. This study aimed to examine this phenomenon among a group of Australian autistic children.

METHODS

Subjects

Urinary porphyrin profiles were obtained from 41 consecutive patients with an ASD presenting to the first author’s psychology clinic from October 2006 through March 2008. Each patient was previously diagnosed with an ASD, by a health professional, based upon accepted international