Porphyrinuria in childhood autistic disorder: Implications for environmental toxicity

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Abstract

To address a possible environmental contribution to autism, we carried out a retrospective study on urinary porphyrin levels, a biomarker of environmental toxicity, in 269 children with neurodevelopmental and related disorders referred to a Paris clinic (2002–2004), including 106 with autistic disorder. Urinary porphyrin levels determined by high-performance liquid chromatography were compared between diagnostic groups including internal and external control groups. Coproporphyrin levels were elevated in children with autistic disorder relative to control groups. Elevation was maintained on normalization for age or to a control heme pathway metabolite (uroporphyrin) in the same samples. The elevation was significant (P < 0.001). Porphyrin levels were unchanged in Asperger’s disorder, distinguishing it from autistic disorder. The atypical molecule precoproporphyrin, a specific indicator of heavy metal toxicity, was also elevated in autistic disorder (P < 0.001) but not significantly in Asperger’s. A subgroup with autistic disorder was treated with oral dimercaptosuccinic acid (DMSA) with a view to heavy metal removal. Following DMSA there was a significant (P = 0.002) drop in urinary porphyrin excretion. These data implicate environmental toxicity in childhood autistic disorder.

Keywords: Autism; Asperger; Porphyrin; Mercury; Pervasive Developmental Disorder

Introduction

Autism is a disorder of reciprocal social interaction, behavioral repertoire, and language and communication. Because the phenotype ranges from manifest disability to specific performance elevation, the term Autistic Spectrum Disorder (ASD) (Wing, 1996; Gillberg and Coleman, 2000) is now commonly used to denote the DSM-IV (American Psychiatric Association, 1994) group of pervasive neurodevelopmental disorders encompassing autistic disorder, Asperger’s disorder, Rett’s disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS). A fraction of cases have a defined genetic cause, but the apparent increase in prevalence of ASD (California Department of Human Developmental Services, 2003; Smeeth et al., 2004; Barbaresi et al., 2005), as reviewed (Blaxill, 2004), is suggestive of an environmental contribution. Changes in awareness and diagnostic criteria may explain some of the rise (Croen et al., 2002; Rutter, 2005), but a true increase in prevalence has not been excluded (Rutter, 2005). Elevated ASD rates in urban versus rural areas (Deb and Prasad, 1994; Palmer et al., 2006; Williams et al., 2006) are consistent with an environmental contribution. Several sporadic reports have suggested an association between heavy metal exposure and ASD (Cohen et al., 1982; Accardo et al., 1988; Shannon and Graef, 1996; Lidsky and Schneider, 2005). Superficial similarity between mercury toxicity and ASD has prompted discussion of mercury exposure in the etiology of the disorders (Bernard et al., 2001), while ASD prevalence in Texas schools correlated with local environmental release of mercury (Palmer et al., 2006).

To address an environmental contribution to ASD, several studies have explored the body burden of heavy metals. Because