

Type 1 Diabetes and Autism

Is there a link?

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The prevalence of diabetes in children and youth <18 years of age is ~1 in 400–500 (1). The prevalence of diabetes for those aged <19 years from 1995–2000 in Ontario was 1.87 per 1,000 (2). Type 1 diabetes is recognized as a T-cell-mediated autoimmune process with a strong genetic contribution (3,4).

In 2003, the prevalence of autism spectrum disorder was reported in one study as 3.4 per 1,000 children (5) and in another as 6.7 per 1,000 children (4 per 1,000 children with autism) aged 3–10 years (6) in the U.S. Like type 1 diabetes, both immune-mediated and genetic factors have been implicated in the development of autism (7,8). Based on recent clinical experiences and on the putative autoimmune etiology of these two conditions, we hypothesized that there would be an increased prevalence of autism spectrum disorder in a population of children with type 1 diabetes.

To investigate this hypothesis, a retrospective chart review of nearly 1,000 children with type 1 diabetes followed at the Diabetes Clinic at The Hospital for Sick Children was performed to identify children with autism spectrum disorder.

RESEARCH DESIGN AND METHODS

Children with both type 1 diabetes and autism spectrum disorder were identified ($n = 9$) by a retrospective chart review of all children with diabetes ($n = 984$ in 2002) attending the

Diabetes Clinic at The Hospital for Sick Children. With respect to autism spectrum disorder, the data selected included age at diagnosis, method of diagnosis, and family history of autism spectrum disorder or learning disorders. For those identified, the diagnosis of autism spectrum disorder had been made previously by either a psychiatrist or developmental pediatrician.

The 95% CI was calculated for the prevalence of autism spectrum disorder in our population of children with type 1 diabetes.

RESULTS — Of 984 individual children with diabetes seen in our Diabetes Clinic in 2002, 9 were identified as having autism spectrum disorder (0.9% [95% CI 0.3–1.5]). There were seven male and two female subjects.

The median age at diagnosis of autism spectrum disorder was 4.8 years (range 3.3–6.8), while that for type 1 diabetes was 8.2 years (range 0.8–13.5). In five children, the diagnosis of autism spectrum disorder was made following evaluation by a staff psychiatrist or developmental pediatrician at The Hospital for Sick Children. The diagnosis was made in two children following evaluation by developmental pediatricians in the community. Three children were also identified as having a family history of some form of developmental disorder.

CONCLUSIONS — Our data suggest that the prevalence of autism spectrum disorder in children with type 1 diabetes attending the Diabetes Clinic at The Hospital for Sick Children, Toronto, may be greater than that in the general population (0.9% [95% CI 0.3–1.5] vs. 0.34–0.67) (4,6). Certain factors may account for this finding, including a common autoimmune pathogenesis. In 1971, Money et al. (9) reported a possible association between autism and a family history of autoimmune disease in a case report. In addition, Denney et al. (10) described a lower percentage of helper-inducer cells and a decreased helper-to-suppressor cell ratio in children with autism, as well as a lower percentage of lymphocytes expressing bound interleukin-2 receptors, following mitogenic stimulation compared with control subjects. These findings were inversely related to the severity of autistic symptoms. Gupta et al. (11) reported findings that suggest that an imbalance of Th1- and Th2-like cytokines may be important in the pathogenesis of autism. Similarly, Plioplys et al. (12) reported on 11 of 17 patients with autism who had findings suggestive of “incomplete activation” of T-cells, a finding also seen in autoimmune diseases. Comi et al. (13) reported an increased incidence of autoimmune diseases in mothers of patients with autism compared with control mothers. A recently reported link between autism and autoimmune thyroid disorder increases the likelihood of finding some shared autoimmune etiologic process (14). Furthermore, autoantibodies implicated in autoimmune thyroid disorders are found with an increased prevalence in patients with type 1 diabetes (15–17).

A possible referral bias, the small sample size, and the absence of specific autism surveillance measures used for all children attending the Diabetes Clinic limit the generalizability of these findings. However, while our findings must be viewed as preliminary, our experience suggests that a large multicenter study involving a large sample size is required to

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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confirm or refute an association between these two conditions.

Our report of an increased prevalence of autism spectrum disorder in a population of children with type 1 diabetes emphasizes the need to recognize a potential association between these two diseases allowing for better overall patient identification and referral for appropriate care. Confirmation of an association between type 1 diabetes and autism spectrum disorder may provide important insights into the pathogenesis of both conditions.

References

- Centers for Disease Control and Prevention/National Center for Chronic Disease Prevention and Health Promotion: National diabetes fact sheet [article online], 2000. Available from <http://www.cdc.gov/diabetes/pubs/facts98.htm>. Accessed 3 March 2004
- To T, Curtis JR, Daneman D: Diabetes in children. In *Diabetes in Ontario*. Hux J, Booth G, Slaughter P, Laupacis A, Eds. Toronto, ICES, 2003, p. 219–230
- Bach JF: Insulin-dependent diabetes mellitus as an autoimmune disease. *Endocr Rev* 15:516–542, 1994
- Devendra D, Liu E, Eisenbarth GS: Type 1 diabetes: recent developments. *BMJ* 328:750–754, 2004
- Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C: Prevalence of autism in a US metropolitan area. *JAMA* 289:49–55, 2003
- Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decoufle P: Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. *Pediatrics* 108:1155–1161, 2001
- Farber JM: Autism and other communication disorders. In *Developmental Disabilities in Infancy and Childhood*. 2nd ed. Capute AJ, Accardo PJ, Eds. Baltimore, MD, Brookes, 1996, p. 347–364
- Szatmari P, Jones MB, Zwaigenbaum L, MacLean JE: Genetics of autism: overview and new directions. *J Autism Dev Disord* 28:351–368, 1998
- Money J, Bobrow NA, Clarke FC: Autism and autoimmune disease: a family study. *J Autism Child Schizophr* 1:146–160, 1971
- Denney DR, Frei BW, Gaffney GR: Lymphocyte subsets and interleukin-2 receptors in autistic children. *J Autism Dev Disord* 26:87–97, 1996
- Gupta S, Aggarwal S, Roshanravan B, Lee T: Th1- and Th2-like cytokines in CD4+ and CD8+ T cells in autism. *J Neuroimmunol* 85:106–109, 1998
- Plioplys AV, Greaves A, Kazemi K, Silverman E: Lymphocyte function in autism and Rett syndrome. *Neuropsychobiology* 29:12–16, 1994
- Comi AM, Zimmerman AW, Frye VH, Law A, Peeden JN: Familial clustering of autoimmune disorders and evaluation of medical risk factors in autism. *J Child Neuro* 14:388–394, 1999
- Malloy C, Morrow A, Meinzen-Derr J, Lord C: Familial autoimmunity as a risk factor for regression in children with autism spectrum disorder: a CPEA study (Abstract). Sacramento, CA, International Meeting for Autism Research, 2004
- Mennon PS, Vaidyanathan B, Kaur M: Autoimmune thyroid disease in Indian children with type 1 diabetes mellitus. *J Pediatr Endocrinol Metab* 14:279–286, 2001
- Park YS, Kim TW, Kim WB, Cho BY: Increased prevalence of autoimmune thyroid disease in patients with type 1 diabetes. *Korean J Intern Med* 15:202–210, 2000
- Prazny M, Skrha J, Limanova Z, Hilgertova J: The evaluation of thyroid and islet autoantibodies in type 1 diabetes mellitus. *Sb Lek* 100:205–211, 1999