HHS Public Access

Author manuscript

J Am Acad Child Adolesc Psychiatry. Author manuscript; available in PMC 2016 April 27.

Published in final edited form as:

J Am Acad Child Adolesc Psychiatry. 2015 November ; 54(11): 957–958. doi:10.1016/j.jaac.2015.07.016.

Clinical correlates of early generalized overgrowth in autism spectrum disorder

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Early generalized overgrowth has been described in a subgroup of children with autism spectrum disorder (ASD)[1–3]. A recent paper in the Journal[2] suggested that overgrowth may be associated with a particular pattern of cognitive and social impairment in ASD.

Chawarska and colleagues[1] initially collected growth data retrospectively from birth to 2 years in 184 boys with DSM-IV Pervasive Developmental Disorders (PDD), developmental delay, or typical development. Using spline function modeling, they identified greater overall rates of somatic growth in children with PDD. In a subgroup of boys with PDD in the top 10% of the distribution for overall body size across the first year of life, they found more severe Autism Diagnostic Observation Scale (ADOS) total scores (p=0.010) and lower Vineland Adaptive Behavior Scale (VABS) socialization scores (p=0.030) at two years of age.

In a follow-up study published in the Journal, the same group[2] collected growth data retrospectively from birth to 2 years of age in toddlers with ASD (n=200) and typically developing controls (n=147). Using the same spline function modeling, they found a more rapid rate of growth in ASD that was associated with lower verbal and non-verbal developmental quotient (VDQ, p=0.004; NVDQ, p=0.01) on the Mullen Scales of Early Learning.

The authors hypothesized that early generalized overgrowth may serve as a biomarker for a distinct subgroup of children with ASD. To follow up this exciting possibility, we used the larger Autism Speaks Autism Treatment Network (AS-ATN) dataset[4]. We examined whether overgrowth, defined by height and weight at entry into the AS-ATN, would define a subgroup of 2–5 year old children that differed clinically from the overall ASD population.

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Disclosures: Dr. McGuire and Ms. Shui have no conflicts to disclose.

All participants had a DSM-IV clinical diagnosis of PDD. Height and weight measurements were converted to percentiles from Center for Disease Control (CDC) 2000 Growth Charts. Three overgrowth groups were created for children greater than or equal to the 97th percentile for height (n=242), weight (n=331), or both height and weight (n=140). Acknowledging that the appropriate boundaries to define overgrowth are uncertain, children were classified as non-overgrowth if they were within the 10th–90th percentile for height (n=1889), weight (n=1922), or both height and weight (n=1527).

Each overgrowth group was compared to the non-overgrowth group on age, race, ethnicity, sex, and parental education level. Variables that differed at a threshold of $p<0.1$ were included as covariates in regression models examining how components of growth related to (1) Mullen VDQ, (2) NVDQ, (3) ADOS severity score, and (4) VABS socialization score.

In contrast with the previous findings[1, 2], we identified higher NVDQ in children with both height and weight >97%ile, which was significant after controlling for age (10.7 points, p=0.0024). Similarly, children above the 97%ile for either weight (4.8 points, p = 0.0325) or height (6.2 points, p = 0.0166) showed higher NVDQ. The height and weight overgrowth group also showed a trend for higher VDQ (8.2 points, p=0.0670). We observed no significant difference in ADOS, VABS, Child Behavior Checklist or parent endorsement of gastrointestinal, neurological, or sleep issues between the overgrowth and comparison groups.

The inconsistent results of this and previous reports[1, 2] could be due to a number of factors. First, we analyzed size at study entry, rather than using retrospective data. We reasoned that data enabling spline modeling are typically not available at a clinic visit and were specifically not available within the AS-ATN. Second, our population was compared to CDC norms, without access to a separate non-ASD population. Third, our population was substantially older at time of measurement. Lastly, our population was substantially larger and represented more sites than the previous reports[1, 2]. Our findings do suggest that macrosomy is more common than would be expected by chance in the ASD population, but the relationship with specific clinical features may be less straightforward than initially hoped.

Acknowledgments

Funding was provided by the National Institute of Mental Health grants MH016434 (KM) and MH094604 (JV); Autism Speaks and cooperative agreement UA3 MC11054 through the U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Research Program (AS); and the Marilyn and James Simons Family Giving (KM).

Dr. Veenstra-VanderWeele has received research support from Seaside Therapeutics, Roche Pharmaceuticals, Novartis, Forest, Sunovion, and SynapDx and has consulted with Roche Pharmaceuticals, Novartis, and SynapDx. He has received support for editorial work from Springer and Wiley.

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