



Pre-schoolchildren with autism spectrum disorders are rarely macrocephalic: A population study



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ABSTRACT

Numerous clinical studies over the past decades have concluded that there is an association between autism spectrum disorders (ASD) and large head size. Lately, some studies have reported conflicting results. The present study was conducted with a view to assess the presence of macrocephaly in a community-representative group of pre-school children with ASD. The prevalence of ASD in this general population was 0.8%.

Thirty-three children (5 girls, 28 boys) recruited after general population screening for ASD, and diagnosed with ASD (two-thirds not globally delayed) were assessed as regards growth parameters; height, weight, and head circumference (HC), at birth and at comprehensive medical-psychiatric diagnostic examinations at a mean age of 3 years. Macrocephaly in the present study was defined as HC above the 97th percentile, and ≥ 2 SD above recorded length/height. Only one of the 33 children (3%) had macrocephaly which is similar to the general population prevalence. Another 9% had a big but proportional head. None of the children were microcephalic. In this community-based study we found no evidence to support a strong link between a large head size and ASD. Conclusions must be guarded because of the relatively small number of ASD cases included.

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1. Introduction

Over the past decades a considerable amount of research has been presented concerning the presence or absence of macrocephaly in children with autism spectrum disorders (ASD). Several studies have concluded that there is an association between ASD, and large head size, regardless of whether the ASD diagnosis has been autism, Asperger syndrome (AS), or atypical autism/Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) (e.g. Cederlund & Gillberg, 2004; Dissayanake, Bui, Huggins, & Loesch, 2006; Fombonne, Rogé, Claverie, Courty, & Fremolle, 1999; Gillberg & de Souza, 2002; Lainhart et al., 2006; van Daalen, Swinkels, van Engeland, & Buitelaar, 2007).

The study by Lainhart et al. (2006) recruited more than 400 children and adults (mean age 10.8 years) with ASD from four different investigation sites in the U.S., and found that approximately 17% of all investigated individuals had macrocephaly, and macrocephaly was as common in the ASD collapsed group as in the subgroup of individuals with classic autism. Fombonne et al. (1999), reported on 126 French children with autism (2–16 years of age) coming from both local and national investigation centers to an ASD assessment unit in Toulouse, France, and found results similar to Lainhart. However, in the subgroup of preschool children in the Fombonne study, only about 9% had macrocephaly. This latter study also indicated that microcephaly might be overrepresented in classic autism, affecting about 15% of all individuals and 6% in the

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group of preschool children. In addition, macrocephaly was more common in the group of children with less severe autism and microcephaly was more common among severely affected children with autism (Fombonne et al., 1999). Gillberg and de Souza (2002) compared 45 consecutive children with AS with 45 children with autism, and 45 children with ADHD, all referred to a Swedish general child neuropsychiatric clinic at ages 1.5–16 years, and found a higher rate of macrocephaly in all groups compared to the normal population, and with the highest rate in the AS group (22%). Dissayanake et al. (2006) assessed the growth charts for the first 3 years of life in 28 individuals diagnosed with AS ($n = 12$) or “high-functioning autism” (HFA) ($n = 16$) at ages 4–11 years, and found no significant difference in growth rate for length/height, weight, or head circumference (HC) across these groups. However, compared to the normally developing control group there was a significantly higher growth rate for length/height and weight in the collapsed ASD group. In addition, a trend toward a higher growth rate in HC was found in the HFA-group in comparison to the normal controls. The Dutch study by van Daalen et al. (2007) reported results from a group of Caucasian preschool children with ASD ($n = 53$), who were partly recruited from a population-based screening, and partly from the clinical monitoring system of well-baby clinics in the Netherlands, and in which 11% of the children had macrocephaly. In a follow-up study from our own center in Gothenburg, of males diagnosed with Asperger syndrome in childhood, macrocephaly, defined by a head size ≥ 97 th percentile, was present in 15% at follow-up at a mean age of 23 years (Cederlund & Gillberg, 2004). However, the rate of macrocephaly (using the same definition in the same group at birth) had not been increased, compared with population norms. In 2012 Muratori et al. presented data from a group of 50 children (40 boys and 10 girls) with ASD (20 children had autism and 30 children had PDD-NOS) referred for assessment to a center for autism and compared them to a group of 100 typically developing children. Data concerning HC, length and weight at birth, at 1–2 months of age, at 3–5 months of age, and at 6–12 months of age were collected retrospectively for the children of both groups. There was no difference at birth across the two groups, albeit both at 3–5, and 6–12 months of age children with ASD had significantly larger HC than controls. At 6–12 months of age macrocephaly was present in 18% of the children in the ASD group compared to 9% in the control group. Surén et al. (2013) reported a rate of macrocephaly of 9% in a sample of 376 children with ASD at 12 months of age recruited from the population-based Norwegian Mother and Child database. In a recent French study Grandgeorge, Lemonnier, and Jallot (2013) investigated 422 children with ASD and compared them to 153 control individuals who participated voluntarily. They found macrocephaly to be present in approximately 6% of the children with ASD, and a little more than 3% had microcephaly. However, in the PDD-NOS subgroup macrocephaly was found in 9% of the individuals. After having performed a review study, Raznahan et al. (2013) argued in favor of using matched controls in studies concerning HC growth in ASD because such studies were found to be more methodological and bias-free compared to studies using general growth charts.

In contrast to the above mentioned studies it has also been argued, although this has received much less media attention, that there is *no* connection between large head size and ASD (e.g. Barnard-Brak, Sulak, & Ivey Hatz, 2011; Davidovitch, Golan, Vardi, Lev, & Lerman-Sagie, 2010). Barnard-Brak and colleagues assessed the HC in approximately 9000 children derived from the “Early Childhood Longitudinal Study Birth Cohort” at 3 time-points (9 months, 24 months, and 36 months of age), and children diagnosed with autism did not differ significantly from normally developing children at any of these time-points. The study by Davidovitch investigated the rate of macrocephaly in a sample of more than 300 clinically assessed children, who had received a diagnosis of autism or PDD-NOS in two different child development centers in Israel, and found a prevalence of macrocephaly of 4.4% at an average age of about 2.5 years.

A few reports addressing the issue of whether or not large head size in ASD is more common at birth or later in the first years of life have also been published (e.g. Courchesne et al., 2003; Dawson et al., 2007; Wu Nordahl et al., 2011). The study by Courchesne et al. (2003) presented the change in HC from birth to 14 months of age in 48 children with ASD, who participated in magnetic resonance imaging studies. They found that children diagnosed with ASD had significantly *smaller* head size at birth than normal controls. However, 59% of the children with an ASD had an increase in head growth after birth up to 6–14 months of age, compared to 6% in the normally developing group. Within the ASD group, children with autism had a more accelerated increase in HC than children with a diagnosis of PDD-NOS. In addition, this study also showed that excessive growth in HC after birth up to 6–14 months of age was related to greater cerebral cortex volume at 2–5 years of age. The study by Wu Nordahl et al. (2011) reported similar results and argued brain enlargement to be associated with regressive autism in boys. Dawson et al. (2007) analyzed longitudinal HC data from 28 children later diagnosed with autism and found a normal head size at birth, accelerating HC up to 12 months followed by normal head growth between 12 and 36 months of age. It has also been argued that children with autism present with a generalized overgrowth at least in the first two years of life (Chawarska et al., 2011).

In contrast to Courchesne et al. (2003) and Dawson et al. (2007), Torrey, Dhavale, Lawlor, and Yolken (2004) reported data on HC growth from 15 children with ASD, who had slightly larger heads at birth than normal controls. At assessment at 4 months of age, HC was not significantly larger in this group compared to controls, in contrast to both weight and height which at the same age were significantly greater than in the control group.

A comparison between Caucasian, Chinese, and South Asian children (Janssen et al., 2007) found Chinese children to have significantly smaller heads than Caucasians. In a paper from the early 1970s, children of different origins (Indian, African, North American, South American, and European) were compared according to HC and results suggested an approximately 1 cm difference in head size between children of Indian and European Caucasoid origin who had the smallest and largest heads, respectively (Meredith, 1971).

Almost all of the studies concerning macrocephaly in children with ASD reported to date have been performed on clinical samples and not on population representative samples. Given the many claims regarding the purportedly strong association

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