Photoanthropometric Study of Dysmorphic Features of the Face in Children with Autism and Asperger Syndrome

Piotr Gorczyca, MD, PhD
Agnieszka Kapinos-Gorczyca, MD, PhD
Katarzyna Ziora MD, PhD
Joanna Oświęcimska MD, PhD

1 Department of Psychiatry, Medical University of Silesia in Katowice, ul. Pyskowicka 49, 42-600 Tarnowskie Góry, Poland.
2 Daily Psychiatric Ward for Children, for Children, NZOZ “Feniks”, ul. Młyńska 8, 44-100 Gliwice, Poland.
3 Department of Paediatrics, Paediatric Endocrinology Unit, Medical University of Silesia in Katowice, ul. 3 Maja 13/15, 41-800 Zabrze, Poland.

Corresponding author:
Piotr Gorczyca, MD, PhD, Department of Psychiatry, Medical University of Silesia in Katowice, ul. Pyskowicka 49, 42-600 Tarnowskie Góry, Poland, Tel/Fax:0048322854358, Email:gormasp@o2.pl

Objective: Childhood autism is a neurodevelopmental disorder characterized by impairments in social interactions, verbal and non-verbal communication and by a pattern of stereotypical behaviors and interests. The aim of this study was to estimate the dysmorphic facial features of children with autism and children with Asperger syndrome.

Methods: The examination was conducted on 60 children (30 with childhood autism and 30 with Asperger syndrome). The photoanthropometric method used in this study followed the protocol established by Stengel-Rutkowski et al.

Results: The performed statistical analysis showed that in patients with childhood autism, the anteriorly rotated ears and the long back of the nose appeared more often. In the group of children with autism, there was a connection between the amount of dysmorphies and the presence of some somatic diseases in the first-degree relatives. There was also a connection between the motor coordination and the age the child began to walk.

Discussion: In patients with childhood autism, there were certain dysmorphies (like the anterior rotated ears and the long back of the nose) which appeared more often. Although the connection was not statistically significant, it seemed to concur with data from the literature.

Conclusion: Formulation of the other conclusions would require broader studies e.g. dealing with a familial analysis of dysmorphic features.

Keywords: Autistic Disorder, Asperger syndrome, Etiology, Feature

Copyright © 2012 by Persian Society of Psychiatry
Published by "Tehran University of Medical Sciences" (www.tums.ac.ir)
All children were psychiatrically examined and their behavior in new surroundings was observed. The criterion for exclusion in the study was the presence of any chromosomal defects manifesting phenotypically, such as Down syndrome. The photo anthropometric method used in this study followed the protocol established by Stengel-Rutkowski et al. (10). This method was successfully used in different studies (11, 12, 13). The obtained data were compared to the norms of this scale (10, 14). (Table 1).

The values below the 3rd and above the 97th percentile were defined as dysmorphic. Additionally, parents were asked to complete a short questionnaire check-list to broaden the anamnestic data. Fifty one questionnaires were received; some parents did not agree to broaden the anamnestic data. Fifty one "Statistica 5.0 Pl" software (StatSoft INC., USA). Statistical analysis was conducted using ANOVA Kruskal-Wallis and U Mann Whitney tests. Correlation analysis was done using the χ² test and the Spearmann index. A level of p<0,05 was accepted as statistically significant. Calculations were conducted using "Statistica 5.0 PI" software (StatSoft INC., USA).

**Results**

We examined 52 boys and 8 girls, aged between 3 and 12 years. In the group of children diagnosed with childhood autism, there were 25 boys and 5 girls (the proportion of boys to girls was 5:1) ages 3-12 (mean: 7.1; SD=2.604). In the group of children diagnosed with Asperger Syndrome, there were 27 boys and 3 girls (the proportion of boys to girls was 9:1) ages 5 to 12 (mean: 9.483; SD=2.325). Both groups were homogeneous as for sex; however, they differed as for age. The number of dysmorphies in the group diagnosed with autism was from 0 to 6 (mean: 2.1), whereas the number was from 0 to 4 (mean: 1.933) in the group with Asperger Syndrome. Both groups were homogeneous in the number of dysmorphies (p=0.6034). Most of the children diagnosed with autism were characterized by having good motor coordination, whereas most of the children with Asperger Syndrome were characterized by having poor motor coordination. Motor development (the onset of walking) and development of speech (first words) of children in both groups are presented in Table 2.

The examined groups did not differ in a statistically significant way concerning the time of the appearance of abnormal behavior, so their parents did not notice anything unusual in the children's behavior. In all children diagnosed with childhood autism such behaviour was observed before they reached 4 years old, whereas in 25% of the children with Asperger Syndrome, this was noticed after they reached the age of 4 (Table 3).

Serious somatic illnesses occurred in the first-degree relatives of 12 (52.17%) of the persons in the study group (cancer, diabetes, asthma, epilepsy, stomach ulcers, ulcerative colitis, Duchenne muscular dystrophy, Parkinson's disease, multiple sclerosis) as well as in 14 (66.67%) of the persons in the Asperger group (malignant tumors, Parkinson's disease, hypothyroidism, systemic lupus erythematosus, stomach ulcers, asthma, diabetes). Mental illnesses of first-degree relatives occurred in 6 (27.27%) of the children diagnosed with autism (schizophrenia, depression, alcohol dependence syndrome) and 10 (43.48%) of the children with Asperger Syndrome (schizophrenia, depression, obsessive-compulsive disorder, alcohol dependence syndrome, mental retardation). The performed statistical analysis showed that in patients with childhood autism the anteriorly rotated ears and the long back of the nose appeared more often (Table 4).

In the group of children with Asperger Syndrome, there was a relationship between the amount of dysmorphies and sex (p=0,0350); females were found to have a larger number of dysmorphies. In the group diagnosed with autism, a connection was found between the amount of dysmorphies and occurrence of serious somatic illnesses in the first-degree relatives. The occurrence of these diseases was connected with a greater number of dysmorphies. In the group diagnosed with childhood autism, there were also connections (approaching statistical significance) between the

**Table 1. The values of photoanthropometric indices in the examined groups***.

| Index                                      | Mean | Min. | Max. | SD  | The coefficient of variation [%] |
|--------------------------------------------|------|------|------|-----|----------------------------------|
| 1. Midface height                          | 0.597| 0.48 | 0.69 | 0.05| 8.37                             |
| 2. Inner canthal distance                  | 0.241| 0.16 | 0.30 | 0.02| 8.30                             |
| 3. Width of the palpebral fissures         | 0.204| 0.17 | 0.24 | 0.015| 7.35                            |
| 4. Length of the back of the nose          | 0.462| 0.33 | 0.58 | 0.05| 10.82                            |
| 5. Interalar distance                      | 0.250| 0.19 | 0.30 | 0.215| 8.60                             |
| 6. Prominence of the upper jaw             | 0.942| 0.83 | 1.05 | 0.04| 4.25                             |
| 7. Nasolabial distance                     | 0.171| 0.11 | 0.22 | 0.03| 17.54                            |
| 8. Width of the mouth                      | 0.333| 0.28 | 0.42 | 0.03| 9.60                             |
| 9. Height of the chin                      | 0.211| 0.14 | 0.30 | 0.03| 14.22                            |
| 10. Prominence of the chin                | 1.027| 0.92 | 1.26 | 0.07| 6.81                             |
| 11. Inclination of the ear insertion line  | 79.983| 64.00| 97.00| 6.61| 8.25                             |
| 12. Length of the ears                     | 0.754| 0.59 | 0.86 | 0.05| 6.63                             |
| 13. Width of the ears                      | 0.334| 0.20 | 0.41 | 0.04| 11.98                            |

* The values of photoanthropometric indices are established by Stengel – Rutkowski et all 1984)
Dysmorphic Feature of the Face in Autism and Asperger Syndrome

Table 2. Motor and speech development in the examined groups

| First steps [age in months] | Childhood autism [n] | Asperger Syndrome [n] |
|-----------------------------|----------------------|----------------------|
| 8-12                        | 12                   | 7                    |
| 13-15                       | 8                    | 11                   |
| 16-18                       | 3                    | 5                    |
| 19-24.                      | 1                    | 2                    |
| >24                         | 2                    | 0                    |
| First words [age in months] | Childhood autism [n] | Asperger Syndrome [n] |
| 8-12                        | 12                   | 15                   |
| 13-15                       | -                    | 4                    |
| 16-24                       | 4                    | 2                    |
| 24-36                       | 4                    | 1                    |
| 36-48                       | 2                    | 2                    |
| >48                         | 1                    | 1                    |
| Lack of speech              | 2                    | 0                    |

Table 3. Appearance of abnormal behaviour in the examined groups

| DIAGNOSIS | Time of the abnormal behaviour appearance [age in months] | 0-3 | 4-6 | 7-12 | 13-24 | 24-36 | 36-48 | >48 | Together |
|-----------|--------------------------------------------------------|-----|-----|------|-------|-------|-------|-----|----------|
| Childhood autism |                                        | 3   | 4   | 3    | 5     | 8     | 3     | 0   | 26       |
| Asperger Syndrome  |                                          | 3   | 3   | 3    | 4     | 0     | 5     | 6   | 24       |
| All                  |                                          | 6   | 7   | 6    | 9     | 8     | 8     | 6   | 50*      |
| Χ² Pearson |                                             | 14,69748 | Df=6 | p=0,02275 |

*Not all parents gave answers in inventory

Table 4. The difference in the frequency of dysmorphology appearance in the examined groups.

| Index                              | % of dysmorphology for the group with childhood autism [n] | % of dysmorphology for the group with AS [n] | Difference in the frequency of dysmorphology appearance [p] |
|------------------------------------|-----------------------------------------------------------|---------------------------------------------|-----------------------------------------------------------|
| 1. Midface height                  | >97th centile: 13.33, <3rd centile: 6.67                 | >97th centile: 0, <3rd centile: 16.67       | p=0.11, p=0.42                                           |
| 2. Inner canthal distance          | >97th centile: 3.33, <3rd centile: 3.33                  | >97th centile: 0, <3rd centile: 3.33        | p=0.14, p=1                                               |
| 3. Width of the palpebral fissures | >97th centile: 26.67, <3rd centile: 0                    | >97th centile: 0, <3rd centile: 3.33        | p=0.14, p=1                                               |
| 4. Interalar distance              | >97th centile: 6.67, <3rd centile: 10.00                 | >97th centile: 0, <3rd centile: 10.00       | p=1                                                      |
| 5. Width of the mouth              | >97th centile: 3.33, <3rd centile: 16.67                 | >97th centile: 0, <3rd centile: 0           | p=0.01, p=1                                               |
| 6. Length of the back of the nose  | >97th centile: 23.33, <3rd centile: 0                    | >97th centile: 0, <3rd centile: 0           | p=0.01, p=1                                               |
| 7. Prominence of the upper jaw     | >97th centile: 0, <3rd centile: 13.33                    | >97th centile: 0, <3rd centile: 0           | p=0.01, p=1                                               |
| 8. Nasolabial distance             | >97th centile: 0, <3rd centile: 6.67                     | >97th centile: 0, <3rd centile: 3.33        | p=0.14, p=1                                               |
| 9. Height of the chin              | >97th centile: 0, <3rd centile: 30.00                    | >97th centile: 0, <3rd centile: 30.00       | p=1                                                      |
| 10. Prominence of the chin         | >97th centile: 3.33, <3rd centile: 6.67                  | >97th centile: 0, <3rd centile: 16.67       | p=0.19, p=1                                               |
| 11. Inclination of the ear insertion line | >97th centile: 0, <3rd centile: 40.00     | >97th centile: 0, <3rd centile: 13.33       | p=0.04, p=0.04                                           |
| 12. Length of the ears             | >97th centile: 3.33, <3rd centile: 6.67                  | >97th centile: 0, <3rd centile: 0           | p=0.14, p=0.49                                           |
| 13. Width of the ears              | >97th centile: 6.67, <3rd centile: 0                     | >97th centile: 0, <3rd centile: 6.67        | p=1                                                      |

In the group of children diagnosed with Asperger Syndrome, there was a relationship between the amount of dysmorphies and the age the child articulated its first words (p=0.0309).

Discussion

In this study, among children diagnosed with autism, the number of boys was five times more than girls. This proportion is in accordance with epidemiology data, which can confirm the representativeness of the study group (15). This large predominance of males is currently believed to be the result of a higher level of fetal testosterone. Its role in the pathogenesis of autism may be found, among other things, in the so-called exposure index for fetal testosterone (2D:4D ratio – the second to the fourth digit), which is lower in persons with autism, and also in a higher level of androgens and the early maturity of adolescents with autism compared with those in the control group (16, 17). The role of testosterone in the pathogenesis of autism is emphasized in the extreme male brain theory by Simon Baron-Cohen (18).

In the group of children diagnosed with Asperger Syndrome, the number of boys was ten times more than girls. Such a large predominance of boys is most likely connected with age, when it is more difficult to diagnose Asperger Syndrome in girls who, as a rule, are characterized by a higher level of social abilities.
As demonstrated in the attached bibliography, among children with AS sent for diagnosis, the proportion of boys to girls is 10:1 (19). Furthermore, in the group of children diagnosed with AS, a connection between the amount of dysmorphies and sex was observed. There were more dysmorphies among females, which could confirm the existence of deeper disorders in girls. This concurs with data of other studies, according to which disorders of neurobiological nature occur more frequently in boys, whereas in girls they result in deeper developmental problems. The threshold of susceptibility for the damaging factors is lower in boys, whereas the occurrence of disorders is preceded by a greater amount of destructive factors in girls. Hence, the disorders in girls are more intensive and more frequently connected with cognitive impairment (20).

The majority of children with autism, in regard to physical development, are characterized by proportionate body build and proper height (21, 22). Nevertheless, different authors describe certain dysmorphic features, commonly occurring singly in autistic persons (23).

In the examined groups of autistic children, there were certain small anomalies like the anteriorly rotated ears (p=0.04) and the long back of the nose (p=0.01) which appeared more often, but the connection was not statistically significant. In other studies, the occurrence of minor physical anomalies (MPAs) in neurological disorders such as schizophrenia, ADHD, fetal alcohol syndrome and cerebral palsy are often described (24, 25). Since the minor physical anomalies are connected more often with structures deriving from the ectoderm, from which the nervous system develops, their presence might indicate its incorrect development, appearing most likely during the first or at the beginning of the second trimester of pregnancy. One can suppose that anatomical anomalies interact with other genetic and environmental factors in creating the symptoms of the illness. The present state of medical knowledge allows us to establish the precise time of the genesis of the concrete deformations, as concrete organs develop in a definite period of pregnancy. Stromland et al. (2002) in their work dealing with children diagnosed with autism, whose mothers took thalidomide during pregnancy, it was established that children with Asperger Syndrome, such behaviour was observed after they reached the age of 4. These results are in accordance with that of other studies. Certain symptoms of Asperger disorder may be present very early, however, because children with AS have better social contact than autistic children, diagnosis is established later - specific difficulties in social interactions as well as narrow and limited interests became more noticeable when the child began school education (31, 32, 33). The latest studies show that the average age of a child with Asperger Syndrome at the time of diagnosis is 11 years old (whereas for a child with autism it is 5.5 years old) (34, 35).

In the studies conducted on children diagnosed with childhood autism, there was a connection between the amount of dysmorphies and motor coordination (a greater number of dysmorphies had a connection with poor motor coordination) as well as when autistic children begin to walk. The motor development of children with autism rarely has been the subject of studies; a motor pattern characteristic for autism has not yet been established. Johnson et al (1992) stated that motor development was distinctly delayed in about 28% of children. In a study by Teitelbaum et al, (1998) all infants whose autism was later diagnosed were found to have certain abnormalities in motor development (29, 30). Delayed motor development may be connected with perinatal complications, additional somatic illnesses or mental retardation. It is likely that such disturbance in child development worsens its adaptability. A greater amount of dysmorphies seems to be connected with a greater degree of developmental disorder.

In our study, we also found that the both examined groups of children differed in the time of the appearance of their abnormal behavior in a statistically significant way, so their parents did not notice anything unusual about their behavior. In 25% of the children with Asperger Syndrome, such behaviour was observed after they reached the age of 4. These results are in accordance with that of other studies. Certain symptoms of Asperger disorder may be present very early, however, because children with AS have better social contact than autistic children, diagnosis is established later - specific difficulties in social interactions as well as narrow and limited interests became more noticeable when the child began school education (31, 32, 33). The latest studies show that the average age of a child with Asperger Syndrome at the time of diagnosis is 11 years old (whereas for a child with autism it is 5.5 years old) (34, 35).

In the studies conducted on children diagnosed with childhood autism, there was a connection between the amount of dysmorphies and motor coordination (a greater number of dysmorphies had a connection with poor motor coordination) as well as when autistic children begin to walk. The motor development of children with autism rarely has been the subject of studies; a motor pattern characteristic for autism has not yet been established. Johnson et al (1992) stated that motor development was distinctly delayed in about 28% of children. In a study by Teitelbaum et al, (1998) all infants whose autism was later diagnosed were found to have certain abnormalities in motor development (29, 30). Delayed motor development may be connected with perinatal complications, additional somatic illnesses or mental retardation. It is likely that such disturbance in child development worsens its adaptability. A greater amount of dysmorphies seems to be connected with a greater degree of developmental disorder.

In our study, we also found that the both examined groups of children differed in the time of the appearance of their abnormal behavior in a statistically significant way, so their parents did not notice anything unusual about their behavior. In 25% of the children with Asperger Syndrome, such behaviour was observed after they reached the age of 4. These results are in accordance with that of other studies. Certain symptoms of Asperger disorder may be present very early, however, because children with AS have better social contact than autistic children, diagnosis is established later - specific difficulties in social interactions as well as narrow and limited interests became more noticeable when the child began school education (31, 32, 33). The latest studies show that the average age of a child with Asperger Syndrome at the time of diagnosis is 11 years old (whereas for a child with autism it is 5.5 years old) (34, 35).

In the studies conducted on children diagnosed with childhood autism, there was a connection between the amount of dysmorphies and motor coordination (a greater number of dysmorphies had a connection with poor motor coordination) as well as when autistic children begin to walk. The motor development of children with autism rarely has been the subject of studies; a motor pattern characteristic for autism has not yet been established. Johnson et al (1992) stated that motor development was distinctly delayed in about 28% of children. In a study by Teitelbaum et al, (1998) all infants whose autism was later diagnosed were found to have certain abnormalities in motor development (29, 30). Delayed motor development may be connected with perinatal complications, additional somatic illnesses or mental retardation. It is likely that such disturbance in child development worsens its adaptability. A greater amount of dysmorphies seems to be connected with a greater degree of developmental disorder.

In our study, we also found that the both examined groups of children differed in the time of the appearance of their abnormal behavior in a statistically significant way, so their parents did not notice anything unusual about their behavior. In 25% of the children with Asperger Syndrome, such behaviour was observed after they reached the age of 4. These results are in accordance with that of other studies. Certain symptoms of Asperger disorder may be present very early, however, because children with AS have better social contact than autistic children, diagnosis is established later - specific difficulties in social interactions as well as narrow and limited interests became more noticeable when the child began school education (31, 32, 33). The latest studies show that the average age of a child with Asperger Syndrome at the time of diagnosis is 11 years old (whereas for a child with autism it is 5.5 years old) (34, 35).

In the studies conducted on children diagnosed with childhood autism, there was a connection between the amount of dysmorphies and motor coordination (a greater number of dysmorphies had a connection with poor motor coordination) as well as when autistic children begin to walk. The motor development of children with autism rarely has been the subject of studies; a motor pattern characteristic for autism has not yet been established. Johnson et al (1992) stated that motor development was distinctly delayed in about 28% of children. In a study by Teitelbaum et al, (1998) all infants whose autism was later diagnosed were found to have certain abnormalities in motor development (29, 30). Delayed motor development may be connected with perinatal complications, additional somatic illnesses or mental retardation. It is likely that such disturbance in child development worsens its adaptability. A greater amount of dysmorphies seems to be connected with a greater degree of developmental disorder.

In our study, we also found that the both examined groups of children differed in the time of the appearance of their abnormal behavior in a statistically significant way, so their parents did not notice anything unusual about their behavior. In 25% of the children with Asperger Syndrome, such behaviour was observed after they reached the age of 4. These results are in accordance with that of other studies. Certain symptoms of Asperger disorder may be present very early, however, because children with AS have better social contact than autistic children, diagnosis is established later - specific difficulties in social interactions as well as narrow and limited interests became more noticeable when the child began school education (31, 32, 33). The latest studies show that the average age of a child with Asperger Syndrome at the time of diagnosis is 11 years old (whereas for a child with autism it is 5.5 years old) (34, 35).

In the studies conducted on children diagnosed with childhood autism, there was a connection between the amount of dysmorphies and motor coordination (a greater number of dysmorphies had a connection with poor motor coordination) as well as when autistic children begin to walk. The motor development of children with autism rarely has been the subject of studies; a motor pattern characteristic for autism has not yet been established. Johnson et al (1992) stated that motor development was distinctly delayed in about 28% of children. In a study by Teitelbaum et al, (1998) all infants whose autism was later diagnosed were found to have certain abnormalities in motor development (29, 30). Delayed motor development may be connected with perinatal complications, additional somatic illnesses or mental retardation. It is likely that such disturbance in child development worsens its adaptability. A greater amount of dysmorphies seems to be connected with a greater degree of developmental disorder.
amount of dysmorphies and the development of speech. A greater number of dysmorphies was connected with the later age at which a child articulated its first words. This connection requires further studies. Our study has some limitations. To eliminate the anomalies running in a family it would be useful to also examine the parents and siblings of the autistic children. We also considered extending our study for the control group but we finally decided to use the standards established by Stengel-Rutkowski et al. from white control children.

We conclude that in the group of children with autism, there was a connection between the amount of dysmorphies and the presence of some somatic disorders in the first-degree relatives. The number of dysmorphies also showed the connection with motor coordination and the age the child began to walk.

References

1. Willemsen-Swinkels SH, Buitelaar JK. The autistic spectrum: subgroups, boundaries, and treatment. Psychiatr Clin North Am 2002; 25: 811-836.
2. Puri BK, Laking PJ, Treasaden IH. Textbook of Psychiatry. 2nd edition. Edinburgh: Churchill Livingstone; 2003.
3. Muhle R, Trentacoste SV, Rapin I. The genetics of autism. Pediatrics 2004; 113: 472-486.
4. Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of autism in a U S metropolitan area. JAMA 2003; 289: 49-55.
5. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children: confirmation of high prevalence. Am J Psychiatry 2005; 162: 1133-1141.
6. Coplan J. Making sense of autistic spectrum disorders. New York: Bantam Books; 2010.
7. Firth U. Autism and Asperger syndrome. Cambridge: Cambridge University Press; 1991.
8. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition. Washington DC: American Psychiatric Association; 1994.
9. Gillberg C. Asperger syndrome in 23 Swedish children. Dev Med Child Neurrol 1989; 31: 520-531.
10. Stengel-Rutkowski S, Schimanek P, Wernheimer A. Anthropometric definitions of dysmorphic facial signs. Hum Genet 1984; 67: 272-295.
11. Butler MG, Hovis CL, Feurer ID. Genetic variants of the human obesity (OB) gene in subjects with and without Prader-Willi syndrome: comparison with body mass index and weight. Clin Genet 1998; 54: 385-393.
12. Midro AT, Zadroza-Tolwinska B. [Epilepsy in a child with ring chromosome 14]. Neurol Neurochir Pol 1993; 27: 99-104.
13. Butler MG, Hovis CL, Angulo MA. Photoanthropometric study of craniofacial traits in individuals with Prader-Willi syndrome on short-term growth hormone therapy. Clin Genet 1998; 53: 268-275.
14. Hovis CL and Butler MG. Photoanthropometric study of craniofacial traits in individuals with Williams syndrome. Clin Genet 1997; 51: 379-387.
15. Stone JL, Merriman B, Cantor RM, Yonan AL, Gilliam TC, Geschwind DH, et al. Evidence for sex-specific risk alleles in autism spectrum disorder. Am J Hum Genet 2004; 75: 1117-1123.
16. Lutchmaya S, Baron-Cohen S, Raggatt P, Knickmeyer R and Manning JT. 2nd to 4th digit ratios, fetal testosterone and estradiol. Early Hum Dev 2004; 77: 23-28.
17. Knickmeyer RC and B aron-Cohen S. Fetal testosterone and sex differences in typical social development and in autism. J Child Neurol 2006; 21: 825-845.
18. Baron-Cohen S. The extreme male brain theory of autism. Trends Cogn Sci 2002; 6: 248-254.
19. Gillberg IC, Gillberg C. Asperger syndrome--some epidemiological considerations: a research note. J Child Psychol Psychiatry 1989; 30: 631-638.
20. Prevalence of autism spectrum disorders--autism and dev elopmental disabilities monitoring network, 14 sites, United States, 2002. MMWR Surveill Summ 2007; 56: 12-28.
21. Weidal L, Coleman M. The autistic and control population of this study: demographic, historical and altitudinal data. In: Coleman M, ed. The autistic syndromes. New York: North-Holland Publishing Company; 1976.
22. Schopfer E, Mesibov GB. Diagnosis and assessment in autism. New York: Plenum Press; 1988.
23. Rodier PM, Bryson SE, Welch JP. Minor malformations and physical measurements in autism: data from Nova Scotia. Teratology 1997; 55: 319-325.
24. McGrath J, El-Saadi O, Grim V, Cardy S, Chapple B, Chant D, et al. Minor physical anomalies and quantitative measures of the head and face in patients with psychosis. Arch Gen Psychiatry 2002; 59: 458-464.
25. Gourion D, Goldberger C, Bourdel MC, Bayle FJ, Millet B, Olie JP, et al. Neurological soft-signs and minor physical anomalies in schizophrenia: differential transmission within families. Schizophr Res 2003; 63: 181-187.
26. Stromland K, Sjogreen L, Miller M, Gillberg C, Wentz E, Johansson M, et al. Mobius sequence--a Swedish multidisciplinary study. Eur J Paediatr Neurol 2002; 6: 35-45.
27. Hardan AY, Keshavan MS, Sreedhar S, Vemulapalli M and Minshew NJ. An MRI study of minor physical anomalies in autism. J Autism Dev Disord 2006; 36: 607-611.
28. Casas KA, Mononen TK, Mikail CN, Hassed SJ, Li S, Mulvihill JJ, et al. Chromosome 2q terminal deletion: report of 6 new patients and review of phenotype-breakpoint correlations in 66 individuals. Am J Med Genet A 2004; 130A: 331-339.
29. Johnson MH, Siddons F, Frith U, Morton J. Can autism be predicted on the basis of infant screening tests? Dev Med Child Neurol 1992; 34: 316-320.

30. Teitelbaum P, Teitelbaum O, Nye J, Fryman J, Maurer RG. Movement analysis in infancy may be useful for early diagnosis of autism. Proc Natl Acad Sci U S A 1998; 95: 13982-13987.

31. Klin A, Volkmar FR, Sparrow SS. Asperger Syndrome. New York: The Guilford Press; 2000.

32. Eisenmajer R, Prior M, Leekam S, Wing L, Gould J, Welham M, et al. Comparison of clinical symptoms in autism and Asperger's disorder. J Am Acad Child Adolesc Psychiatry 1996; 35: 1523-1531.

33. Paul R. Communication Development and Assessment. In: Chawarska K, Klin A, Volkmar FR, eds. Autism Spectrum Disorders in Infants and Toddlers: Diagnosis, Assessment and Treatment. New York: The Guilford Press; 2008.

34. Howlin P, Asgharian A. The diagnosis of autism and Asperger syndrome: findings from a survey of 770 families. Dev Med Child Neurol 1999; 41: 834-839.

35. Cederlund M, Gillberg C. One hundred males with Asperger syndrome: a clinical study of background and associated factors. Dev Med Child Neurol 2004; 46: 652-660.

36. Ingudomnukul E, Baron-Cohen S, Wheelwright S, Knickmeyer R. Elevated rates of testosterone-related disorders in women with autism spectrum conditions. Horm Behav 2007; 51: 597-604.

37. Mouridsen SE, Rich B, Isager T, Nedergaard NJ. Autoimmune diseases in parents of children with infantile autism: a case-control study. Dev Med Child Neurol 2007; 49: 429-432.

38. Croen LA, Grether JK, Yoshida CK, Odouli R, Van de Water J. Maternal autoimmune diseases, asthma and allergies, and childhood autism spectrum disorders: a case-control study. Arch Pediatr Adolesc Med 2005; 159: 151-157.

39. Comi AM, Zimmerman AW, Frye VH, Law PA, Peeden JN. Familial clustering of autoimmune disorders and evaluation of medical risk factors in autism. J Child Neurol 1999; 14: 388-394.

40. Ashwood P, Van de Water J. Is autism an autoimmune disease? Autoimmun Rev 2004; 3: 557-562.