

Twin pair discordant for autism

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1. Muhle2004 (cited)

2. Neuroscience site (cited)

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8. Kestenbaum2008 (cited)

10. Autism-encyclopedia

Background: Autism is one of the most common neurodevelopment disorder characterized by deficiencies in social interactions and communication skills, as well as repetitive and stereotyped patterns of behavior. Recent epidemiological data show that autism is observed in 1 child in 300. In 10-25% of the cases, autism is linked to chromosomal abnormalities. Twin studies help to identify the relative contributions of genetic liability and environmental risk factors for autism.

11. Twin-wikipedia

Case presentation: A pair of 4-year-old twin boys was investigated. One twin was early diagnosed as autistic disorder based on the language delay. Chromosome analysis in cultured peripheral blood lymphocytes from parents and twins was performed following standard protocols. The twin zygosity was determined according to blood test: ABO blood type system, Rh blood group system and HLA haplotype. There was no family history of autism.

Conclusion: Our patient appeared to be a sporadic case of autism. In the future, the patient will require molecular genetic testing for confirming the diagnosis, long-term follow-up and treatment of manifestations if necessary.

Keywords: autism, twins, autistic phenotype

3. Fombonne2005 (NOT cited)

4. Twins Site (NOT cited)

5. Betancur2007 site (NOT cited)

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Introduction

Autism is one of the most common neurodevelopment disorder characterized by deficiencies in social interactions and communication skills, as well as repetitive and stereotyped patterns of behavior [1]. Recent studies estimate the prevalence of autism at 13 per 10,000, Asperger's disorder is approximately 3 per 10,000, and childhood disintegrative disorder is very rare at about 0.2 per 10,000. The assessment process, sample size, publication year, and geographic location of studies all have an effect on prevalence estimates. [2]. Developmental disorders usually appear before the age of three. The study of familial cases and twins shows the strong involvement of genetic factors in autism [3]. In 10-25% of the cases, autism is linked to identified genetic diseases, such as tuberous sclerosis or fragile X syndrome, or to chromosomal abnormalities. Autism is not a disease but a syndrome with multiple non-genetic and genetic causes. By autism, is meaning the wide spectrum of developmental disorders characterized by impairments in 3 behavioral domains: 1) social interaction; 2) language, communication, and imaginative play; and 3) range of interests and activities [4].

The main support for genetically influenced is derived from family and twin studies.

Twin studies reported 60% concordance for classic autism in monozygotic (MZ) twins versus 0 in dizygotic (DZ) twins, the higher MZ concordance attesting to genetic inheritance as the predominant causative agent [4].

Case presentation

A pair of 4-year-old twin boys was evaluated and diagnosed by a multidisciplinary team (psychiatric exam, language skills tests, MRI). The parents became aware of the indifference to other people, passiveness and aloofness of one of their sons, even towards them. The examination included a psychiatric assessment and a neurological examination in addition to neurophysiological, neuroimaging and chromosomal evaluation. One of the twins had a history of speech delay. He was diagnosed with autism when he was two years old and still exhibits all characteristics of the classic disorder, including deficits in reciprocal social interactions and communication (speech and language), stereotyped behavior and restricted interests and activities. Chromosome analysis revealed normal karyotype 46,XY for both twins. Physical characteristics of the twins were very similar and

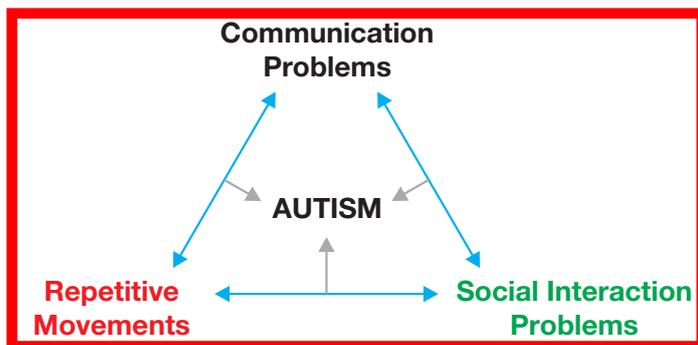


Fig. 1 Spectrum of developmental disorders

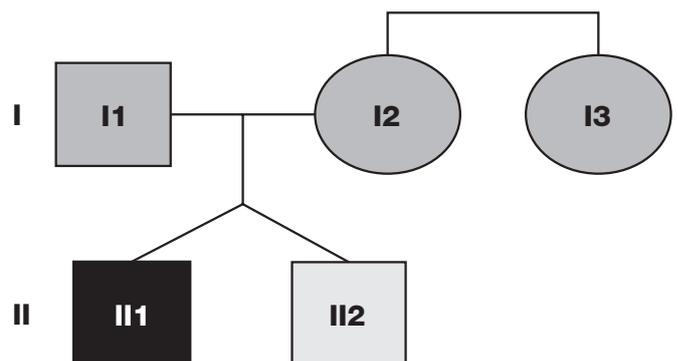


Fig. 2 Family Pedigree: II1 male twin with autism

Table 1 Twins expressed different phenotypes

TWIN 1 – AUTISM	TWIN 2 – Non Hodgkin's lymphoma of the nasopharynx
Expressive and receptive language delays (no single words at age 2; no phrases by 33 months) Lack of social or emotional reciprocity Persistent preoccupation with parts of objects No hearing and visual impairment No facial dysmorphic features HLA A2, B18, DR13 Rh + A blood group Normal karyotype 46,XY No genital abnormality Normal primary dentition	Marked impairment in the ability to initiate or sustain a conversation with others Normal social or emotional reciprocity No hearing and visual impairment HLA A2,B18,DR13 Rh+ O blood group Normal karyotype 46,XY No genital abnormality Normal primary dentition

it might be mistaken for identical twins. The twin zygosity test according to ABO blood type system, Rh blood group system and HLA haplotype was conclusive identifying the boys as non-identical twins (Table 1). Like any other siblings, the twins had an extremely small chance having the same genetic profile.

Male fraternal twins were born to unrelated healthy parents in their mid-thirties. Gestation was uneventful and delivery was at full-term by caesarean section. There was no family history of autism (Figure 2). Both twins showed language impairment and didn't interact with anyone, but interact each other. Twins found comfort in the television. One twin met criteria for autism (marked impairments in communication, social interactions, restricted interests, and activities) and his co-twin did not. The co-twin was diagnosed with non Hodgkin's lymphoma of the nasopharynx. The boys had normal intelligence for their age.

Discussion

The cause of autism is unclear; it is known that genetics do play a role. Usually, many families with an autistic child also have one or more perfectly healthy. The disorder is seen often in identical twins: different studies have shown that if one identical twin has autism then there is a 63-98% chance that the other twin will have it. For non-identical twins or fraternal twins, the chance is between 0 -10% that both twins will develop autism. The chance that siblings will be affected by autism is about 3%. Autism is seen more often in boys; four or five boys will have autism compared to one girl. But girls with autism are often more severely affected than boys and score lower on intelligence tests. Autism does not seem to affect any racial, ethnic or social group more than others [5].

Twin studies seemed to point to a genetic cause for the disease; however, the increased risk amongst fraternal twins (though not as high as that of identical) seems to indicate that perhaps something about being a twin could also be a factor. This means that environmental factors in the womb, placental development, or even the experience of

being raised with a same-age sibling could have some triggering effect for autism [6]. Usually, many families with an autistic child also have one or more perfectly healthy children.

Autism susceptibility locus, termed AUTS1, contains several potential genes: FOXP2, RAY1/ST7, and IMMP2L, as well as the glutamate receptor GRM8, CADPS2, and WNT2 [7].

A multimodal treatment plan is considered optimal in order to achieve a successful therapeutic outcome [2].

Conclusions

1. Twins are discordant for autism.
2. Our autistic patient appeared to be a sporadic case.

Acknowledgements

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