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# Genetic Counseling in Autistic Phenotypes

Agnes Cristina Fett-Conte

*Medical School - FAMERP/FUNFARME, São José do Rio Preto, São Paulo  
Brazil*

## 1. Introduction

Autism is a neurobehavioural disorder that includes impairment in social interaction and language development and communication deficits accompanied by repetitive and stereotyped behaviours. More recently this term has been used to define a very broad behavioural phenotype which is classified as different disorders that comprise the Pervasive Developmental Disorders (PDD) according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition-DSM-IV (American Psychiatric Association [APA], 1994). It contains the criteria for diagnosis and specific characteristics of each disease, including Autism, Asperger's syndrome, Childhood Disintegrative Disorder, Rett syndrome and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS).

However, with the exception of Rett syndrome, the others make up a continuous spectrum rather than clinically defined diagnostic categories due to the wide variation of clinical signs and symptoms and the subjectivity of the criteria for differential diagnosis. For this reason these disorders have been included in a general conceptual category, Autism Spectrum Disorders (ASDs) (Snow & Lecavalier, 2011; Witwer & Lecavalier, 2008). Hence, the proposals for DSM-V, being prepared by the APA, which is scheduled to be published in 2012 or 2013, recommend that Rett syndrome is not considered among the ASDs, that the designation PDD is no longer used and that ASD is considered a single category that includes Autism, Asperger's syndrome, Childhood Disintegrative Disorder and PDD-NOS. That is, the disorders that compose the autistic spectrum would no longer have specific names (APA, 2011).

Rett syndrome almost exclusively affects girls and is characterized by normal development until about six months followed by regression of motor and social skills. The triad dementia-ataxia-autism is observed as is a characteristic pattern of deceleration in the rate of head growth, loss of acquired manual skills, poorly coordinated gait, involuntary movements of the hands and the trunk and autistic features. Epilepsy may be present and an abnormal respiratory pattern is typical. The prevalence among women is between 1:10,000 and 1:15,000 with most cases caused by a sporadic mutation in the *MECP2* gene, located on Xq28. In some cases, the etiology is due to mitochondrial DNA mutations (Gonzales & LaSalle, 2010; Nissenkorn et al., 2010; Temudo et al., 2010). The peculiar nature and specific etiology, linked to a genetic defect with consequent brain damage, are among the reasons for not being considered within the ASDs.

Childhood Disintegrative Disorder is basically characterized by normal development of children until at least two years of age followed by a process of loss of previously acquired intellectual and behavioural skills, which results in autistic behaviour (Homan et al., 2011).

Asperger's syndrome differs from other diagnoses because of the absence of delay in language development, in general a preserved cognitive development, frequently prodigious memory, as well as "pedantic" speech, inadequate social interaction and, in many cases, disinterest in interpersonal relationships (Koyama & Kurita, 2008).

Since the reports of Kanner in 1943 on "autistic disturbances of affective contact", Autism has been extensively discussed and investigated. Currently regarded as a developmental disorder that manifests before thirty months of age, it is characterized by abnormal responses to auditory and visual stimuli and underdeveloped or absent speech. Serious communication and social interaction problems occur and behaviour is ritualistic, aggregating abnormal routines with resistance to change. Approximately 75% of cases are associated with mental retardation, 15 to 40% with seizures and 20 to 50% with electroencephalographic abnormalities (Tuchman et al., 2010).

PDD-NOS is a diagnosis of exclusion made when an individual presents severe impairment of reciprocal social interaction and verbal or nonverbal communication skill development, but does not satisfy the criteria for other PDDs. Atypical Autism, for which the etiology and prevalence remain unknown, is also included in this category (Chiappedi et al., 2010; Koyama & Kurita, 2008).

ASDs occur in approximately 1:150 live births and in all ethnic groups and social classes, and thus can be considered a public health problem. There are discussions as to whether there is a real progressive increase in the prevalence of these diseases in the population and it is speculated that there are several risk factors. However, this increase appears to result from the fact that diagnosis is being made earlier as education and healthcare staff are more attentive to the symptoms, besides the diffusion of information, leading to the identification of a greater number of cases (Liu et al., 2010; Shen et al., 2010; Nassar et al., 2009). There are several diagnostic scales that use "checklists" and are effective in the rapid identification of possible cases of ASD. The degree of behavioral and cognitive functioning is highly variable and early diagnosis is of paramount importance because stimulation programs achieve much more significant results when interventions occur in the early development stages. If diagnosis and intervention are delayed, the results are not very promising (Biederman et al., 2010; Marteleto et al., 2008).

But if the classification of the autism phenotype is so difficult and so discussed, the etiology is even more so. Knowledge about the etiology of ASDs is increasing, but causes remain elusive for most cases. The truth is that autism has many etiologies.

ASD associated with a known cause is called syndromic autism. There is an expanding list of medical conditions in the literature associated with autistic manifestations, ranging from disruptions caused by varying environmental agents to several mutations and well-defined syndromes, chromosomal abnormalities and metabolic diseases. In cases where the cause is identified, the autistic manifestation is considered secondary (Benvenuto et al., 2009). Among these, prenatal infections, prenatal exposure to physical and chemical agents and genetic disorders may be cited (Ratajczak, 2011; Zhang et al., 2010). However, the biological mechanisms involved in these associations are unclear.

The clinical heterogeneity of ASDs probably reflects the complexity of the genetic profile. There is no doubt that different genetic mechanisms contribute to the pathogenesis of ASDs. Thus, when the many different etiologies of autistic phenotype are referred to, the principal focus is on genetic aspects. Heritability is estimated in 90% and the monozygotic twin concordance rate is as high as 95%. The situation is complicated by significant inter-individual heterogeneity, the numerous loci involved and gene-environment interactions (Caglayan, 2010).

Another interesting aspect is related to the phenomenon of genetic anticipation. Since the first descriptions by Kanner, particular personality traits in relatives of autistic patients have been recognized. The findings of familial aggregation of minor variants suggest that genes confer susceptibility at variable severity, which is often "light", known as *broad phenotype*, and independently segregates among relatives (Losh et al., 2008; Schmidt et al., 2008).

This suggests that this complex combination of genetic and environmental factors, is what really defines the risk for ASDs. The commonly accepted empirical risk estimate for a couple with one affected child is 2–8%, in the absence of a definable condition (Selkirk et al., 2009).

Karyotype analysis shows changes involving all chromosomes in 3 to 6% of ASD cases. However, the functional significance of these changes also remains unknown given the variation in the size of the regions involved and the diversity of loci. Moreover, the majority of rearrangements are sporadic, some are detected in other asymptomatic family members or are *de novo* in individuals with a positive family history of ASDs (Marshall et al., 2008; Sykes & Lamp, 2007).

Many genes are likely to contribute to the etiology of ASDs, especially in cases of non-syndromic autism, as they present mutations or polymorphisms. The identification is becoming easier as a result of advances in genetic technology. It is believed that the emergence of the autistic phenotype in most cases depends on a small additive effect of multiple genes, but all with expressions in the central nervous system. Among these are the *CENTG2* gene mapped at 2q37.2, the *SHANK3* gene mapped at 22q13.3, the *GABRB3* gene mapped at 15q11-13, the *SLC6A4* gene located at 17q11.2 and the *NLGN3* gene mapped at Xq13.1 (Cuscó et al., 2009).

Many studies recommend that the laboratory evaluation of ASD cases should initially include an analysis of G banded karyotype, preferably high resolution and a molecular evaluation of the *FMR1* gene. But even at high resolution, abnormalities smaller than ~5Mb cannot be detected by karyotyping, which is problematic, particularly in subtelomeric chromosomal regions that are rich in genes susceptible to rearrangements. For this reason, karyotypic evaluation by the Fluorescent in situ Hybridization (FISH) technique is indicated to overcome some limitations and clarify certain karyotypic findings. However, negative results obtained with these techniques have not ruled out other types of genetic alterations.

Genetic screens represent a powerful tool when dealing with monogenic disorders characterized by direct genotype-phenotype correlations. Current guidelines for clinical genetic evaluation of patients recommends carrying out a detailed physical examination, hearing evaluation, obtaining a detailed personal and family history, screening for inborn errors of metabolism and neuroimaging studies, as well as karyotype and fragile-X DNA testing (Lintas & Persico, 2008; Wassink et al., 2007). The identification of genes linked to susceptibility and investigation of pathogenic mechanisms is crucial in clinical practice and for adequate genetic counseling of families, but the specifications and limitations of each test should be considered. Some genetic testing, even as part of research protocols for ASDs, can only be time consuming and not appropriate in many cases.

More recently tests to identify cryptic genomic changes have been proposed. The development of array-based CGH (Comparative Genomic Hybridization) and MLPA analysis (Multiplex Ligation-dependent Probe Amplification) has enabled detection of microdeletions and microduplications in patients with ASDs. These have been referred to as copy number variants (CNVs) and seem to play a key role in the etiology of many cases, more commonly among patients with non-dysmorphic ASDs (Benvenuto et al., 2009; Christian et al., 2008). But despite the promising genetic findings, the data are still

inconclusive which is due to genetic heterogeneity, the likely involvement of many genes that interact, epistatic interactions, gene-environment interactions, variability in gene expression, the influence of epigenetic mechanisms and the fact that the expression of some genes is influenced by specific regulatory regions located at relatively long distances, even on other chromosomes, which makes the selection of candidate genes difficult (Zahir & Brown, 2011; Vorstman et al., 2006). The fact that the cost of these tests is high and the availability is low has to be considered as this makes access for many patients difficult.

The high prevalence and complexity of the ASDs have motivated several studies using different research strategies. Genetic factors are the most studied and its potential cause in many cases has resulted in a significant increase in the number of referrals to clinical geneticists and genetic counselors.

Genetic counselors are able to help families that have children with syndromic autism and even in cases with uncertainty regarding etiology. But, genetic counseling for families of ASD individuals is a difficult procedure. The most important aspect is that genetic counseling is not only a question of giving technical information related to all the complexity of the aforementioned features. Even so, technical information can be offered in several contexts such as healthcare and educational booklets and even in television shows.

Genetic counseling is the process of providing information to individuals and families about the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. It is a communication process. As such it should be understood as a "two-way street", i.e. as a situation of "exchange". Counselors have no guarantee or control that their "message" to counselees is understood as intended, nor even about the consequences of the process. Thus, besides the communication of biological and clinical information, counselors must prioritize the educational and psychological aspects of the process, so that all the information and emotional support given to counselees can support their decision making and help to reduce anxiety and guilt. It is essential to remember that nondirectiveness is crucial in this process (Kessler, 2001) as is the context, the environment chosen for the process to develop.

Nondirectiveness is not a question of whether to give advice or not or to say what the counselor thinks is best or not. It is a form to promote and to enhance the autonomy and self-directedness of counselees. It is necessary to provide accurate, complete and unbiased information and to have an empathic relationship between those involved, professionals and family. Nondirectiveness and ethical principles applied to genetic counseling are very well documented in a publication of the World Health Organization in 1998 (World Health Organization [WHO], 1998).

There are different methods to promote the identification of the most relevant aspects that must be addressed with the families. The counselor should convey all the useful information requested, as well as information that should have been requested by counselees, but was not.

All circumstances of genetic counseling are in a complex context that involves personal dynamics and social interactions with the meaning and perception being very different among those involved (i.e., counselees and counsellor). Invariably, however, stress and anxiety are present in this context. It should be noted that coping strategies differ between individuals, ranging from seeking information or avoiding new information to reactions of anger or indifference, which are psychological defences against an aversive event that causes pain. Often, the cascade of psychological effects that begins is unpredictable. Certainly, at least in the first session of genetic counseling, the counselor is faced by shocked

and very vulnerable individuals with a great sense of loss, guilt and shame. Family issues, structure, emotional dynamics, religion, patterns of communication, kinds of interactions, ethnicity and social support must be considered during the counseling process because all these issues will influence the counseling.

The diagnosis of autism is really a major stressor for families who have to adapt to a reality that, in addition to being new, is very heterogeneous, complex, and difficult and can result in conflict. This requires professionals working in this area to invest more in psychosocial genetic counseling skills. These issues and their applications to genetic counseling were detailed by Weil (2000).

Genetic counseling generally involves a chronicity situation which is absolutely true in the case of autism. Chronic diseases can produce consequences such as pain, discomfort, low self-esteem, uncertainty about the future, suicidal thoughts, fear, panic, general and specific disorders of conduct, academic performance deficits, difficulties in interpersonal and family relationships, anxiety, and depression among others. The emotional distress associated with these diseases, if ignored, can lead to a significant reduction in the quality of life of patients and their families and negatively affect the absorption of important information and adherence to treatment. Thus, family members should always be considered at risk for developing some kind of emotional disorder. These considerations underscore the nature of genetic counseling as something far beyond the process of medical diagnosis and the establishment of the risk of occurrence/recurrence. Hence, skilled and experienced professionals are needed to perform this task, giving priority to communications and humanization of care. In the past, communication skills were not considered a priority. However, today these skills have become a professional demand and even the legal obligation of every professional in healthcare.

Genetic counseling is developed in a continuous and integrated manner. Division in phases is only for teaching purposes and can be summarized as: the reception and identification of patient/family, understanding of the problem/complaint, the identification of antecedents, establishment and confirmation of the diagnosis, assessment of genetic risk, discussion about options and decisions, and follow up. Psychological support from the counselor is essential for each phase, whether in a single session or several.

There are not a great number of reports about genetic counseling in ASDs. Maybe one of the reasons is related to the misunderstanding about the heritability of these disorders as mentioned above. Like other diseases, some cases are inherited and others are not. Then, what to do in each case since genetic causes may play an important role in the etiology of ASDs?

The clinicians have to identify specific causes or exclude them to provide effective counseling and this is not always an easy job. Two situations must always be considered: syndromic autism and non-syndromic autism (idiopathic or primary). In the first one, there is a known cause related to the behavioural phenotype and that often can be identified by dysmorphic features. It may be associated with well-known monogenic disorders, chromosomal alterations and environmental events. Genetic counseling should be directed to information related to the cause, genetic or not. Someone could say that if the cause is not genetic, the patient certainly will not go to a genetic counseling service, but in practice this is not true. In non-syndromic cases, determined after detailed investigations, the approach will be different, discussing in particular the polygenic predisposition and the environmental contribution to the autistic phenotype.

## 2. Genetic counseling in genetic disease associated to autism

Approximately 10% of autistic patients have a diagnosis of single gene diseases or chromosomal abnormalities; there are several molecular pathways potentially involved in the alterations that affect normal neurodevelopmental events. In cases of chromosomal defects, for example, these can cause alterations in neuronal migration and brain growth, with subsequent altered cortical organization, synaptic and dendritic changes and the ASD phenotype. Metabolic disorders produce an accumulation of toxic metabolites which can cause a reduction of myelin, neuronal loss, alterations in dopaminergic or serotonergic neurotransmission and ASD (Benvenuto et al., 2009).

The most common genetic diseases associated with ASDs include Fragile-X syndrome, Tuberous Sclerosis, invdup(15) or idic(15), Prader-Willi and Angelman syndromes, Down syndrome, Joubert syndrome, macrocephaly and overground syndromes, Turner syndrome, Williams syndrome, Timothy syndrome, Smith-Magenis syndrome, Phelan-McDermid (22q13.3 deletion) syndrome, Cohen syndrome, Sanfilippo syndrome, mitochondrial cytopathies, among others (Caglayan, 2010; Moss & Howlin, 2009). And this list just keeps growing!

A Fragile X syndrome is diagnosed in almost 5% of the children with ASDs. Faced with this, it is considered the most common genetic etiology of the autistic phenotype. It is the most common cause of inherited intellectual deficiency in men. It results from a full mutation that affects approximately 1 in 2500 males and 1 in 8000 females. The molecular basis involves a dynamic and unstable mutation characterized by the repeat expansion of the trinucleotide (CGG)<sub>n</sub> in the 5' untranslated region of the first exon of the *FMR-1* gene (Fragile-X Mental Retardation 1) mapped at Xq27.3. When the number of CGG repeats is greater than 200, the allele is classified as a full mutation. CpG island hypermethylation of the promoter causes gene inactivation. Persons with the syndrome produce little or no detectable expression of the encoded protein called Fragile X Mental Retardation Protein or FMRP which is essential for normal brain function. It is involved in synaptic maturation and its loss may alter neuronal plasticity. Brain damage results in, among other things, autistic behaviour. Individuals with intermediate CGG expansions in the range of 55–200 repeats are known as fragile X premutation carriers and are at increased risk for a related disorder known as Fragile X-Associated Tremor and Ataxia Syndrome (FXTAS) that affects primarily men over the age of 50. The presence of the premutation in women can also cause premature ovarian failure (Hampson et al, 2011).

All the diseases associated with autism have specific molecular biological mechanisms with different genes involved and different types of inheritance pattern. The fact is that the autism phenotype is one of the clinical manifestations of the disease itself, which in one way or another, changes the structure and/or function of the brain. For this reason, it is spoken of as association rather than comorbidity because the events are not random in the same patient. Given this scenario, genetic counseling should be directed according to information relevant to that specific syndromic diagnosis with explanations of the causes, risks and consequences. Conduct is not so different when the etiology of autism arises from the action of a toxic environmental agent.

The autism phenotype, however, is a major complicating factor when combined with a genetic disease because the parents, who are usually very distressed, can confuse the risk of disease recurrence with risk of autism among those affected by it. Not all of those affected have the autism phenotype. It is important that counselors, in addition to background and

needs, identify the expectations of their genetic counseling clients. However, this scenario includes hundreds of possibilities of events and different strategies to solve them. Some of the genetic conditions are inherited while others are not. In most cases there is an important variability in clinical manifestations. If the disease is genetic it is incurable although often there may be symptomatic and palliative treatments.

Autism phenotype can be associated with autosomal recessive disease, which was originated from parents who carry the deleterious gene. This is one of situations of genetic counseling that inherently evoke guilt. The dominant culture of the family, especially if its members are Latino, produces the feeling of being punished for some sin. In this case the guilt can be a response to new and adverse reality over which one has no control. This can be exacerbated if during the explanation the counselor emphasize features such as that the probability of the outcome was very low.

Sometimes it is difficult for parents to 'see' the genetic disease of their children since the autistic symptoms appear more strongly than the dysmorphic features. By a lack of standardized diagnostic procedures in many syndromes and the absence of laboratory markers, the diagnostic process often stems from interpretation of a set of clinical signs and the experience of the geneticist. For some families, accustomed to different clinical procedures, this can also cause anxiety.

In some cases there is a probable diagnostic hypothesis, however, the test(s) required to arrive at an accurate diagnosis may not be accessible to the family. This can greatly hinder the process of genetic counseling and create stress in the family and counselor. The molecular revolution observed in the last three decades has introduced many procedures that are not still available in public health programs of several countries and only the most economically advantaged families can access them, which does not correspond with the reality of most people. While it lasts, intercountry collaboration programmes should be stimulated (WHO, 2010).

A large number of families consult the Internet before the counseling to obtain information about the diagnoses, treatment, and tests and so many clients arrive for genetic counseling with notions of the condition for which they are to have counseling (Peters & Petrill, 2011). This creates a series of expectations. Not always, however, information is obtained from reliable sources and it is for the counselor to clarify false beliefs or possible misinterpretation.

Also, it must be emphasized that the search for a solution makes the Internet a tool that frequently causes more harm than good. The demand for treatment has increased gradually and cognitive behavioural intervention programmes aimed at trying to improve social interaction and communications are encouraged (Wood et al., 2009). The design of these interventions is to act during the critical period of postnatal neuronal plasticity (within the first three years of life). But there are other not empirically proven therapies; for this reason, sites selling solutions for autism have proliferated. Couples come to genetic counseling requesting an opinion and explanation from the counselor on "magic formulas"; they become anguished and even feel guilty when they realize that this solution is unfeasible, especially as some of them have very high costs. It is for the counselor to reduce the anxiety of parents and explain that this is not about being for or against any type of alternative therapy, but that most have no scientific basis and some may even pose health hazards. Families need to understand the evidence for efficacy (or lack thereof) and potential side effects. More accurate and earlier diagnosis or the elucidation of etiological factors does not mean effective therapies in the short term.

### 3. Genetic counseling in autism of unknown etiology

On taking into account all technologies, an underlying genetic diagnosis is identified in around 10–15% of ASDs cases while cytogenetically visible chromosomal rearrangements are found in 2–6% of ASDs individuals (Bremer et al, 2011; Kumar & Christian, 2009). Hence, for most individuals (90%) with the autistic phenotype, there is no known genetic or environmental cause, which defines them as non-syndromic or 'idiopathic' as previously mentioned. Often this condition is established after negative results obtained from a medical evaluation to identify medical issues that affect the development and behavior of nonverbal children, physical examination about metabolic, medical, or neurologic conditions, careful examination of personal history, a detailed investigation of gestational antecedents and dysmorphic signs and after performing an odyssey of multiple testing.

Genome-wide studies have implicated numerous minor risk alleles with low and high penetrance but few common variants and with many contributing loci. Among the candidates are genes that code for important proteins in synaptic structure, function and maintenance. Genetic mutations in these genes result in an aberrant synaptic process that could produce the ASDs phenotypes. However, the frequency of these mutations is so low that widespread screening does not seem to be clinically justified. Some, however, deserve to be investigated because of clinical findings such as mutations in the *PTEN* gene in children with macrocephaly (Lintas & Persico, 2008).

As etiological factors are progressively being discovered, it is natural to think that the number of idiopathic cases will also gradually decrease. The increased resolution of CGH array testing in combination with new technologies, such as whole genome sequencing and bioinformatics programs, will play an important role in helping us to further understand the complex genetic basis of autism. The implementation of these high resolution techniques in the genetic research of ASDs may discover specific genotypes and subtypes of ASDs for which new diagnostic and therapeutic strategies can be developed. For this reason the identification of genetic abnormalities is a high priority in the study of ASD (Bremer et al., 2011).

For now, non-syndromic cases are much more common than other forms with estimates in the general population reported at approximately 1 in 100. In these cases, ASD is considered a complex disease of multifactorial pattern inheritance (Harrington, 2010; Maenner & Durkin, 2010)[4] M.J. Maenner and M.S. Durkin, Trends in the prevalence of autism on the basis of special education data, *Pediatrics* 126 (2010), pp. e1018–e1025. Full Text via CrossRef | View Record in Scopus | Cited By in Scopus (1). About 70% of probands with autism of unknown cause has a first- or second-degree relative with autistic symptoms, and 15% has fathers with Asperger syndrome. The empiric aggregate risk to sibs of individuals with autism of unknown cause varies across studies but is generally considered to range from 5% to 10% for autism and 10% to 15% for milder symptoms, including language, social, and psychiatric disorders. For families with two or more affected children, the recurrence risk approaches 35% (Miles et al., 2010).

All this information should be thoroughly discussed with the members of the family at their level of understanding. Obviously, faced with such uncertainty and heterogeneity, the counselor may feel uncomfortable to report these risks. It is essential that the family understands that when a child is diagnosed with an ASD, a range of etiological options are involved, which means the possibility of many different diseases. An aggravating factor is that the information may generate anxiety; most families have social and institutional barriers to carrying out more sophisticated tests.

#### 4. Psychosocial aspects of genetic counseling in autism

Throughout its development, the family goes through many changes. Each phase of the so-called life cycle (acquisition, adolescence, maturity and final) has its own peculiarities and difficulties inherent to the transformations that occur. During the acquisition phase, with the arrival of children, accepting parenting is already difficult. The family system "grows" as a whole and new links and forms of communication are needed. Moreover, the "myth of happy motherhood" is common, influenced by sociocultural aspects. This myth may become unreachable and a crisis may result from this expectation, as the ideal social value is not achieved. If motherhood is culturally associated with well-being and achieving, when the son or daughter is not compatible with the one desired by the parents, as is the case of children born with a vulnerability, this condition does not only change the psychophysiological functioning of the mother and her quality of life, but can also result in negative consequences for the whole family. Parenthood is a relational experience of profound psychological meaning, experienced in family relationships, which are transformed over the entire life and that are restructured with the normal cycles of family development and, occasionally, by unforeseen events (Cervený & Berthoud, 1997).

The arrival of a child with ASD can be considered an unexpected contingency at any stage that the family is going through, because these are serious psychiatric illnesses, which require special needs and require much understanding and patience due to the peculiarity of the symptoms. Given this reality, some authors have reported that mothers of children with disabilities tend to depression, which may be associated with hopelessness and worsened quality of life. This is also observed in the fathers and siblings of individuals with ASDs, with the degree of symptoms reflecting the severity of the autism of the affected relative (Orsmond et al., 2009; Orsmond & Seltzer, 2009). Carter and collaborators (2009) studied stability and individual change in depressive symptoms among mothers raising young children with ASD. They observed that child problem behaviors and delayed competence, maternal anxiety symptoms and angry/hostile mood, low parenting efficacy and social supports, and coping styles were associated with depression severity. Only maternal anxiety and parenting efficacy predicted individual change. Many mothers do not appear to adapt, supporting the need for early intervention for maternal well-being.

In particular, mothers experience the reality of having an autistic child permeated by feelings of nullity, loneliness and solitude. They also stop living their daily lives to live the everyday life of the child. Brothers and sisters have more stressful conditions of life, which include early responsibilities, anxiety and feelings of inferiority (Benderix & Sivberg, 2007).

Pearson et al. (2006) found that autistic individuals have more symptoms of depression, withdrawal from social life, atypical behaviour and immature social skills. Besides, they are at particularly high risk of comorbidities involving emotional and behaviour disorders, with direct consequences on their family. Family members have to adapt to a reality that, in addition to being new, is very heterogeneous, complex and difficult and that can result in conflicts that require intervention (Kelly et al., 2008). The disease eventually becomes the focus and other problems become unimportant; family members live only the disease and end up getting sick too (Balieiro & Cervený, 2004).

What is observed in practice is that when a child is diagnosed with ASD, parents experience a variety of very complicated feelings that are often unrelated to interventions involving the child, but related to the parents' particular vision of the world (Wachtel & Carter, 2008). After all, few other diseases can pose such a great threat to the family as these do, because autism

is still seen as an intense "stressor" (Woodgate et al., 2008; King et al., 2006). But when, for example, a better relationship is established between the mother and child, the autistic symptoms may reduce (Smith et al., 2008).

As ASDs are related to a great need for care that directly affects the development not only of the individual but also of their families, the resources available to families must be evaluated very well (Montalbano & Roccella, 2009; Montes & Halterman, 2008). It is important to strengthen social networks and the availability of resources such as specialized schools, stimulation therapy clinics and family psychotherapy (Smith & Elder, 2010; Cahill & Glidden, 1996). Family support is associated with increased optimism that, in turn, predicts higher levels of positive feelings. Even the child psychiatrist should be encouraged to participate in the social support network of parents, helping them on the long journey of raising their children (Wachtel & Carter, 2008).

The paediatrician's role is crucial, because with more frequent contact with the child and the bond of trust with the family, the doctor will be able to detect symptoms early and to guide the investigation and treatment. Most important, according to De Ocampo and Jacobs (2006), is to establish close cooperation and communication between the family and all the experts who care for the child.

There are many gaps in the scientific knowledge which justifies the need to define future research on families of children with these diseases. Health professionals must strive to study them and create effective support strategies.

## **5. Genetic counselor and counselee: a model and an example of case**

Genetic counseling, although governed by traditional guidelines that recommend certain actions, phases and intentions, varies much in the way it is developed, from centre to centre, region to region and from country to country. Not only the emphasis on some particular goal may vary but the composition of the team and the different forms of participation of each of its members may change.

Many kinds of questions can be used in different ways to increase the understanding, respect and empathy on both sides, counselor and counselees. The counselor is part of the system in which he acts and his personality is a determinant of how the process will be conducted within the basic goals of genetic counseling. Some counselors are more paternalistic (I suffer with you and if I could do anything for the situation to be different ...), and some are more authoritarian (You have to understand that I am experienced in this matter and definitely can help you...). There are also the many peculiarities of each team; never will the counseling given by one counselor in one situation be the same as that given by another. Also, counseling performed by one team for one family with a particular type of problem will not be identical to that for another family with exactly the same problem. The process is so dynamic that it cannot be predicted.

We will briefly describe a model of genetic counseling which occurred in a community genetic service of a low-income country (Brazil). It involves a context characterized by certain cultural, legal and religious limitations such as the cultural fear of genetic disorders due to stigma and legal restrictions in respect to selective abortion, among others. The service in question is located in a referral centre for health in a city of the most developed state of the country (São Paulo). It has an interdisciplinary team comprised of three counselors, three psychologists, physicians of different specialties, a social worker and two nurses. One of its peculiarities is that the genetic counselor and psychologist work together during counseling sessions of families, in a transdisciplinary way.

Briefly, the model can be described by the different phases through which the family passes after its arrival in the service:

- After presenting at the reception, the family is asked to stay in a waiting room. There the family is approached by a psychologist, who presents himself, establishes a rapport (contact, dialogue) and investigates the characteristics, expectations and basic needs of the family. The psychologist makes observations about the emotional state (anger, sadness, anxiety, etc.), the main coping strategies (emotional, cognitive and behavioural), psychological functions (guidance, judgement, attention, language, mood, level of understanding, etc.) and beliefs or fears. Questions such as these are used: "What is the reason for your referral to this service?", "Who referred you?" "What do you know about genetic counseling?", "How do you feel?", and "What do you expect from genetic counseling?". The family should be guided and informed on the practical, structural and dynamic operation of genetic counseling, its meaning, as well as the role of the different professionals involved. During the psychological approach a more relaxed atmosphere should be created.
- Before the counselor has contact with the family, he is informed by the psychologist on the data collected in the waiting room. The counselor has elements to promote a more focused and effective intervention, using a more targeted and personalized approach.
- On being called for counseling, the psychologist who established the initial rapport with the family in the waiting room, introduces the family members to the counselor, enters the room and participates in the genetic counseling process. Everyone sits in a circle, with a small table moved to the side, just for the counselor's note taking. The central table is considered an "obstacle" to establishing a relationship as it may suggest difference in level/hierarchical which always causes awkwardness. The psychologist accompanies the discussion, observes and only intervenes quickly and objectively on psychological aspects when requested or when he believes it is absolutely necessary. The phases of genetic counseling develop. It is up to the counselor to give psychological support inherent to the process. It is important to motivate the family to return for a follow up consultation, to perform exams, comply with treatment and to offer supports linked to the most urgent difficulties, contacting a social assistant and professionals/support institutions. When necessary, refer members of the family for a more detailed psychological assessment or for psychotherapy.
- In all consultations, the counselor and the psychologist caring for the family should be the same as the first visit and even when the process is completed the team should be available to explain future doubts that may arise through further meetings or by telephone.

All the professionals involved in the care of families of individuals with ASDs surely pass through difficult situations of intense learning that require much skill and compassion. Perhaps I can illustrate what this means using a true case.

On one day in November 2010 ... The psychologist informed the counselor that the family that she was about to meet comprised of a father, a mother, a three-year-old child with a diagnosis of autism made one week previously, and another five-year-old apparently healthy son. He said that the family was psychologically very weak. The mother, aged 32, expressed much sadness and spoke only when questioned. The father, 39 years old, expressed great anger, was extremely anxious and said that he did not know why they had been referred for genetic counseling, which he thought was a waste of time. Both were well educated; she is a computer engineer and university professor, and he is a judge. They had already researched

on the Internet many details about the problem and were very shocked and confused. In the waiting room the psychologist explained to them about the dynamics of the process and the benefits they might obtain with the clearing up of their doubts and specific guidance. The father rejected obstinately attempts of contact and the mother reported that she was feeling very lonely. As they spoke, the eldest son always listened in silence. When asked how he felt by the psychologist, the son answered "tired".

When called and led by the psychologist to the consultation room, the counselor noted the seemingly arrogant and cold attitude of the father, who entered the room in front of his wife that was holding the hands of both children, and sat down before anyone else. The children were seated in the centre of the circle where some toys had been placed so that they could play and so they would stay there. The counselor noted the autism phenotype of the child with repetitive stereotypic movements, isolation, lack of speech, among other things, without dysmorphic signs. The mother reported that the diagnosis was made by the team of psychiatrists and neurologists that had requested exams, including biochemistry, imaging, hearing evaluation, among other tests, which were normal. The pregnancy and delivery occurred without complications. Also, there was no parental consanguinity or other risk factors involved. She said that before the completion of the diagnosis of childhood autism, other professionals had partial or wrong diagnoses, which left her very confused.

Both the father and mother started giving much information without being requested, including some technical information about autism. They started a kind of "competition", both on involving who spoke first and on the level of knowledge that each one had. Thus, the genetic counselor had an opportunity to observe and evaluate the couple's dynamics. At one point the counselor interrupted them and said, in an attempt to move on directly to emotional issues, "I am realizing how much you are frightened by the diagnosis that you received. Before I explain to you about the diagnosis, I would like to know more about your feelings. What made you so upset? Do you think it is very hard for you to talk about this now?" The couple, as they were caught by surprise, agreed to talk about it and the counselor asked the mother to speak first. Crying a lot, she reported that she was trying to understand everything that was happening and that she was not able to concentrate on her work anymore. She felt very guilty because her family was no longer the same, her eldest son was in trouble at school and that she felt very lonely. She did not know anyone with a child with the same problem and that, initially, the worst that she thought was that her son was deaf. She confessed that she always only wanted to have one child and that the second pregnancy was not planned. She had rejected the child and she felt that was being punished for this. She even felt that she was being punished too for an abortion she had as a teenager. She would like to talk to other people about their son but she had made a deal with her husband that they would not reveal the child's diagnosis to anyone; not before trying to help him to get better.

The counselor told her she had some mistaken ideas and meanings but it was good to see that she was seeking help. Those feelings, though difficult, were natural and expected, as in general, no person is prepared to have a child that is different to what they expected and very few people are ready for this possibility. The counselor continued saying that much of the information that they would receive starting from the first session, might certainly help in this difficult emotional period that the entire family was going through. The father interrupted saying "Speaking of information, I need you to tell me why my son is autistic!" The counselor felt upset with the authoritative behavior of the father and his attempts to

hide his emotions. The mother broke in with the phrase "It is impossible to live with him" to which the father replied "You cannot talk about us because is our son who needs help!"

Then the counselor told the father that she noted that he was also seeking help albeit in a different way. The counselor explained the relative proportions of autism cases in the population that might be attributable to various mechanisms of genetic transmission and that the vast majority of cases of autism remain idiopathic. The counselor asked the father how possible information about the cause of the autism of their son could help him, and why he preferred not to reveal the diagnosis to the child's relatives and friends. He replied that by discovering the cause there would certainly be drugs/specific therapies that would improve their son's condition and that people would look less and would not feel sorry for their son. The anxiety about the manifestations of the autistic child was clear. He added saying that the child was very "stubborn"; he was being seen by a speech therapist and occupational therapist and was taking psychiatric drugs and did not improve much except for being less aggressive. In a possible attempt to justify their ways, the father said many members of his family were stubborn, especially his father. He had been educated in a traditional manner. His father was very angry and never admitted that his children, all male, were weak.

The counselor noticed that the psychological defenses of father were not entirely unconscious. He was being "defensive" and his behavioral probably was related to a great sense of loss.

The counselor provided some practical explanations about autism and coping with affected children, explained the importance of knowing other families, some support institutions and the etiology of ASDs. In 90% of the cases, the etiologies of ASDs are not known.

As the parents had some technical knowledge from other sources, but did not understand it very well, the counselor re-organized the information and clearly explained it, in particular, in respect to idiopathic cases. It was explained that some more sophisticated genetic testing methods that the child had not been done, but they also had a low probability of identifying the cause of the disease. The counselor congratulated the parents because they were adhering to the proposed treatment plan and explained the lack of specific remedies linked to a possible cause in this case and in most others. Finally, that she understood the frustration of the father, his difficulties in understanding the behaviour of his child, who was not stubborn, but he just could not "understand" what his father wanted from him.

At this point the father began to cry copiously and the psychologist intervened saying that he was among friends who wanted to help him, and that he was in the right place to express his emotions without shame or fear of being judged. The counselor asked his wife to hold the hand of her husband and in so doing the eldest son stood up and hugged his father, a move which, to everyone's surprise, was followed by the autistic son, who sat on the father's lap.

After this time, the challenges and clashes that marked the start of the session were replaced by interest to explore and discuss all information. They expressed interest in performing the tests that were missing and in doing psychotherapy. The counselor reiterated that she perceived the sense of responsibility and parental love, fundamental for the family's adjustment to the new reality. The session was adjourned with the family thanking the team for their help and patience, who thanked them for their trust. A return visit was set for 45 days.

At the next session the parents came back hand in hand, the mother was more confident and the father more pleasant. The new tests also showed normal results and the counselor

restated some information. The parents were very satisfied with psychotherapy and had chosen couples therapy. The autistic child had begun equine therapy and the parents were excited and hopeful. They said that they had organized a lunch for relatives and close friends, where they would tell their child's diagnosis and how they counted on the understanding and help of all.

The counselor and psychologist expressed their admiration and congratulated the mother and father for their initiative and expressed their satisfaction with the many positive developments. The team of professionals knew the family's feelings of love and of commitment to each other would support them through what lay ahead. At the end of the session, the psychologist could not contain himself and asked their eldest son: "And you, how are you feeling?" He just smiled and hugged his autistic brother...

## 6. Conclusion

ASDs have become a public health problem but there are many misunderstandings about the heritability of these disorders. The detection of genetic alterations may contribute to the diagnosis, allow an understanding of biological mechanisms involved in the pathogenesis, assist in genetic counseling of families and guide prevention and educational planning. Health care practitioners need to be able to provide information about general principles of human genetics as well as the epidemiological and molecular aspects of genetics regarding Autism Spectrum Disorders. In addition, they need to understand the limitations of genetic testing and the psychological conditions of the families. Knowledge of the genetic factors involved and of the psychological effects of these diseases is crucial for the establishment of intervention strategies that promote the bio-, psycho- and social well being of those affected and their families. Besides providing technical information necessary for the family to have a better understanding about the disease, genetic counseling can alleviate some of the common mistaken beliefs and provide support to families, assisting in the transformation and adaptation of the members. It is very important that psychoeducation programmes be created for parents, focused on handling stress and emotions, modifying false beliefs and solving the daily problems that arise from ASDs.

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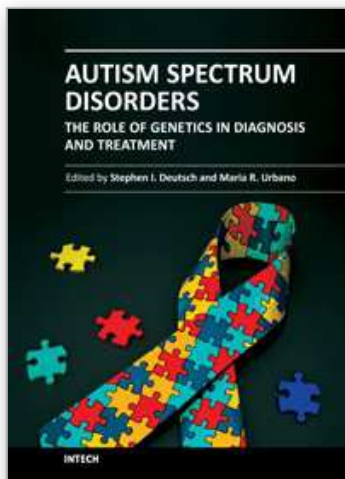
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## **Autism Spectrum Disorders: The Role of Genetics in Diagnosis and Treatment**

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Estimated prevalence rates of autism spectrum disorders (ASDs) have increased at an alarming rate over the past decade; current estimates stand as high as 1 in 110 persons in the population with a higher ratio of affected males to females. In addition to their emotional impact on the affected persons and their family members (in fact, the latter are often unrecognized unaffected “patients” themselves), the economic and social impacts of ASDs on society are staggering. Persons with ASDs will need interdisciplinary approaches to complex treatment and life planning, including, but not limited to, special education, speech and language therapy, vocational skills training and rehabilitation, social skills training and cognitive remediation, in addition to pharmacotherapy. The current book highlights some of the recent research on nosology, etiology, and pathophysiology. Additionally, the book touches on the implications of new research for treatment and genetic counseling. Importantly, because the field is advancing rapidly, no book can be considered the final word or finished product; thus, the availability of open access rapid publication is a mechanism that will help to assure that readers remain current and up-to-date.

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#### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

#### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

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