Review Synthetic Report

Genetic and socio-anthropological regards in infantile Autism

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Abstract  Infantile autism is an early onset neurodevelopmental disorder defined by significant deficits in social interaction and communication and stereotypic behavior. Advances in autism genetic continue to expand the list of medical diseases associated with autism. The etiology and contributing genetic and environmental factors for autism are still poorly understood. Linkage analyses for autism susceptibility loci have suggested the involvement of multiple genes from different chromosomes. The socio-anthropological approach contributes to an understanding of autism focusing mainly on development, socialization, communication and behaviour of the autistic children. This approach assures the comprehension of cultural and social factors influencing the social representations of autism and employs a variety of strategies of integration of the autistic children in different social contexts. Autism damages the social competence of the patient and his or her interaction with others. Impairments associated to the cognitive, emotional, linguistic and social interaction will be reduced if adequate strategies of intervention are applied in the social context of autistic children. Dermatoglyphic studies are considered to be beneficial in the early diagnosis of some syndromes genetically determined. The dermatoglyphic investigation performed on autistic children has put into evidence multiple distortions with deep pathological significance in the digital and especially in the palmary picture. This review is an attempt where converge two disciplines, genetics and socio-anthropology, in order to give an interdisciplinary raise for helping the understanding of this pathology.

Key words : autism, genetic, socio-anthropology, socialization, communication, dermatoglyphics.
Introduction

Infantile autism is a neurodevelopmental defined disorder (Skaar et al., 2005; Watts, 2008) initially described by the psychiatrist Leo Kanner in 1943 (Coplan and Jawad, 2005). It is characterized by qualitative impairments in social interaction, social communication and social imagination with stereotypical, ritualistic and often stereotyped repetitive behaviours and mannerisms and major defects in language development and in other communication skills (Baird et al., 2003; Muhle et al., 2004; Skaar et al., 2005; Watts, 2008).

There are 5 subtypes of Pervasive Developmental Disorders (PDD):

1) Autistic disorder (autism),

2) Asperger disorder (language development at the expected age, no mental retardation), 3) disintegrative disorder (behavioural, cognitive and language regression between ages 2 and 10 years after complete normal early development, including language)

4) PDD not otherwise specified (individuals who have autistic features and do not fit any of the other subtypes)

5) Rett disorder (a genetic disorder of postnatal brain development, caused by a single-gene defect predominantly affecting girls) (Fombonne, 2001; Skaar et al., 2005; Mercandante et al., 2006; Myers et al., 2007).

Autistic disorder is the most severe form of autism spectrum disorders (ASDs) which include Asperger’s syndrome and PDD NOS or atypical autism (Hertz-Picciotto et al., 2006; Newschaffer et al., 2009; Grigorenko, 2009).

The onset of autism occurs before the age of 3 years with symptoms continuing for life (Durand et al., 2007; Geschwind, 2008; Grigorenko, 2009). Approximately 70% of individuals with autistic disorder have some degree of mental retardation and about half are nonverbal or have very impaired speech (Hertz-Picciotto et al., 2006). The current prevalence of autism spectrum disorders is estimated at 6 per 1000 (1.3 per 1000 for autism itself). Autism is more common in boys occurring 4 times as often as in girls with an average male - to – female ratio of 4.3:1 (Trottier et al., 1999; Barnby et al., 2005; Rosen et al., 2007; Fatemi, 2008; Watts, 2008; Newschaffer et al., 2007).

The present report is a synthetic review drawing together recent data and conclusions on the genetics and the socioanthropology of autism.
The Genetics of autism

Evidence for a Genetic Basis

The scientific research on autism during the last 30 years supports the role of genetic factors in its etiology (Geschwind, 2008; Losh et al., 2008). Monozygotic twins show 60% concordance in contrast to only 3% to 5% concordance in dizygotic twins with a heritability estimate of 90% (Losh et al., 2008; Hertz-Picciotto et al., 2006). In spite of this high heritability, there is no particular model of genetic transmission nor identifiable major gene that present the cause of autism (Geschwind, 2008). However a strong familial aggregation of autism was noted: the recurrence rate obtained is of 5% to 8% within families, a 25- to 40- fold increase in risk over the general population.

The clinical characterizations performed in several family and twin studies, documented among relatives a phenotype similar in quality to the defining features of autism but much milder in expression (Losh et al., 2008). The last results of research in autism reveal significant genetic heterogeneity: several dozen distinct genetic disorders or identified chromosomal abnormalities can result in autism (Geschwind, 2008). Linkage, association and cytogenetic studies have been conducted to elucidate the association between specific genes and autism (Talebizadeh et al., 2002; Hertz-Picciotto et al., 2006).

Genetic diseases associated with autism

Genome-wide linkage analysis was initially viewed as a valuable approach for looking for genes causing autism because this approach has the advantage of scanning the genome for disease-associated loci in the absence of a priori hypothesis about the genetic architecture of the disease (Bukelis et al., 2007; Losh et al., 2008). The most frequent genetic syndromes associated with autism are fragile-X syndrome (FXS) and Tuberous sclerosis.

FXS is an X-linked genetic disorder characterized by development pathways that influence physical development, cognitive ability and behavioural outcomes (Eliez et al., 2001). It is caused by an increased number of trinucleotide (CGG) repeats in the gene FMR1 coding for the fragile X mental retardation protein (Winnepenninckx et al., 2003).
The tuberous sclerosis complex TSC, is an autosomally dominant neurocutaneous disorder, which is the result of genetic mutations on either TSC1 on 9q34 or TSC2 on 16p13.3 and characterized by ash leaf depigmented manifestations (Muhle et al., 2004; Benvenuto et al., 2009). It was shown that 20-40% of individuals with FXS have an ASD while 43-86% of patients with TSC have an ASD (Benvenuto et al., 2009).

The relationship between autism, epilepsy and regression is complex. An epileptic disorder must be considered in all children with a low functioning ASD (Minshew, 1991; Muhle et al., 2004; Benvenuto et al., 2009). Neurofibromatosis, a common autosomal dominant disorder characterized by neurologic and cutaneous manifestations, is much less frequently associated with autism than is TSC or FXS (Muhle et al., 2004). Several patients with Kabuki syndrome have been found to have autism or autistic-like behaviour, with difficulties in both communication and peer interactions (Akin Sari et al., 2008). Other rare single-gene defects have been associated with autism in a number of case studies (Muhle et al., 2004, Bukelis et al., 2007).

Chromosomal abnormalities and candidate genes

A genome-wide screen with 264 microsatellites markers performed in 51 multiplex families using non-parametric linkage methods revealed 11 chromosomal regions positively linked to autism (Muhle et al., 2004). Four of these regions overlapped with regions on chromosomes 2q, 7q, 16p and 19p identified by the first genome-wide scan of autism performed by the International Molecular Genetic Study of Autism Consortium (Philippe et al., 1999). A potential susceptibility region with positive results for three adjacent markers, on chromosome 15 (q11–q15) was identified (Philippe et al., 1999). Chromosomal rearrangements in 15 q11-15 q13 region might be the most cytogenetic abnormality in ASD, accounting for 1-2% of patients (Schroer et al., 1998; Benvenuto et al., 2009).

The presence of an autism susceptibility locus within the distal long arm of chromosome 7 (7q) has been indicated (Muhle et al., 2004; Skaar et al., 2005). Two loci 7q22 and 7q31 contain several genes implicated in the pathogenesis of autism. Increased risk for autism can be linked to a functional polymorphism in the RELN gene (found within the 7q22 locus) and in the MET gene (found within the 7q31 locus) (Skaar et al., 2005; Losh et al., 2008; Benvenuto et al., 2009).
The candidate-gene reelin (RELN) encodes a signalling protein that plays a pivotal role in the migration of several neuronal cell types and in the development of neuronal connections (Skaar et al., 2005). Alterations in RELN protein affect cortical and cerebellar development and the cerebellar abnormalities are considered to be robust pathologic findings in autism (Muhle et al., 2004).

Several candidate-genes for autism have been identified in 2q37.3 band. Furthermore, a correlation has been described between autism and a de novo cryptic deletion of chromosome 2p25.2 (Benvenuto et al., 2009). The gene SHANK3 localized on chromosome 22q13 has been associated with autism. A mutation of this gene was found, it encodes an abnormal protein responsible for synaptic or dendritic changes leading to autism with sever language and social deficits (Durand et al., 2007; Losh et al., 2008; Benvenuto et al., 2009).

Neuroligins, cell adhesion molecules that play a prominent role in synaptic maturation and function are regarded as plausible candidates implicated in autism (Grigorenko, 2009). A link between neuroligins and autism was first supported by findings of mutations in the X-linked neuroligins, NLGN3 and NLGN4 in two autistic sib pairs (Losh et al., 2008; Grigorenko, 2009). Neurexins encode a family of neuronal proteins that interact with neuroligins to promote synaptic functioning (Grigorenko, 2009). Neurexin mutations were detected in a recent genome screen conducted by the Autism Genome Project Consortium and recently a number of rare coding variants in a scan of NRXN1 were also identified (Losh et al., 2008; Grigorenko, 2009).

**Structural variants: an additional mechanism**

Recent research in autism genetics has led to an increased appreciation of the de novo and inherited copy number variations CNVs (Abraham and Geschwind, 2008). Whole genome-scanning by array-based technology has detected CNVs which are copy-number changes involving a DNA fragment and represent micro deletions and duplications that are undetectable in the routine cytogenetic analysis (Benvenuto et al., 2009).
De novo CNVs were detected in 24% of individuals with autism (Losh et al., 2008) and in 3% and 10% of autistic children from multiplex families and autistic children from simplex families respectively (Geschwind, 2008). It is too early to predict with from these data the contribution of de novo CNVs to ASD susceptibility. It will be necessary to define the role of CNVs accurately, to have larger sample sizes obtained from independent and clearly defined populations (Geschwind, 2008).

**Socio-anthropology of the autism**

How do specialists talk about and represent the fact of being sick? It seems that the opinion of the patient of his/her disease is based on a profane subjective representation and is associated with his/her individual experience. By investigating the systems of knowledge and recognition of the disease, several studies were managed to propose a conception of the health of a normal or a pathological subject (Adam and Herzlich., 1996; Levin and Browner, 2005). But really the question became more complex when the scientific papers turned to the mental handicap (Jodelet, 1989; Poulin and Levesque, 1995; Rejeb, 2008) which is not yet fully developed to give access to these details. As a category of incapacity affecting the person, the mental handicap still remains enigmatic for research as well as for specialists and the public. So if we are able, regardless of current research relativity, to obtain specialized and objective knowledge then who can give us access to the profane said knowledge?

Being a patient is human which means that being mentally handicapped is human too (Courtial et al., 2007). The simultaneous appeal to the learned and profane representations allows establishing a relation of co-presence between these two logics. The studies carried out since Canguilhem (1943) and based on pathological and normal cases, contributed to producing scientific knowledge of the disease. In this context, Binswanger (1971) treated health from a cultural and anthropological angle. But this could not deal fully with the mental handicap. This can explain the criticism levelled by Heidgger at Binswanger: the phenomologist prefers to speak about “suffering” rather than “mental illness” (Benvenuto, 2006).
In fact, many scientists think that environmental factors interact with genetic predispositions to contribute to autism (Sigman, 2006). Matson and Lo Vullo (2009) have showed in their review that the ASD presented a topic of considerable scientific interest. According to this review, the principal trends of research in autism have been oriented towards many fields: (1) genetics (2) perception and cognition (3) neurobiology and physiology (4) review / overview (5) nosology (6) neuropsychology (7) social skills (8) generic treatements (9) diagnosis (10) developmental run (11) comorbid psychopathology (12) scale development, (13) pharmacology (14) challenging behaviors (15) etiology (16) theory of mind (17) epidemiology.

But we can indeed notice that the socio-anthropological approach is not the theoretical and methodological appropriate framework used to include this pathology; although the anthropological approaches of the study of autism are contributing to a better understanding (Lawlor, 2010). Mostly autism is confronted with the challenge to report its multi-dimensional level (Chamak, 2005).

We claim that socio-anthropology presents a major and outstanding contribution and sets a remarkable place by in research assuring an understanding which helps to penetrate into the worlds of the learned and profane mental handicap. Most importantly, it allows to exceed the various evident analyses which are sometimes simplistic. The socio-anthropologic approach treats the environmental factors associated to autism and also conquers new horizons in this disease which remains among the mental handicaps the least investigated in spite of the rich bibliography found on this theme.

This approach in addition to giving access to socio-cultural classifications of autism, makes it possible to determine various elements which relate to the social or to the individual such as the speeches, the practices, the temporality, the subjectivity, the transmission of the representations among individuals. The report of the plurality of the representations for the same disease and very often at the same individual level or at the same population level makes one wonder about factors responsible for the choice of the contents of the representation. Furthermore, the socio-anthropological treatment points out the analysis of development, socialization, communication and behavior (Levy et al., 2009).
Socio cultural classification of the autism

A socio-cultural approach to autism, considers autism from three social angles: (1) participating in conversational turn-taking and sequences; (2) formulating situational scenarios and (3) socio-farming interpreting meanings of indexical forms and behavior (Ochs et al., 2004). This classification wraps the main socio-cultural dimensions of the disease. Several studies treated the interactive aspect of the autistic subjects (Hewitt, 1998, Machalicek et al., 2006, Wesley et al., 2010). For instance in their study, Leaf et al (2009) define the interactive fitness by focusing the treatment on the following domains:

- Play
- Conversation
- Emotional
- Choosing the same friends

This typology allows to determine the diagnosis of the degree of interactive fitness of the autistic child and to observe the process of evolution by using a protocol taking into account the following items: academic skills, communication skills, functional life skills, social play and skills. To appreciate the expected contribution of these researches, we have to bear in mind that "Language difficulties exhibited by autistic children vary from the complete absence of vocal speech to limited proficiency in social situations. Recent studies have revealed that more than half children diagnosed with autism at 2 years could not produce judgments at 9 years of age (Fischer, 2010).

Autism as a socio-linguistic impairment

Conversation for the autistic persons and with them is a double challenge. We know that the main incapacities are linguistic, communicative and social ((Hewitt, 1998, Ochs et al., 2004, Solomon, 2008). In a comparative perspective, the social cognition is thus underdeveloped in autism, but hyper-developed to dysfunction in psychosis (Crespi et al., 2007). DSM-IV ‘Diagnosis Statistical Manuel- Fourth Edition) includes social reciprocity and inflexible thinking/ restricted interests but no history of clinically significant language delay for diagnosis conversational disorders (Paynter and Peterson, 2010). Ochs et al. (2004) note that social cultural knowledge constitutive of
membership in human societies and lay out framework for analyzing abilities/disabilities in relation to norms, preferences, and expectations that are tied to participation in culturally configured social situation. Those autistic impairments are related to social competence, especially the ability to take the perspective of others (Ochs and Solomon, 2004).

Thus, the studies have given an important clarification with regard to understanding how to proceed linguistically with this category. Hewitt (1998) in her study supports the well-known claim that simple syntax and short utterances are easier for individuals with disorders to process, and should be used as much as possible in communicating with this population in order to optimize comprehension. The situation of conversation between autistic people and non-autistic persons is too complex and contradictory to pursue conversational continuity and understanding (Solomon and Bagatell, 2010; Gouvousis et al., 2010). But it is not also evident to assure this understanding because the autistic subjects are less aware of the other perspectives and options. The socio-emotional complexity of their conversational situation explains difficulties of verbal trade (Ochs et al., 2004).

**Autism as a socio-emotional impairment**

The autistic children were probably less sensitive emotionally to the information conveyed by the social environment representing a deficit in emotional perception that would likely lead to social problems (Hughes, 2008). The communication impairment which partially defines autism is closely related to the impairment of social interaction, and includes impaired use of language even when language is present (Boucher, 2003). From another ethnographical point of view, Solomon(2008) has considered that children with ASD are seen as actively participating in the co-construction of their worlds of life by communicating with others, rather than to be assisted by others or to be managed or treated. Rejeb (2008) advanced concerning the infantile mental handicap, an explanation helping to understand the relationship of the autistic child with his social world and particularly with his family. This analysis showed well that the handicap is seen as «a visible focus of stigma» and it intervenes in interference with the family context to provoke disorders of interaction. Other studies also showed well that the depression of the parents having an autistic child is associated with the deficiencies of their child and especially with the behavioral stereotype and with the problems of the social communication (Hughes, 2008; Volkmar, 2005).
Autism as a socio-cognitive impairment

Children and adults with autism have also been shown to have deficits in their understanding of pretence, irony, non-literal language and deception (Hill and Frith, 2003). To understand this relationship of autism in the mental development, several studies, such as that of Hill and Frith (2003), made appeal to the theories of mind (ToM) like cognitive theories—mentalizing deficit, weak central coherence and executive dysfunction. The cognitive capacity of the autistic children can be improved when they have been integrated with normal peers (Paynter and Peterson, 2010). So, innovating the interventions to acquire socio-cognitive and social skills can help these children to succeed socially with their peers (Heyes, 2001). In addition, Boucher (2003) indicates that the essential causes of the linguistic deficiency are psychological.

Socialization and taking charge of Autism's child.

When dealt with autism through socio-anthropologic approach, the problem of the socialization and taking charge can be overcome. The various deficiencies constitute a load to parents and the family. As we have already indicated, autism presents too «a visible focus of stigma". Our socio-anthropological conception of childhood allows understanding this result. This conception is defined as situations of socialization in perpetual construction following processes which can function in a cultural register, essentially values and significations. We can advance the following remark: all the steps of the childhood depend on the adult, the social history of the family and the various systems of socialization (Figure 1) (Rejeb, 2009).

All experiences of socialization are influenced by the different variables mentioned in figure1. Al Anbar et al. (2010) propose that identifying parents’ beliefs about their child’s illness may be an important step in formulating family interventions to reduce distress and enhance well-being. Also Whittingham et al. (2009) in their study, focused on the role of parental attributions in predicting treatment outcomes.
The diagnosis by dermatoglyphics: anthro-po-genetic assignment

Our review seeks to deal with the question of pathologic/normal, health/illness and thus to improve health care system in relation to autism. It is so necessary to establish some methods and techniques for an early identification of children at risk of having autism: an adequate therapy should be applied prior to the manifestation of any symptoms (Tarca and Barabolski, 2003).

Dermatoglyphics are the patterned traceries of the epidermal ridges on fingers, palms and soles. Dermal ridge configurations begin to develop about the 13th week of gestation. The pattern formation is complete by the 19th weeks (Hassanzadeh Nazarabadi et al., 2007) and after this period, dermatoglyphics remain unchanged and thus appear to constitute enduring evidence of prenatal insult. A relationship was established between embryonic stress and the presence of the simplest digital patterns which are archs (Babler, 1978).
Many studies have shown that dermatoglyphics can be used as a tool of diagnosis of some genetic diseases and syndromes genetically determined (Rosa et al., 2001; Hassanzadeh Nazarababi et al., 2007). Dermatoglyphic studies are considered to be beneficial in autism, thus several studies of dermatoglyphs of the digito-palmar complex in autistic patients have been published ((Tarca and Barabolski, 2003; Milicic et al., 2003). Compared to control subjects, autistic patients have shown that both their fingers and palms present many distortions with deep clinical significance. Increased number of arches, reduced number of whorls and lowered ridge counts were observed. Other abnormalities of ridge structure and a complete suppression of transverse crease were noted (Tarca and Barabolski, 2003). These results could be used for an early identification of autism in order to establish an adequate therapy.

Conclusions

From the current review, it is possible to conclude that:

Autism is well known as a complex developmental disorder characterized by significant disturbances in social communicative and behavioural functioning. Autism is a multifactorial disease caused by genetic and environmental factors. Several chromosomal loci contribute to genetic susceptibility in autism. Autism damages the social competence of the patient and his or her interaction with others. Impairments associated to the cognitive, emotional, linguistic and social interaction will be reduced if adequate strategies of intervention are applied in the social context of autistic children. Furthermore, the cognitive capacity of the autistic children can be improved when they are integrated with normal peers. The autistic children can be able to co-construct their world by communicating with others. The question of pathologic/normal, takes on importance in raising health care system in association with autism. The socio-anthropology approach contributes to a better understanding of autism. This approach focuses mainly on development, socialization, communication and behaviour of the patient. The dermatoglyphic investigation performed on autistic children have put into evidence multiple distortions with deep pathological significance in the digital and especially in the palmary picture which can contribute to a more complete knowledge of the dermatoglyphic nomogram and thus, autism could be diagnosed early.
References


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