

REVIEW ARTICLE

Autism Spectrum Disorders in Iran

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Abstract

Objective

Autistic disorder, Asperger syndrome, and PDD-Not Otherwise Specified are subsets of autism spectrum disorders (ASDs), which are characterized by impairments in social communication and stereotyped behavior. This article reviews the prevalence, etiology, diagnosis, and treatment of ASDs in Iran.

Materials & Methods

We searched PubMed, ISI Web of Science, and 4 Iranian databases (IranPsych, IranMedex, Irandoc and Scientific Information Database (SID) to find Iranian studies on ASDs. The results of 39 investigations, comprising original, review and editorial articles; proceedings; and available dissertations were categorized by prevalence, etiology, diagnosis, and treatment.

Conclusion

Several preliminary investigations have been done to evaluate the prevalence of ASDs, and risk factors and effective variables have been studied with regard to etiology. The diagnostic evaluation of ASDs, especially based on EEG, and several pharmacological and behavioral interventions for ASD have been implemented in Iran. Mental health, stress levels, and personality characteristics were examined in the parents of children with ASDs, which were focused on mothers.

Keywords: Autism spectrum disorders (ASDs); prevalence; etiology; diagnosis; treatment; Iran

Introduction

Pervasive Developmental Disorders (PDD) is severe developmental abnormalities in many fundamental psychological functions that are characterized by persistent social impairment, speech disorders, and exotic motor movements. Autism Spectrum Disorders (ASDs), which is one of the PDD and includes autistic disorder, Asperger syndrome and PDD not otherwise specified, are characterized by abnormalities in social interaction, verbal and non verbal communications and having repetitive and stereotyped behaviors (1, 2, 3). ASDs have multiple etiologies, from genetic to environmental factors (4, 5).

Less attention has been paid to the study of ASDs especially their epidemiology in developing countries. In fact, most studies on ASD prevalence have been performed in the United States and Europe (6). Totally, recent scientific researches indicated that the rates of ASDs are rising. In primary school children, the rate estimated of ASD prevalence is 157 per 10,000 children in the United Kingdom (7). The only study on adults with ASDs calculated a prevalence of 98 per 10,000 in England (8). A study

on 8 years old children with ASDs estimated that 90 per 10,000 participants were affected in the United States (9). In a comprehensive review, the prevalence rate was approximately 20 per 10,000 for autistic disorder, 30 per 10,000 for PDD-NOS, and 2 per 100,000 for Asperger syndrome (10). In contrast, the rates of Asperger syndrome are 36 and 48 per 10,000 children in Sweden (11, 12).

ASD prevalence rates vary across the world. Accordingly, these differences are related to the age of participants, diagnostic criteria, and the geographical locations. Also, lower prevalence rates of ASDs in developing countries can be explained by the scarcity in services and the lack of awareness about ASD (13).

Because cultural factors play an essential role in the prevalence, diagnosis, and treatment of ASDs, they should be examined (14). Thus, research on ASDs in Iran will be reviewed in this article.

Materials & Methods

A systematic literature review was performed to identify ASD studies in Iran. Accordingly, PubMed, ISI Web of Science, and 4 Iranian databases (IranPsych, IranMedex, Irandoc, and Scientific Information Database (SID)) were searched to find Iranian studies on ASDs using a combination of 2 groups of terms. The first group included the terms: autism spectrum disorders, autism, autistic disorder, PDD-Not Otherwise Specified, and Asperger, combined with OR; the second group consisted of Iran or its major cities. The names of famous Iranian researchers in the ASD field and their curriculum vitae were also searched to find scientific studies on ASDs in Iran. Case reports were excluded; the results of 39 investigations, including original, review, and editorial articles; proceedings; and available dissertations were categorized based on prevalence, etiology, diagnosis, and treatment.

Literature Review

There are epidemiological and clinical studies about the frequency, etiology, diagnosis, and treatment of ASDs in Iran.

Prevalence of ASDs

While there is no advanced study on ASD prevalence

in Iran (15), Ghanizadeh's preliminary investigation in school children (2008) indicated a rate of 19 per 1000 for probable autistic disorder and 5 per 1000 for probable Asperger syndrome, which is more than the reported rates across the world (16). Also, Nejatisafa (2003) performed the first preliminary study to investigate the frequency of ASDs in university students; while the scores were significantly higher for men than women, the frequency was 120 of 1000 adult participants (17).

A study demonstrated the highest prevalence of ASDs for autistic disorder, then Asperger syndrome, and PDD-NOS; also, it indicated that boys were 4 times more likely than girls to have autistic and Asperger disorders (18). The prevalence of autistic students is 0.366% among exceptional students (19).

Etiology of ASDs

With regard to etiology, the relationships between ASDs and some effective factors have been investigated. In a recent study, the theory of mind development was significantly affected by gender and IQ; thus, low-functioning autistic children had the poorest performance in the theory of mind development compared with high-functioning autistic children and the normal group (20). In the other study, IQ was an important factor in determining the visual memory of meaningless shapes in children and adolescents with ASDs; so a significant difference was observed in the visual memory of meaningless shapes between children and adolescents with ASDs and the normal group by entering the IQ effect, but the results were contrary by eliminating it. However, IQ variation did not correlate with facial memory in children with ASDs. There was no significant difference in facial memory between children with ASDs and the normal group in this study (21).

In a clinical study, no significant correlation was observed between age, the diagnosis and severity of symptoms with gender in children with ASDs (22).

Sasanfar (2010) investigated parental age and education level as risk factors and suggested that higher paternal age, but not maternal age, and higher education level increase the risk for autism. However, it seemed that parents with high education usually sought diagnostic and therapeutic services more than less educated parents (23).

In another Iranian study, no correlation was observed between autism and celiac diseases in autistic children compared with age- and sex-matched normal groups (24).

The brain stem has a critical role in processing hearing inputs and has been investigated using an auditory brain stem response tool in children with slight and severe autism compared with a normal group. This research indicated brain stem abnormalities in severe autistic children, which can intensify autism symptoms (25).

Diagnostic evaluation of ASDs

Several studies have diagnosed abnormalities by quantitative electroencephalography (qEEG) analysis in children with ASDs in comparison with normal participants. Considering that the spectrogram showed more abnormalities in the left brain hemisphere and prefrontal lobe in children with ASDs compared with normal children, the relaxed eye-opened condition in the

alpha band was the best condition under which 2 groups could be discriminated (26).

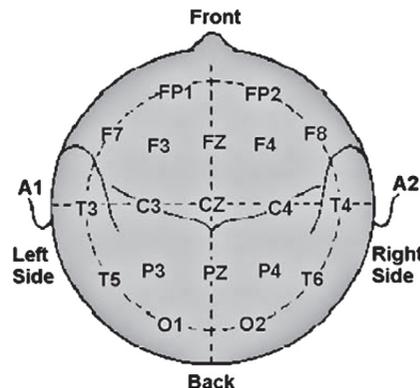


Fig 1. International EEG electrode placement system (27)

Also, more abnormalities in the connectivity of temporal lobes with other lobes in the gamma frequency band have been based on coherence values in children with ASDs (28).

Table 1: The spectrogram criteria values of the EEG for children with autism spectrum disorder (ASD) and control children for all electrodes in the alpha band (8–13 Hz) (28)

Electrodes	ASD children (Mean±SD)	Control children (Mean±SD)	P Value
Fp1*	0.238±0.156	0.381±0.131	0.018
Fp2	0.256±0.165	0.357±0.157	0.122
F7*	0.245±0.131	0.376±0.146	0.021
F3**	0.197±0.076	0.442±0.103	0.000
Fz	0.237±0.106	0.309±0.175	0.192
F4	0.270±0.174	0.309±0.137	0.529
F8	0.300±0.198	0.337±0.118	0.583
T3**	0.254±0.136	0.405±0.130	0.007
C3*	0.251±0.156	0.401±0.121	0.013
Cz*	0.267±0.146	0.407±0.173	0.030
C4	0.291±0.182	0.310±0.190	0.796
T4	0.313±0.175	0.391±0.219	0.308
T5*	0.238±0.156	0.396±0.150	0.014
P3	0.300±0.154	0.411±0.133	0.063
Pz	0.310±0.196	0.395±0.147	0.231
P4	0.340±0.194	0.407±0.179	0.373
T6	0.319±0.170	0.388±0.123	0.258
O1	0.304±0.169	0.381±0.151	0.234
O2	0.308±0.161	0.293±0.163	0.821

** p<0.01 and * p<0.05

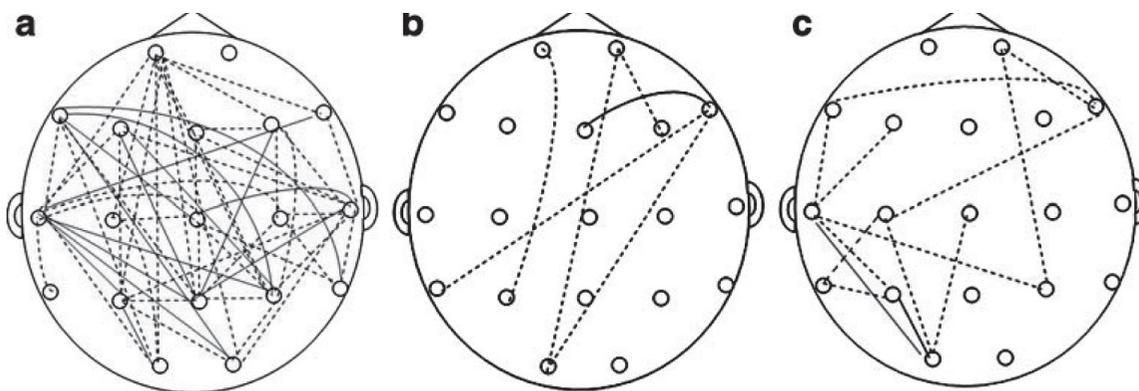


Fig 2. Result of connectivity in 171 pairs of electrodes in frequency bands in the two groups control children and children with ASD disorders ($p < 0.05$) shown with dotted lines and ($p < 0.01$) shown with solid lines. a) gamma frequency band, b) alpha frequency band, c) beta frequency band (28)

Another research implicated the gamma frequency band as the best discriminant in children with Asperger compared with the normal group. Additionally, the prefrontal and right temporal lobes had more abnormalities based on

the spectrogram, and the coherence values showed more abnormalities in the connectivity of the right temporal lobe as compared with the other lobes in the gamma frequency band in Asperger children (29).

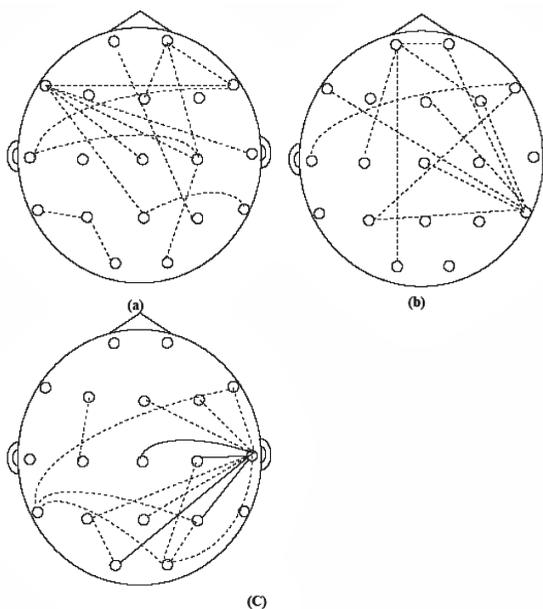


Fig 3. Results of connectivity in 171 pairs of electrodes that had significant differences in frequency bands. Significant differences with $p < 0.05$ between control subjects and Asperger patients shown with dotted lines and with $p < 0.01$ shown with solid lines. a) alpha, b) beta and c) gamma frequency band.(29)

In another study, chaos theory was used to introduce a neural network model for EEG-based assessment of ASD with a precision of 90% (30).

The differential diagnosis for social interaction and stereotyped behaviors was investigated between autistic and trainable mentally retarded children, which showed higher mean scores on qualitative damage to social interaction and stereotyped behaviors in autistic children compared with trainable mentally retarded children (31).

Treatment of ASDs

Although there is no strong evidence of dopamine involvement in autism, neuroleptics have been used for a long time to decrease aggression, stereotypic behaviors, and impulsivity. Low-potency neuroleptics were soon abandoned, due to their cognitive and sedative side effects. Among high-potency neuroleptics, haloperidol has been studied most frequently. Several controlled studies showed its benefits over placebo among young children treated with 1 to 2 mg daily to improve attention and reduce hyperactivity, anger outbursts, and stereotypies (32, 33). However, problematic side effects, in the form of acute dystonic reactions, withdrawal dyskinesias, and tardive dyskinesias, were noted.

Typical neuroleptics have been replaced with atypical antipsychotics that combine dopamine (D2) and serotonin (5-HT₂) receptor antagonist actions (32-35). Following several open-label studies that suggested the efficacy of risperidone, a 12-week, double-blind, placebo-controlled trial was conducted with 31 adults (mean age 28 years) with autism and PDD-NOS. Significantly, at a mean dosage of 2.9 mg daily, more responders (57% vs 0%) were observed in the risperidone than in the placebo group, and improvements were noted in irritability, anxiety or nervousness, aggression, repetitive behaviors, and depression. There were no improvements on objective measurements of social behavior and language, suggesting that the drug targets nonspecific behavioral problems that are associated with autism (36, 37). The drug was well tolerated.

More recently, a multicenter, 8-week, double-blind, placebo-controlled trial of risperidone (dosage range 0.5 to 3.5 mg daily) was completed in 101 children with autism aged 5 to 17 years (mean age 8.8 years) who presented with clinical levels of tantrums, aggression,

and self-injurious behavior. Significant benefits of the active medication were observed for the 2 primary outcome measures of reduced irritability scores (57% vs 14%) and a rating of "much improved" or "very much improved" on a Clinical Global Improvement (CGI) scale (69% vs 12%). Side effects, such as fatigue, drowsiness, increased appetite, and drooling, were more common in the risperidone group, as was a significantly higher weight gain (2.7 vs 0.8 kg).

Promising open-label studies have been conducted with olanzapine, quetiapine, clozapine, and ziprasidone; several randomized studies are currently underway. Atypical neuroleptics, therefore, appear to be promising agents that can be used to treat behavioral symptoms that often occur among autism patients. Yet, despite their good tolerability, these drugs are associated with some undesirable adverse effects, such as tachycardia in young children on risperidone and sedation for all atypicals, the most serious of which is substantial weight gain. There are no long-term studies on the drugs' efficacy and tolerability (35-39).

Several pharmacological, behavioral, and social interventions for children with ASDs have been implemented in Iran. Akhondzadeh (2010) administered a double-blind, placebo-controlled trial to assess the effects of pentoxifylline added to risperidone in the treatment of autistic disorder, reducing scores for irritability, lethargy/social withdrawal, stereotyped behavior, hyperactivity/noncompliance, and inappropriate speech (40).

In another study, he examined the efficacy of piracetam added to risperidone in autistic disorder and determined that a combination of atypical antipsychotic medications and a glutamate agent, such as piracetam, has synergistic effects in the treatment of autism (41). Also, the combination of topiramate with risperidone reduced scores for irritability, stereotypic behavior, and hyperactivity/noncompliance compared with risperidone alone in autistic children (42). In another double-blind, placebo-controlled trial, the 5-HT₂ antagonist cyproheptadine plus haloperidol was evaluated in the treatment of autistic disorder. The results suggested that the combination of cyproheptadine with a conventional antipsychotic may be more effective than a conventional antipsychotic alone for autistic children (43). In a comparison of celecoxib added to risperidone with

risperidone plus placebo, significant differences were observed between the 2 groups, showing reduced scores for irritability, lethargy, and stereotyped behavior in autistic children who took celecoxib plus risperidone (44). Ghanizadeh (2011) hypothesized that the glycine site on the N-methyl-D: -aspartic acid (NMDA) glutamate receptor can be tested as a new target for the treatment of autism (45). He also introduced neurotensin as a novel agent for autism (46).

In a nonpharmacotherapeutic intervention, social stories as a social skill were evaluated in autistic children, and the results indicated that this intervention was effective in decreasing autistic behavior and improving social development in autistic children (47). In another study, the home-based Lovaas approach was performed for the treatment of autism, and the results showed that it was effective in improving social interaction, speech and language, and play and behavior skills in autistic children (48). Also, the effect of ABA (Applied Behavior Analysis) was demonstrated on autistic children, who had acquired significant improvements in suitable behaviors (49). In another study, 3 therapeutic interventions (drug, education, and combined therapy) were administered to autistic children, and the results showed that while risperidone therapy was effective primarily on stereotyped behavior and hyperactivity, education according to the Lovaas approach improved social communication and language development (50). The effectiveness of parent-child interaction therapy was investigated in 4 young children with high-functioning autism, and the results showed a decrease in their behavioral problems (51).

Parental Studies

Because it seems that parents of children with ASDs experience stresses, such as stigma, blame, and insufficient social support in developing countries (52, 53), several studies have been performed to investigate parental problems, especially those of mothers, in Iran. A scientific report indicated a significant difference in parenting stress and coping strategy (emotion-focused and problem-focused) variables between mothers with autistic children and mothers who had normal children; also, a significant correlation was observed between stress levels and emotion-focused coping strategies

in mothers with autistic children (54). Another study investigated personality characteristics and attachment style in mothers with autistic children in comparison with mothers who had normal children and showed a significant difference in neuroticism versus emotional stability but not in other characteristics; also, no significant difference was observed in attachment style between the 2 groups. Based on these results, while mothers with autistic children could be in the neurotic group, mothers with normal children were almost always in the emotionally stable group (55). The correlation between personality characteristics and coping strategies was studied in parents who had children with ASDs and indicated no significant difference in coping strategies between fathers and mothers of children with ASDs; however, original thinking, sociability, and vigor characteristics differed significantly between them (56). Samadi (2009) evaluated the general health and stress levels in parents who had children with ASDs and showed that mothers had significantly higher scores than fathers (57). In another study, parental stress was compared in mothers of autistic children with mothers who had normal children, and the results indicated higher parental stress scores for mothers of autistic children (58). The results of another study showed that 27.5% of mothers with autistic children had mental disease, and a significant correlation was observed between insufficient coping strategies and mental health (59).

Some interventions were performed to reduce mental problems in mothers with autistic children. A preliminary investigation showed that the symptoms of stress, depression, and anxiety in mothers with autistic children were relatively reduced by guided imagery via music (60). In another study, group counseling was administered to a group of mothers with autistic children, and the results indicated significant differences in family performance and marital satisfaction scores in mothers who had received group counseling compared with the control group (61).

In conclusion, It appears that autism spectrum disorders are unknown in developing countries, and parents who have children with ASDs suffer from a lack of social support. Although several studies on ASDs have been performed recently in Iran, they are not sufficient, especially with regard to ASD epidemiology.

Because of the essential role of cultural factors bettering increasing our understanding and treatment of ASDs, more comprehensive research on the prevalence, etiology, diagnosis, and treatment of ASDs should be performed in Iran.

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