

Broader Autism Phenotype in Iranian Parents of Children with Autism Spectrum Disorders vs. Normal Children

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Objective: The aim of the present study was to compare the broader autism phenotype in Iranian parents of children with autism spectrum disorders and parents of typically developing children.

Method: Parents of children with ASD and parents of typically developing children were asked to complete the Persian version of the Autism Spectrum Quotient (AQ). In the ASD group, families included 204 parents (96 fathers and 108 mothers) of children diagnosed as having autism (Autistic Disorder, or AD) (n=124), Asperger Syndrome (AS) or High Functioning Autism (HFA) (n=48) and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) (n=32) by psychiatrists based on the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV-TR) criteria. In the control group, 210 (108 fathers and 102 mothers) parents of typically developing children. Parents of typically developing children were selected from four primary schools. Based on family reports, their children did not have any psychiatric problems. Total AQ score and each of the 5 subscales were analyzed using two-way ANOVAs with sex and group as factors.

Results: The mean age of ASD fathers was 40.6 years (SD=5.96; range 31-54), and of ASD mothers was 34.7 years (SD=4.55; range 28-45). The mean age of control fathers was 37 years (SD=4.6; range 29-45) and of control mothers was 34.11 years (SD=4.86; range 28-45). Group differences were found in age ($p<0/001$). On total AQ, a main effect for group and sex was found. ASD parents scored higher than controls ($F(1,410)=77.876$, $P<0/001$) and males scored higher than females ($F(1,410)=23.324$, $P<0/001$). Also, Group by Sex interaction was significant ($F(1,410)=4.986$, $P<0/05$). Results of MANOVA analysis displayed significant differences between ASD's subgroups on total AQ and subscales scores ($F(15, 1121) = 13.924$, $p<0.0005$; Wilk's Lambda=0.624, partial $\eta^2=0.145$). Pairwise comparisons between ASD's subgroups and Normal group showed that mean scores for the Asperger group are significantly more than other groups in total AQ, attention switching and communication subscales ($p<0.05$). The frequencies of BAP ($X^2=52.721$ (DF=1), $P<0/001$), MAP ($X^2=17.133$ (DF=1), $P<0/001$) and NAP ($X^2=12.722$ (DF=1), $P<0/001$) in ASD parents were significantly more than control parents. The frequencies of Broader Autism Phenotype (BAP) ($X^2=3.842$ (DF=1), $P>0/05$) and Medium Autism phenotype (MAP) ($X^2=0.060$ (DF=1), $P>0/05$) did not significantly differ in ASD fathers and mothers, but the proportion of fathers in Narrow Autism Phenotype (NAP) range was more than mothers ($X^2=14.344$, $P<0/001$).

Conclusion: Results of the present study revealed that parents of children with ASD scored significantly higher than control parents on total AQ and its subscales and the rates of BAP, MAP and NAP were higher in ASD parents than in controls. In addition, in ASD's subgroups, the parents of Asperger children scored significantly more than other subgroups (Autism and PDD-nos) and the normal group on total AQ and some subscales.

Key words: *Autistic disorder, Child, Iran, Parents*

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Autism spectrum disorders (ASD) are developmental disorders characterized by impairments in social interactions, verbal and nonverbal communication, emotional and restricted patterns of behaviors (1-4). It has been reported that prevalence of ASD is increasing

(5, 6). Fombone (7) has reported different prevalence estimates ranging from 2.5 to 72.6 per 10,000 with a median rate of 11.3 per 10,000. The estimated screening prevalence of autism spectrum disorders in school aged children population in Iran is about 1.9% (8). Although research studies have generated much

evidence to suggest that genetic and neurobiological factors play an important role in the pathogenesis of autism, its etiology is still unclear (9-11). Familial recurrence of the disorder is 100-fold higher than in the general population (12). Recent studies have shown that autistic deficits exist on a spectrum, from clinical to subclinical manifestations (13).

The Broader Autism Phenotype (BAP) has been used to describe personality characteristics subtly similar to individuals diagnosed with autism and often found in relatives of individuals with ASD which represents a genetic liability for the disorder (14).

Primary studies on BAP found that up to 20% of siblings of probands with autism exhibited a deficit in one or more core areas associated with ASD, social interaction, communication, and restricted and repetitive behaviors (15).

Subsequent studies of family members have suggested that the BAP is associated with specific personality features, such as rigidity, aloofness, and hypersensitivity to criticism (16,17) interpersonal difficulties such as deficits in the number and quality of friendships (6-18) cognitive deficits such as impaired executive functioning (19,20) weak central coherence (21) and pragmatic language deficits (22).

In addition, Research suggests that the BAP is more likely to be found in male relatives and family members of verbal as opposed to nonverbal individuals with ASD (15).

Recently, a variety of instruments, such as structured interviews, rating scales and self-report questionnaires have been developed to assess the BAP, including the Autism Family History Interview (AFHI), the Broad Autism Phenotype Questionnaire (BAPQ), Broader Phenotype Autism Symptom Scale (BPASS) and Social Responsiveness Scale (SRS). These instruments have been used in several studies but each one has a different weakness (e.g. versions are not available for use across different ages, administrators must be specially trained, time consuming to administer, not normally distributed) (23). The Autism Spectrum Quotient (AQ) is another instrument used in several studies. AQ was designed as a self-administered, forced-choice questionnaire for quantifying the number of autistic traits an individual possesses across five domains (social skill, attention switching, attention to detail, communication and imagination) in both clinical and non-clinical samples (24). Recent studies indicate that subclinical characteristics of autism identified by the AQ are normally distributed in the general population (25, 26) and are associated with personality traits (28) and interpersonal deficits (29) that are part of the BAP. This questionnaire is an effective tool indistinguishing individuals with Asperger's Syndrome and high-functioning autism from typically-developing individuals (24, 27, and 30) and identifying the broader autism phenotype in parents of individuals with ASD (31). The AQ shows consistent results across different age groups (32, 33) across time in independent samples (34) and has good cross-cultural stability (28,30).

These characteristics render the AQ a versatile and reliable tool for measuring the BAP.

Bishop et al. (2004) found that the AQ identified significantly higher rates of autistic traits in parents of children with ASD on the social skill and communication subscales (31). This finding was not confirmed by Scheeren and Stauder (2008), who did not find any difference in AQ scores in 25 parents of children with high-functioning autism compared to 25 parents of typically developing children (35).

A much larger study with adequate power was reported by Wheelwright et al. (2010) in which 571 fathers and 1,429 mothers took part. Both mothers and fathers of ASC children scored higher than control parents on total AQ score, and on four out of five of the subscales (social skills, communication, attention switching and imagination). Additionally, the study introduced the concepts of the 'medium autism phenotype' (MAP) and 'narrow autism phenotype' (NAP) to describe phenotypes characterized by a medium or large number of autistic traits, respectively as detected by AQ scores. Most parents of children with ASC scored in the BAP, MAP and NAP ranges (36). These results are confirmed by Ruta et al. (2012) (23). The aim of the present study was to compare the broader autism phenotype in Iranian parents of children with autism spectrum disorders and parents of typically developed children.

Materials and Method

Participants

Parents of children with Autism spectrum disorders (ASD) and parents of typically developing children were asked to complete the Persian version of the Autism Spectrum Quotient (AQ). All parents were biologically related to their child and are of Iranian nationality. In the ASD Group, families included 204 parents (96 fathers and 108 mothers) of children diagnosed as having autism (Autistic Disorder, or AD) (n = 124), Asperger Syndrome (AS) or High Functioning Autism (HFA) (n = 48) and pervasive developmental disorder not otherwise specified (PDD-NOS) (n = 32) by psychiatrists based on the DSM-IV-TR criteria. All families had only one autistic child and all children were boys. ASD parents were selected from a child psychiatric clinic and an autism center in Tehran from 2011 to 2012.

In the control group, families included 210 (108 fathers and 102 mothers) parents of typically developing children who were selected from 4 primary schools. Based on family reports, their children did not have any psychiatric problem.

Instrument

The Autism Spectrum Quotient (AQ) was designed as a self-administered, forced-choice questionnaire for quantifying the number of autistic traits in people with normal intelligence. It comprises of 50 questions, made up of 10 questions assessing 5 different areas: social skills (items 1,11,13,15,22,36,44,45,47,48); attention switching (items 2,4,10,16,25,32,34,37,43,46);

attention to detail (items 5,6,9,12,19,23,28,29,30,49);communication (items 7,17,18,26,27,31,33,35,38,39); imagination (items 3,8,14,20,21,24,40,41,42,50). Each of the items listed above scores 1 point if the respondent records the abnormal or autistic-like behavior either mildly or strongly. Scoring for each item is as follows: Abnormality = poor social skill, poor communication skill, poor imagination, exceptional attention to detail, poor attention-switching/strong focus of attention. Approximately half the items were worded to produce a 'disagree' response, and half an 'agree' response, in a high scoring person with AS/HFA. This was to avoid a response bias either way. Following this, items were randomized with respect to both the expected response from a high-scorer, and with respect to their domain (13).In Ruta et al. (2012) study, Cronbach's alpha coefficients reported are as follows: AQ total = 0.76; communication = 0.64; social skills = 0.68; imagination = 0.52; local details = 0.58,; attention switching = 0.54; and good test-retest reliability was reported (Pearson r = 0.79).

Validation of the Persian Autism Spectrum Quotient

To maintain the meaning of words and sentences between English and Persian, a back-translation was conducted. First, the AQ was translated to Persian by one of the authors. Subsequently, a bilingual translator translated the questionnaire back to English. This translated version of the questionnaire was compared with the original version of the AQ by one of the authors. To test if the questionnaire was comprehensible and to assess its principal psychometric properties, a pilot study was conducted with a group of 50 males and 50 females from the general population (mean age = 33.6 years, SD = 4.93).

The mean and SD total AQ scores were 18.91 and 3.36. Cronbach's alpha coefficients demonstrated a fair internal consistency (AQ total = 0.71). BAP, MAP and NAP scores were calculated using the same method as Wheelwright et al. (2010) and Ruta et al. (2012). The combined male and female mean and standard deviation values obtained from the pilot study were used as reference values.BAP was defined as AQ scores between 1 and 2 SDs above the mean (AQ scores of 22–26); MAP was defined as AQ scores between 2 and 3 SDs above the mean (AQ scores of 27–30); and NAP was defined as AQ scores 3 SDs or higher above the mean (AQ scores of +31).

Data Analysis

Data analysis was performed using the SPSS-18.Total AQ score and each of the 5 subscales were analyzed using two-way ANOVAs, with sex and group as factors. We also used MANOVA to compare scores of ASD's subgroups and the normal group on total AQ and subscales.

Results

The mean age of ASD fathers was 40.6 years (SD=5.96; range 31-54), and of ASD mothers was 34.7 years (SD = 4.55; range 28-45). The mean age of control fathers was 37 years (SD =4.6; range 29-45) and of control mothers was 34.11 years (sd= 4.86; range 28-45). Group differences were found in age (p<0/001).Table 1 shows the mean and SD total AQ scores and it's subscale for controls and ASD parents. Higher scores indicate more autistic traits. The distribution of total AQ scores in ASD fathers versus control fathers, and ASD mothers versus control mothers are presented in Figs. 1and 2.

Table 1. Mean and standard deviation scores on the total AQ* and subscales in controls and ASD parents**

	ASD group		Control group	
	Fathers n=96	Mothers n=108	Fathers n=108	Mothers n=102
Social skills	3.416 (1.76)	3.03 (1.98)	2.66 (1.45)	2.70 (0.96)
Attention switching	6.04 (1.54)	5.88 (0.99)	5.11 (1.45)	4.88 (1.71)
Attention to details	5.09 (1.58)	5.4 (2.15)	5.44 (2.48)	6.3 (2.03)
Communication	3.29 (1.97)	2.11 (1.45)	2.16 (1.26)	2.17 (1.55)
Imagination	5.58 (1.94)	4.29 (1.79)	3.83 (1.12)	2.17 (1.04)
Total AQ scores	23.425 (5.454)	20.75 (4.11)	19.22 (2.13)	18.25 (3.13)

* The Autism Spectrum Quotient

** Autism Spectrum Disorders

Table 2. F values from ANOVAs with between subject factors of Group and Sex and effect sizes

	Group main effect F(410)	Group effect size Partial Eta squared	Sex main effect F(410)	Sex effect size Partial Eta squared	Group by sex interaction F(410)	Group by sex effect size Partial Eta squared
Total AQ	**77.86	0.160	**23.324	0.054	*4.986	0.012
Social skills	*11.937	0.028	1.183	0.003	1.792	0.004
Attention switching	**46.191	0.101	1.792	0.004	0.071	0.000
Attention to details	*8.952	0.021	*7.914	0.019	1.661	0.004
Communication	*11.739	0.028	**14.33	0.034	**14.814	0.035
Imagination	**167.247	0.29	**96.788	0.191	1.527	0.004

*P<0/05

** P<0/001

Table 3. Mean and standard deviation scores on the total AQ* and subscales in ASD subgroups and Normal group

Variable	Diagnosis	Mean.	Sd.	N
Social skills	Autism	3.129	0.143	124
	Asperger	3.500	0.230	48
	PDD-NOS	3.125	0.281	32
	Normal	2.686	0.110	210
Attention switching	Autism	5.903	0.129	124
	Asperger	6.417	0.207	48
	PDD-NOS	5.500	0.254	32
	Normal	5.000	0.099	210
Attention to details	Autism	4.903	0.189	124
	Asperger	5.500	0.303	48
	PDD-NOS	6.275	0.371	32
	Normal	5.857	0.145	210
Communication	Autism	2.677	0.140	124
	Asperger	3.500	0.225	48
	PDD-NOS	1.375	0.276	32
	Normal	2.171	0.108	210
Imagination	Autism	4.839	0.152	124
	Asperger	5.083	0.244	48
	PDD-NOS	4.875	0.299	32
	Normal	3.029	0.117	210
Total AQ scores	Autism	21.452	0.351	124
	Asperger	24.000	0.565	48
	PDD-NOS	21.150	0.692	32
	Normal	18.743	0.270	210

Table 4: Pairwise comparisons between ASD's subgroups and Normal group

Variable	Group	Comparison groups	Mean Difference	Std.Error	Sig.
Social skills	Autism	Asperger	-0.371	0.271	0.171
		PDD-nos	0.004	0.316	0.990
		Normal	0.443*	0.180	0.014
	Asperger	PDD-nos	0.375	0.363	0.303
		Normal	0.814**	0.255	0.001
		PDD-nos	0.439	0.302	0.147
Attention switching	Autism	Asperger	-0.513*	0.244	0.036
		PDD-nos	0.403	0.285	0.158
		Normal	0.903**	0.163	0.000
	Asperger	PDD-nos	0.917*	0.328	0.005
		Normal	1.417**	0.230	0.000
		PDD-nos	0.500	0.273	0.067
Attention to details	Autism	Asperger	-0.597	0.357	0.095
		PDD-nos	-1.372**	0.416	0.001
		Normal	-0.954**	0.238	0.000
	Asperger	PDD-nos	-0.775	0.479	0.107
		Normal	-0.357	0.336	0.228
		PDD-nos	0.418	0.398	0.295
Communication	Autism	Asperger	-0.823*	0.265	0.002
		PDD-nos	1.302**	0.309	0.000
		Normal	0.506*	0.177	0.004
	Asperger	PDD-nos	2.125**	0.356	0.000
		Normal	1.329**	0.249	0.000
		PDD-nos	-0.796*	0.296	0.007
Imagination	Autism	Asperger	-0.245	0.288	0.396
		PDD-nos	-0.036	0.335	0.914
		Normal	1.810**	0.192	0.000
	Asperger	PDD-nos	0.208	0.386	0.590
		Normal	2.055**	0.271	0.000
		PDD-nos	1.846**	0.321	0.000
Total AQ scores	Autism	Asperger	-2.548**	0.665	0.000
		PDD-nos	0.302	0.776	0.698
		Normal	2.709**	0.443	0.000
	Asperger	PDD-nos	2.850*	0.893	0.002
		Normal	5.257**	0.626	0.000
		PDD-nos	2.407**	0.743	0.001

* p<0.05

** p≤ 0.001

Table 5: The frequencies of BAP*, MAP and NAP*** in ASD**** and control parents**

	ASD fathers	ASD mothers	Control fathers	Control mothers
BAP (22-26)	48	40	12	12
MAP (27-30)	8	8	0	0
NAP (+31)	12	0	0	0

*Broader Autism Phenotype

**Medium Autism Phenotype

***Narrow Autism Phenotype

**** Autism Spectrum Disorders

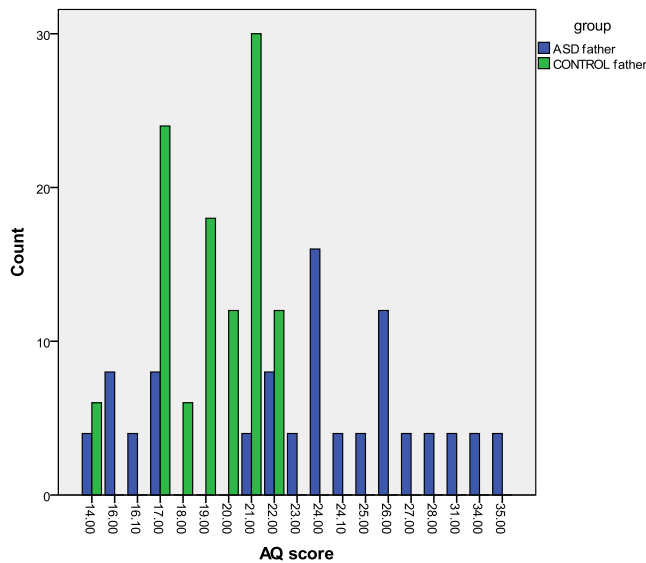


Fig. 1 the Autism Spectrum Quotient scores in ASD and control fathers

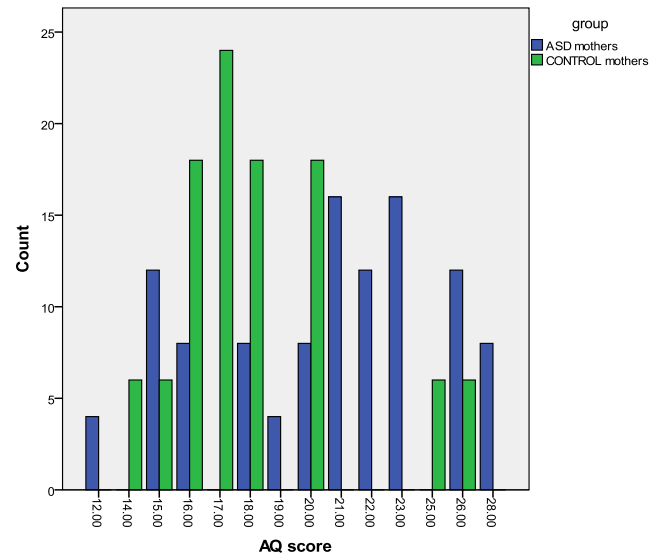


Fig. 2 the Autism Spectrum Quotient scores in ASD and control mothers

F values from ANOVAs with between subject factors of Group and Sex and effect sizes are reported in table 2. On total AQ, a main effect for group and sex was found. ASD parents scored higher than controls ($F(1,410) = 77.876, P < 0.001$) and males scored higher than females ($F(1,410) = 23.324, P < 0.001$). Also, Group by Sex interaction was significant ($F(1,410) = 4.986, P < 0.05$). On the social skills domain, there was a significant main effect of Group ($F(1,410) = 11.937, P < 0.05$), but not for Sex ($F(1,410) = 1.183, P = 0.277$) and Group by Sex interaction ($F(1,410) = 1.792, P = 0.181$). On the attention switching domain, there was a significant main effect of Group ($F(1,410) = 46.191, P < 0.001$), but not for Sex ($F(1,410) = 1.792, P = 0.181$) and Group by Sex interaction ($F(1,410) = 0.071, P = 0.790$).

On the attention to details domain, there was a significant main effect of Group ($F(1,410) = 8.952, P < 0.05$) and Sex ($F(1,410) = 7.914, P < 0.05$), but not for Group by Sex interaction ($F(1,410) = 1.661, P = 0.198$). On the communication domain, there was a significant main effect of Group ($F(1,410) = 11.739, P < 0.05$), Sex ($F(1,410) = 14.330, P < 0.001$) and Group by Sex interaction ($F(1,410) = 14.814, P < 0.001$).

On the imagination domain, there was a significant main effect of Group ($F(1,410) = 167.247, P < 0.001$) and Sex ($F(1,410) = 96.788, P < 0.001$), but not for Group by Sex interaction ($F(1,410) = 1.527, P = 0.217$). A MANOVA analysis was conducted to clarify whether there are significant differences on total AQ and subscales in ASD's subgroups and Normal group. Table 3 demonstrates Mean and standard deviation

scores on the total AQ and subscales in ASD's subgroups and Normal group.

Results of MANOVA analysis reveals that there are significant differences between groups on total AQ and subscales scores ($F(15, 1121) = 13.924, p < 0.0005$;

Wilk's Lambda = 0.624, partial $\eta^2 = 0.145$). Pairwise comparisons between ASD's subgroups and Normal group (see table 4) shows that mean scores for Asperger group are significantly more than other groups in total AQ, attention switching and communication subscales ($p < 0.05$). The frequencies of BAP, MAP and NAP, the corresponding chi-square and p-values are shown in table 5.

The frequencies of BAP ($\chi^2 = 52.721, DF = 1, P < 0.001$), MAP ($\chi^2 = 17.133, DF = 1, P < 0.001$) and NAP ($\chi^2 = 12.722, DF = 1, P < 0.001$) in ASD parents were significantly more than control parents. The frequencies of BAP ($\chi^2 = 3.842, DF = 1, P = 0.062$) and MAP ($\chi^2 = 0.060, DF = 1, P = 0.806$) did not significantly differ in ASD fathers and mothers, but the proportion of fathers in the NAP range was more than mothers ($\chi^2 = 14.344, DF = 1, P < 0.001$).

Discussion

The aim of the present study was to compare the broader autism phenotype in Iranian parents of children with autism spectrum disorders with that of parents of typically development children. The results of the present study show that Autism Spectrum Quotient (AQ) is a suitable tool for comparing autistic features in parents of children with autism spectrum disorders with that of typically developed children.

In the Iranian sample, parents of children with Autism Spectrum Disorders (ASD) scored significantly higher than control parents on total AQ and its subscales. These findings are in accordance with previous studies which reported that parents of people with ASD obtained higher scores than controls on total AQ (23, 31, and 36). On differences in subscale scores, Wheelwright et al. (2010) reported that ASD parents scored significantly higher than control parents on four subscales of social skills, communication, attention

switching and imagination (36). In another study, Ruta et al. (2012) found that parents of people with ASD obtained higher scores than controls on two subscales of social skills and communication and autistic mothers scored higher than control mothers on imagination subscale (23). Also, Bishop et al. (2004) reported that parents of people with ASC obtained higher scores than controls on two subscales of the AQ (social skills and communication) (31).

Results of the present study also demonstrated a sex difference in scores, reported by Ruta et al. (2012). Males scored higher than females on total AQ scores and on imagination, communication and attention to details subscales (23).

In both groups, males scored higher than females on total AQ scores and on imagination subscale, while in communication subscale autistic fathers scored higher than autistic mothers and control fathers scored higher than control mothers in attention to details subscale.

In accordance with these results, Ruta et al (2012) found that males scored higher than females on total AQ scores and on social skills subscale in both groups, and in ASD group fathers scored higher than mothers on the communication subscale. A significant difference was observed between males and females on imagination subscale in the control group (23). In another study, Dawson et al. (2007), using the Broader Phenotype Autism Symptom Scale, found that ASD fathers scored significantly higher than ASD mothers on the Expressiveness and Conversational skills domains (37). In this study, we also found that in ASD's subgroups, the parents of Asperger children scored significantly more than other subgroups (Autism and PDD-nos) and the normal group on total AQ and some subscales. This finding is related to previous studies that have shown family members of verbal individuals with ASD have more traits of autism (15).

This study also revealed that the rates of BAP, MAP and NAP were higher in ASD parents than in controls. Also, ASD fathers displayed the highest rate of NAP. These findings are in accordance with Wheelwright et al. (2010) and Ruta et al. (2012) studies. Both studies demonstrated that the rates of BAP, MAP and NAP, as measured by the AQ were higher in ASC parents than in controls. Also, ASC fathers displayed the highest rate of MAP and NAP (23, 36).

According to Ruta et al. (2012), the MAP and NAP dimensions may be useful in identifying a different loading of quantitative traits within the more general concept of the broader phenotype in autism families and to relate these quantitative endophenotypes to susceptibility genes. A candidate gene association study of autistic traits using the AQ has been conducted in the general population indicating differences in allele frequency in common single nucleotide polymorphisms (SNPs) related to neural growth, sex steroid hormones, and social reward (Chakrabarti et al. 2009). The same approach might be applied to families with autism with high incidence of MAP and NAP to stratify the samples for autism risk loci analyses (23).

Conclusion

Results of the present study replicate findings from previous studies. In the Iranian sample, parents of children with ASD scored significantly higher than control parents on total AQ and its subscales and in ASD's subgroups, the parents of Asperger children scored significantly more than other subgroups (Autism and PDD-nos) and the normal group on total AQ and some subscales. In addition, the rates of BAP, MAP and NAP were higher in ASD parents than in controls. We also found that males show more autistic traits than females.

Results of the present study revealed that AQ is able to distinguish parents of children with autism spectrum disorders and parents of typically development children, which indicates that people who had more autistic features are at a greater risk to have autistic children. This tool may be very useful in predicting the likelihood of children born autistic.

Among the limitations of this study are small sample size and the use of nonrandom sampling method. Also, in the ASD group, all children were boys. Future research should test these findings with a large random sample population that include both boys and girls.

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