

## Supplement 1

### Method

#### Study samples

The following criteria were applied to patient selection: 1) met the 'autism' diagnosis by the ADI-R algorithm or 'ASD' by the ASD1 and ASD2 criteria according to Risi et al.;<sup>1</sup> 2)  $\geq 4$  and  $\leq 20$  years old when the ADI-R was administered (because of the instability of verbal/non-verbal status and repetitive behaviours in very young children, and poor recall for the 'ever' items for the older ASD patients); 3) were selected for genotyping so ethnicity could be estimated using the genotype data; 4) had verbal/non-verbal status recorded; 5) had no missing values for any of the 28 ADI-R algorithm items.

#### Genetic markers

The genetic markers had a mean inter-marker distance of 0.68cM (standard deviation (SD)=1.00), and a mean minor allele frequency of 0.31 (SD=0.12). The Rutgers genetic map<sup>2</sup> was used as the basis for linear interpolation for the genetic locations of the SNPs using the physical locations from NCBI build 35.<sup>3</sup> Because the linkage analysis program Merlin<sup>4</sup> assumes a no-interference model, the Kosambi map was converted into the Haldane map and results are reported on the Kosambi scale. The marker allele frequencies were calculated using the founders from all the AGPI families or Caucasian families. Because 84% of the parents were genotyped in AGPI, differences in allele frequency estimates due to ethnic variation should have little effect on the linkage results.

#### Simulations

Marker data for the whole genome was simulated based on the marker informativeness, spacing and missing data patterns in the original AGPI dataset assuming no linkage to the factors. One thousand simulations of the genotype data were generated. The original factor scores, covariates, and pedigree structures were preserved. According to Lander and Kruglyak,<sup>5</sup> genome-wide suggestive evidence for linkage was defined as 'statistical evidence that would be expected to occur one time at random in a genome scan' (i.e., 1,000 times in 1,000 simulations,

or the 1,000th maximum LOD score with one maximum LOD score selected from each simulation), and genome-wide significant evidence for linkage was 'expected to occur 0.05 times in a genome scan' (i.e., 50 times in 1,000 simulations, or the 50th maximum LOD score). The accuracy of the simulation results is conditioned on the assumptions that the map positions are correct and the marker allele frequencies are known.

## References

1. Risi S, Lord C, Gotham K *et al.* Combining information from multiple sources in the diagnosis of autism spectrum disorders. *J Am Acad Child Adolesc Psychiatry.* 2006;45:1094-103.
2. Kong X, Murphy K, Raj T, He C, White PS, Matise TC. A combined linkage-physical map of the human genome. *Am J Hum Genet.* 2004;75:1143-8.
3. McEntyre J, Ostell J, editors. *The NCBI Handbook.* Bethesda, MD, USA: National Library of Medicine (US), National Center for Biotechnology Information (NCBI); 2002-2005.
4. Abecasis GR, Cherny SS, Cookson WO, Cardon LR. Merlin--rapid analysis of dense genetic maps using sparse gene flow trees. *Nat Genet.* 2002;30:97-101.
5. Lander E, Kruglyak L. Genetic dissection of complex traits: guidelines for interpreting and reporting linkage results. *Nat Genet.* 1995;11:241-7.

Table S1. Factor loading patterns for the patients from the Autism Genome Project phase II

	ADI-R items	Factor1: Social interaction & communication	Factor2: Joint attention	Factor3: Peer interaction	Factor4: Non-verbal communication	Factor5: Repetitive sensory- motor behaviour	Factor6: Compulsion/ restricted interests
Social domain	Direct gaze	0.10	<b>0.62</b>	0.24	0.00	0.16	0.05
	Social smiling	0.21	<b>0.62</b>	0.16	0.20	0.11	0.26
	Range of facial expressions used to communicate	0.28	<b>0.42</b>	0.18	0.21	0.08	0.34
	Imaginative play with peers	<b>0.70</b>	0.19	<b>0.39</b>	0.14	0.21	-0.02
	Interest in children	0.27	0.26	<b>0.67</b>	0.10	0.10	0.06
	Response to approaches of other children	0.19	0.29	<b>0.77</b>	0.06	0.17	-0.03
	Group play with peers	<b>0.51</b>	0.17	<b>0.53</b>	0.15	0.09	0.12
	Showing and directing attention	<b>0.47</b>	<b>0.49</b>	0.10	0.23	0.22	-0.14
	Offering to share	<b>0.43</b>	0.34	0.27	0.18	0.19	-0.07
	Seeking to share enjoyment with others	0.27	<b>0.53</b>	0.15	0.16	0.16	-0.09
	Use of other's body to communicate	0.07	0.11	0.11	0.21	<b>0.44</b>	-0.24
	Offering comfort	<b>0.49</b>	0.34	0.20	0.23	0.12	0.15
	Quality of social overtures	0.23	<b>0.62</b>	0.31	0.09	0.21	-0.04
	Appropriateness of social responses	0.30	<b>0.49</b>	0.30	0.10	0.24	0.10
Communication	Pointing to express interest	<b>0.35</b>	0.34	0.12	<b>0.38</b>	0.26	-0.25
	Nodding	0.21	0.18	0.09	<b>0.87</b>	0.26	-0.13
	Head shaking	0.26	0.14	0.12	<b>0.85</b>	0.12	0.12
	Conventional/instrumental gestures	<b>0.49</b>	0.32	0.14	<b>0.41</b>	0.18	0.11
	Spontaneous imitation of actions	<b>0.64</b>	0.24	0.12	0.18	0.10	0.12
	Imaginative play	<b>0.68</b>	0.20	0.33	0.09	0.25	0.03
	Imitative social play	0.25	0.32	<b>0.50</b>	0.08	0.10	-0.09
Behaviour	Unusual preoccupations	0.02	-0.07	-0.02	0.08	0.15	<b>0.40</b>
	Circumscribed interests	-0.02	0.01	-0.02	-0.12	-0.01	<b>0.36</b>
	Compulsions/rituals	0.07	0.13	0.05	0.05	0.13	<b>0.42</b>
	Hand and finger mannerisms	0.11	0.14	0.06	0.07	<b>0.40</b>	0.14
	Other complex mannerisms or stereotyped body movements	0.02	0.09	0.10	0.02	<b>0.38</b>	0.05
	Repetitive use of objects or interest in parts of objects	0.22	0.10	0.05	0.10	<b>0.47</b>	0.24
	Unusual sensory interests	0.16	0.10	0.03	0.09	<b>0.50</b>	0.15
Common variance explained (%) – before rotation		70.7	10.9	7.9	6.0	4.9	4.1
Common variance explained (%) – after rotation		24.5	22.4	17.4	16.4	11.9	7.5

Note: Bold if loading  $\geq 0.35$ . ADI-R = Autism Diagnostic Interview-Revised.

Table S2. Factor loading patterns for 100 random samples from the patients of the Autism Genome Project phase I

	ADI-R items	Factor1: Social interaction & communication		Factor2: Joint attention		Factor3: Non-verbal communication		Factor4: Repetitive sensory- motor behaviour		Factor5: Peer interaction		Factor6: Compulsion/ restricted interests	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Social domain	Direct gaze	0.11	0.05	<b>0.55</b>	<b>0.04</b>	0.06	0.03	0.19	0.04	0.18	0.04	0.22	0.06
	Social smiling	0.26	0.06	<b>0.64</b>	<b>0.04</b>	0.17	0.03	0.10	0.03	0.19	0.04	0.18	0.05
	Range of facial expressions used to communicate	0.22	0.06	<b>0.52</b>	<b>0.05</b>	0.16	0.03	0.12	0.04	0.15	0.05	0.20	0.05
	Imaginative play with peers	<b>0.64</b>	<b>0.06</b>	0.23	0.07	0.12	0.03	0.15	0.03	0.33	0.07	-0.09	0.04
	Interest in children	0.26	0.07	<b>0.35</b>	<b>0.05</b>	0.09	0.03	0.12	0.03	<b>0.65</b>	<b>0.05</b>	0.07	0.04
	Response to approaches of other children	0.23	0.07	0.32	0.05	0.12	0.03	0.16	0.03	<b>0.65</b>	<b>0.04</b>	0.09	0.04
	Group play with peers	<b>0.40</b>	<b>0.07</b>	0.22	0.06	0.15	0.03	0.04	0.03	<b>0.53</b>	<b>0.06</b>	0.05	0.04
	Showing and directing attention	<b>0.45</b>	<b>0.08</b>	<b>0.44</b>	<b>0.08</b>	0.25	0.03	0.19	0.04	0.17	0.06	-0.06	0.05
	Offering to share	<b>0.47</b>	<b>0.07</b>	0.30	0.07	0.24	0.04	0.18	0.04	0.19	0.06	-0.04	0.05
	Seeking to share enjoyment with others	0.31	0.08	<b>0.47</b>	<b>0.07</b>	0.27	0.04	0.13	0.04	0.23	0.06	0.01	0.05
	Use of other's body to communicate	0.17	0.05	0.11	0.04	0.20	0.04	<b>0.43</b>	<b>0.04</b>	0.13	0.04	-0.13	0.05
	Offering comfort	<b>0.46</b>	<b>0.06</b>	0.34	0.07	0.15	0.03	0.16	0.03	0.16	0.05	0.00	0.05
	Quality of social overtures	0.31	0.07	<b>0.59</b>	<b>0.05</b>	0.17	0.03	0.16	0.03	0.19	0.05	0.04	0.04
Appropriateness of social responses	0.31	0.07	<b>0.55</b>	<b>0.05</b>	0.06	0.03	0.14	0.03	0.21	0.05	0.02	0.05	
Communicatio	Pointing to express interest	0.26	0.06	0.34	0.06	0.33	0.04	0.27	0.04	0.13	0.05	-0.02	0.05
	Nodding	0.13	0.04	0.19	0.04	<b>0.93</b>	<b>0.02</b>	0.23	0.03	0.14	0.03	0.00	0.03
	Head shaking	0.21	0.04	0.21	0.04	<b>0.81</b>	<b>0.02</b>	0.15	0.03	0.06	0.03	0.05	0.03
	Conventional/instrumental gestures	<b>0.46</b>	<b>0.06</b>	<b>0.38</b>	<b>0.06</b>	<b>0.40</b>	<b>0.03</b>	0.15	0.03	0.20	0.05	0.06	0.04
	Spontaneous imitation of actions	<b>0.59</b>	<b>0.05</b>	0.25	0.06	0.09	0.03	0.17	0.04	0.07	0.05	0.07	0.05
	Imaginative play	<b>0.69</b>	<b>0.04</b>	0.20	0.06	0.11	0.03	0.23	0.04	0.19	0.06	0.04	0.04
	Imitative social play	<b>0.42</b>	<b>0.07</b>	0.32	0.06	0.04	0.03	0.16	0.03	0.33	0.06	0.09	0.04
Behaviour	Unusual preoccupations	0.10	0.05	0.02	0.04	0.13	0.04	0.15	0.05	0.04	0.04	<b>0.40</b>	<b>0.07</b>
	Circumscribed interests	-0.04	0.03	0.09	0.04	-0.10	0.03	-0.07	0.03	0.03	0.04	<b>0.52</b>	<b>0.07</b>
	Compulsions/rituals	-0.02	0.04	0.09	0.05	0.02	0.03	0.16	0.04	0.02	0.04	<b>0.41</b>	<b>0.06</b>
	Hand and finger mannerisms	0.10	0.03	0.15	0.04	0.09	0.03	<b>0.56</b>	<b>0.04</b>	0.10	0.04	0.08	0.05
	Other complex mannerisms or stereotyped body movements	0.11	0.03	0.10	0.04	0.07	0.03	<b>0.48</b>	<b>0.04</b>	0.04	0.03	0.12	0.04
	Repetitive use of objects or interest in parts of objects	0.34	0.04	0.07	0.04	0.08	0.03	<b>0.56</b>	<b>0.04</b>	0.04	0.04	0.15	0.05
	Unusual sensory interests	0.05	0.04	0.11	0.04	0.08	0.03	<b>0.60</b>	<b>0.04</b>	0.04	0.04	0.06	0.05
Common variance explained (%) – before rotation		70	1	11	0.6	8	0.5	7	0.4	4	0.3	3	0.3
Common variance explained (%) – after rotation		24.2	5	23.9	4	16.7	0.8	15	0.7	13.7	2	6.5	0.6

Note: Bold if loading  $\geq 0.35$ . ADI-R = Autism Diagnostic Interview-Revised.

Table S3. Comparison of the factor loading patterns for the patients from the Autism Genome Project (AGP) phases I and II (coefficients of congruence)

	AGPII_1	AGPII_2	AGPII_3	AGPII_4	AGPII_5	AGPII_6
AGPI_1	0.77	<b>0.99</b>	0.75	0.58	0.64	0.24
AGPI_2	<b>0.98</b>	0.77	0.76	0.58	0.68	0.16
AGPI_3	0.59	0.55	0.41	<b>0.99</b>	0.57	0.02
AGPI_4	0.58	0.57	0.47	0.52	<b>0.98</b>	0.23
AGPI_5	0.71	0.70	<b>0.97</b>	0.43	0.53	0.12
AGPI_6	0.19	0.32	0.25	0.12	0.31	<b>0.84</b>

Note: Bold type for the highest coefficients by row and column. AGPI = patients from AGP phase I; AGPII = patients from AGP phase II.

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Table S4. Covariate effects for the derived factors using the patients from the Autism Genome Project (AGP) phase I (regression coefficient (p value))<sup>a</sup>

Covariate	Categorical level <sup>2</sup>	Sample size	Factor1: Joint attention	Factor2: Social interaction & communication	Transformed Factor3: Non-verbal communication	Factor4: Repetitive sensory-motor behaviour	Factor5: Peer interaction	Factor6: Compulsion/re stricted interests
Age at ADI-R (months)		1,236	<b>0.02 (1E-16)</b>	<b>0.01 (3E-07)</b>	-0.01 (0.009)	0.002 (0.5)	0.006 (0.07)	<b>0.01 (3E-07)</b>
(Age at ADI-R) <sup>2</sup>		1,236	<b>-0.00008 (2E-11)</b>	<b>-0.00005 (3E-05)</b>	-0.00004 (0.02)	-0.00001 (0.2)	-0.00002 (0.1)	<b>0.00004 (8E-05)</b>
Gender	Female	246	0.2 (0.0003)	-0.1 (0.02)	0.06 (0.4)	-0.08 (0.1)	-0.06 (0.3)	<b>-0.2 (1E-04)</b>
Verbal/non-verbal status	Non-verbal	338	<b>0.3 (2E-07)</b>	<b>0.5 (4E-18)</b>	0.2 (0.005)	<b>0.6 (1E-32)</b>	<b>0.2 (9E-06)</b>	<b>-0.3 (1E-10)</b>
Ethnicity	Non-Caucasian	202	0.08 (0.3)	0.1 (0.03)	-0.2 (0.006)	0.08 (0.2)	0.1 (0.1)	-0.1 (0.02)
AGP site	CANAGEN	80	0.3 (0.001)	-0.2 (0.04)	-0.1 (0.3)	0.01 (0.9)	0.2 (0.1)	0.3 (0.003)
	CPEA	182	0.02 (0.8)	<b>-0.7 (5E-20)</b>	0.2 (0.02)	-0.1 (0.1)	-0.1 (0.2)	0.2 (0.01)
	DUKE	50	-0.4 (0.003)	-0.3 (0.03)	0.06 (0.7)	-0.02 (0.9)	-0.1 (0.4)	-0.1 (0.2)
	IMGSAC	330	0.2 (0.01)	-0.07 (0.3)	-0.03 (0.7)	<b>-0.2 (1E-04)</b>	0.1 (0.07)	0.2 (0.0009)
	INSERM	22	-0.4 (0.04)	-0.4 (0.04)	-0.3 (0.3)	-0.5 (0.003)	0.2 (0.4)	-0.3 (0.1)
	Mt. Sinai	14	0.3 (0.2)	-0.4 (0.09)	0.5 (0.08)	-0.05 (0.8)	-0.07 (0.8)	-0.2 (0.4)
	Stanford	64	<b>0.5 (8E-06)</b>	0.1 (0.2)	-0.03 (0.8)	0.3 (0.006)	0.4 (0.0004)	<b>0.6 (3E-09)</b>
	UNC	58	0.3 (0.007)	<b>-0.5 (8E-05)</b>	0.1 (0.4)	-0.2 (0.1)	0.2 (0.1)	0.02 (0.8)
	Vanderbilt	16	0.2 (0.3)	-0.2 (0.3)	-0.03 (0.9)	-0.4 (0.06)	-0.2 (0.4)	-0.2 (0.3)

Note: ADI-R = Autism Diagnostic Interview-Revised; CPEA = Collaborative Programs of Excellence in Autism; IMGSAC = International Molecular Genetic Study of Autism Consortium; INSERM = Institute National de la Santé et de la Recherche Médicale; UNC = University of North Carolina.

<sup>a</sup>Bold if p value  $\leq 0.0001$ . For the categorical covariates, the group which has the largest sample size, i.e., male for gender, verbal for verbal/non-verbal status, Caucasian for ethnicity, and Autism Genetics Resource Exchange (AGRE) for AGP site, was used as a reference.

Table S5. Heritability estimates for the derived factors using the families from the Autism Genome Project phase I (heritability estimate  $\pm$  standard error (p value))<sup>a</sup>

	All (618 families)		Caucasian (517 families)	
	No covariate	4 covariates <sup>b</sup>	No covariate	4 covariates <sup>b</sup>
Factor 1: Joint attention	0.61 $\pm$ 0.08 ( $8 \times 10^{-14}$ )	0.52 $\pm$ 0.08 ( $2 \times 10^{-10}$ )	0.56 $\pm$ 0.09 ( $3 \times 10^{-10}$ )	0.50 $\pm$ 0.09 ( $1 \times 10^{-8}$ )
Factor 2: Social interaction & communication	0.63 $\pm$ 0.07 ( $3 \times 10^{-15}$ )	0.58 $\pm$ 0.08 ( $5 \times 10^{-13}$ )	0.57 $\pm$ 0.08 ( $1 \times 10^{-10}$ )	0.49 $\pm$ 0.09 ( $2 \times 10^{-8}$ )
Factor 3: Non-verbal communication	0.50 $\pm$ 0.08 ( $4 \times 10^{-10}$ )	0.49 $\pm$ 0.08 ( $8 \times 10^{-10}$ )	0.48 $\pm$ 0.08 ( $2 \times 10^{-8}$ )	0.47 $\pm$ 0.08 ( $5 \times 10^{-8}$ )
Factor 4: Repetitive sensory-motor behaviour	0.46 $\pm$ 0.08 ( $6 \times 10^{-9}$ )	0.51 $\pm$ 0.08 ( $2 \times 10^{-10}$ )	0.46 $\pm$ 0.09 ( $1 \times 10^{-7}$ )	0.54 $\pm$ 0.08 ( $6 \times 10^{-10}$ )
Factor 5: Peer interaction	0.32 $\pm$ 0.08 (0.00005)	0.33 $\pm$ 0.08 (0.00003)	0.27 $\pm$ 0.09 (0.001)	0.29 $\pm$ 0.09 (0.0006)
Factor 6: Compulsion/ restricted interests	0.69 $\pm$ 0.07 ( $9 \times 10^{-18}$ )	0.64 $\pm$ 0.07 ( $2 \times 10^{-15}$ )	0.70 $\pm$ 0.08 ( $9 \times 10^{-16}$ )	0.65 $\pm$ 0.08 ( $1 \times 10^{-13}$ )

Note: <sup>a</sup>The degree of statistical significance for all the heritability estimates decreased when only Caucasian families (n=517) were used compared to when all the families (n=618) were used, possibly due to the decrease in sample size. The effect of covariates on heritability estimates varied for different factors. For example, for analyses using the Caucasian families, after adjusting for covariates, the heritability estimates decreased for the joint attention, social interaction & communication, and compulsion/restricted interests factors, increased for the repetitive sensory-motor behaviour factor, but remained the same for the non-verbal communication and peer interaction factors.

<sup>b</sup>After adjustment for 4 covariates: gender, age at Autism Diagnostic Interview-Revised (ADI-R) assessment, age squared, and verbal/nonverbal status.

Table S6. Factor loading patterns when 2 to 5 factors were retained for the patients from the Autism Genome Project phase I

	ADI-R items	2 factors		3 factors			4 factors				5 factors				
		Fac1	Fac2	Fac1	Fac2	Fac3	Fac1	Fac2	Fac3	Fac4	Fac1	Fac2	Fac3	Fac4	Fac5
Social domain	Direct gaze	<b>0.51</b>	0.20	<b>0.49</b>	0.28	-0.01	<b>0.43</b>	0.12	0.16	<b>0.45</b>	<b>0.40</b>	0.11	0.15	0.13	<b>0.46</b>
	Social smiling	<b>0.63</b>	0.27	<b>0.65</b>	0.20	0.09	<b>0.59</b>	0.23	0.08	<b>0.39</b>	<b>0.59</b>	0.22	0.06	0.13	<b>0.42</b>
	Range of facial expressions used to communicate	<b>0.53</b>	0.25	<b>0.54</b>	0.22	0.08	<b>0.48</b>	0.20	0.11	<b>0.36</b>	<b>0.48</b>	0.19	0.10	0.09	<b>0.39</b>
	Imaginative play with peers	<b>0.65</b>	0.26	<b>0.69</b>	0.15	0.09	<b>0.74</b>	0.07	0.21	-0.17	<b>0.69</b>	0.07	0.19	0.28	-0.15
	Interest in children	<b>0.69</b>	0.16	<b>0.69</b>	0.13	0.00	<b>0.66</b>	0.09	0.08	0.20	<b>0.46</b>	0.10	0.10	<b>0.62</b>	0.19
	Response to approaches of other children	<b>0.65</b>	0.19	<b>0.65</b>	0.16	0.02	<b>0.62</b>	0.11	0.11	0.20	<b>0.42</b>	0.13	0.14	<b>0.62</b>	0.20
	Group play with peers	<b>0.62</b>	0.17	<b>0.65</b>	0.06	0.06	<b>0.64</b>	0.10	0.06	0.04	<b>0.50</b>	0.12	0.07	<b>0.48</b>	0.03
	Showing and directing attention	<b>0.59</b>	<b>0.41</b>	<b>0.65</b>	0.21	0.23	<b>0.64</b>	0.27	0.21	0.02	<b>0.65</b>	0.25	0.19	0.12	0.04
	Offering to share	<b>0.53</b>	<b>0.37</b>	<b>0.58</b>	0.20	0.21	<b>0.58</b>	0.22	0.22	-0.04	<b>0.58</b>	0.21	0.20	0.15	-0.03
	Seeking to share enjoyment with others	<b>0.56</b>	<b>0.36</b>	<b>0.62</b>	0.17	0.21	<b>0.58</b>	0.29	0.12	0.15	<b>0.56</b>	0.28	0.11	0.18	0.16
	Use of other's body to communicate	0.22	<b>0.42</b>	0.24	<b>0.37</b>	0.21	0.25	0.20	<b>0.41</b>	-0.08	0.23	0.20	<b>0.41</b>	0.11	-0.09
	Offering comfort	<b>0.55</b>	0.29	<b>0.58</b>	0.19	0.12	<b>0.58</b>	0.15	0.20	0.02	<b>0.59</b>	0.13	0.18	0.12	0.04
	Quality of social overtures	<b>0.62</b>	0.31	<b>0.65</b>	0.21	0.12	<b>0.61</b>	0.22	0.15	0.25	<b>0.61</b>	0.20	0.12	0.13	0.27
	Appropriateness of social responses	<b>0.63</b>	0.20	<b>0.63</b>	0.18	0.02	<b>0.61</b>	0.11	0.12	0.21	<b>0.59</b>	0.10	0.11	0.16	0.24
Communication	Pointing to express interest	<b>0.39</b>	<b>0.49</b>	<b>0.45</b>	0.29	0.31	<b>0.42</b>	<b>0.35</b>	0.27	0.08	<b>0.43</b>	0.34	0.25	0.09	0.09
	Nodding	0.17	<b>0.86</b>	0.33	0.26	<b>0.87</b>	0.26	<b>0.92</b>	0.23	-0.01	0.23	<b>0.94</b>	0.24	0.13	-0.02
	Head shaking	0.19	<b>0.77</b>	<b>0.35</b>	0.22	<b>0.76</b>	0.29	<b>0.80</b>	0.19	0.01	0.31	<b>0.78</b>	0.18	0.05	0.02
	Conventional/instrumental gestures	<b>0.56</b>	<b>0.50</b>	<b>0.64</b>	0.21	0.34	<b>0.62</b>	<b>0.39</b>	0.20	0.06	<b>0.61</b>	<b>0.38</b>	0.18	0.15	0.08
	Spontaneous imitation of actions	<b>0.53</b>	0.26	<b>0.54</b>	0.23	0.06	<b>0.56</b>	0.07	0.26	-0.03	<b>0.60</b>	0.05	0.23	0.04	-0.01
	Imaginative play	<b>0.61</b>	0.30	<b>0.62</b>	0.28	0.07	<b>0.66</b>	0.06	0.33	-0.09	<b>0.66</b>	0.05	0.31	0.16	-0.08
	Imitative social play	<b>0.64</b>	0.16	<b>0.62</b>	0.20	-0.04	<b>0.62</b>	0.02	0.18	0.12	<b>0.55</b>	0.02	0.18	0.28	0.12
Behaviour	Unusual preoccupations	0.13	0.19	0.11	0.26	0.03	0.07	0.10	0.20	0.25	0.06	0.10	0.21	0.05	0.24
	Circumscribed interests	0.11	-0.12	0.05	0.08	-0.19	0.00	-0.10	-0.03	<b>0.41</b>	-0.03	-0.10	-0.01	0.03	<b>0.40</b>
	Compulsions/rituals	0.12	0.10	0.07	0.27	-0.06	0.02	0.02	0.19	<b>0.36</b>	0.00	0.02	0.20	0.03	<b>0.35</b>
	Hand and finger mannerisms	0.23	0.37	0.18	<b>0.56</b>	0.07	0.17	0.10	<b>0.53</b>	0.15	0.16	0.10	<b>0.54</b>	0.08	0.14
	Other complex mannerisms or stereotyped body movements	0.18	0.32	0.13	<b>0.51</b>	0.05	0.12	0.08	<b>0.49</b>	0.13	0.12	0.07	<b>0.49</b>	0.04	0.12
	Repetitive use of objects or interest in parts of objects	0.31	<b>0.39</b>	0.26	<b>0.59</b>	0.05	0.27	0.06	<b>0.62</b>	0.05	0.29	0.05	<b>0.61</b>	0.03	0.05
	Unusual sensory interests	0.15	<b>0.37</b>	0.09	<b>0.59</b>	0.07	0.09	0.10	<b>0.57</b>	0.13	0.09	0.10	<b>0.57</b>	0.03	0.12

Note: Bold if loading  $\geq 0.35$ . ADI-R= Autism Diagnostic Interview-Revised.



Table S7. Factor loading patterns when 2 to 5 factors were retained for the patients from the Autism Genome Project phase II

	ADI-R items	2 factors		3 factors			4 factors				5 factors				
		Fac1	Fac2	Fac1	Fac2	Fac3	Fac1	Fac2	Fac3	Fac4	Fac1	Fac2	Fac3	Fac4	Fac5
Social domain	Direct gaze	<b>0.57</b>	0.07	<b>0.55</b>	0.08	0.17	0.24	0.06	<b>0.64</b>	0.12	0.25	0.03	<b>0.63</b>	0.16	0.04
	Social smiling	<b>0.57</b>	0.25	<b>0.50</b>	0.23	<b>0.36</b>	0.26	0.22	<b>0.52</b>	0.33	0.25	0.26	<b>0.60</b>	0.10	0.27
	Range of facial expressions used to communicate	<b>0.51</b>	0.25	<b>0.43</b>	0.20	<b>0.40</b>	0.32	0.19	<b>0.33</b>	<b>0.38</b>	0.31	0.26	<b>0.39</b>	0.07	<b>0.35</b>
	Imaginative play with peers	<b>0.71</b>	0.31	<b>0.68</b>	0.34	0.15	<b>0.76</b>	0.30	0.16	0.13	<b>0.77</b>	0.27	0.14	0.21	0.03
	Interest in children	<b>0.69</b>	0.07	<b>0.69</b>	0.11	0.07	<b>0.63</b>	0.08	0.32	0.05	<b>0.63</b>	0.06	0.31	0.11	0.00
	Response to approaches of other children	<b>0.72</b>	0.04	<b>0.74</b>	0.08	0.01	<b>0.63</b>	0.06	<b>0.40</b>	-0.01	<b>0.63</b>	0.00	<b>0.36</b>	0.17	-0.09
	Group play with peers	<b>0.68</b>	0.19	<b>0.66</b>	0.21	0.17	<b>0.74</b>	0.17	0.15	0.16	<b>0.73</b>	0.18	0.16	0.09	0.12
	Showing and directing attention	<b>0.58</b>	<b>0.42</b>	<b>0.55</b>	<b>0.44</b>	0.11	<b>0.40</b>	<b>0.43</b>	<b>0.42</b>	0.07	<b>0.41</b>	<b>0.38</b>	<b>0.41</b>	0.22	-0.06
	Offering to share	<b>0.58</b>	0.30	<b>0.56</b>	0.33	0.10	<b>0.49</b>	0.31	0.31	0.07	<b>0.49</b>	0.27	0.30	0.18	-0.03
	Seeking to share enjoyment with others	<b>0.52</b>	0.28	<b>0.51</b>	0.30	0.09	0.29	0.30	<b>0.50</b>	0.04	0.29	0.25	<b>0.49</b>	0.16	-0.05
	Use of other's body to communicate	0.20	0.33	0.20	<b>0.35</b>	-0.01	0.12	<b>0.35</b>	0.20	-0.03	0.12	0.22	0.11	<b>0.44</b>	-0.25
	Offering comfort	<b>0.57</b>	0.34	<b>0.51</b>	0.33	0.28	<b>0.47</b>	0.31	0.25	0.26	<b>0.47</b>	0.34	0.29	0.11	0.19
	Quality of social overtures	<b>0.67</b>	0.18	<b>0.66</b>	0.21	0.13	<b>0.37</b>	0.20	<b>0.64</b>	0.07	<b>0.38</b>	0.14	<b>0.62</b>	0.21	-0.04
Appropriateness of social responses	<b>0.66</b>	0.20	<b>0.61</b>	0.20	0.26	<b>0.42</b>	0.19	<b>0.49</b>	0.22	<b>0.42</b>	0.16	<b>0.47</b>	0.23	0.11	
Communication	Pointing to express interest	<b>0.42</b>	<b>0.52</b>	<b>0.42</b>	<b>0.58</b>	-0.02	0.32	<b>0.57</b>	0.32	-0.05	0.32	<b>0.48</b>	0.29	0.25	-0.21
	Nodding	0.21	<b>0.89</b>	0.17	<b>0.92</b>	0.09	0.17	<b>0.91</b>	0.12	0.07	0.16	<b>0.86</b>	0.15	0.25	-0.13
	Head shaking	0.25	<b>0.79</b>	0.18	<b>0.76</b>	0.23	0.23	<b>0.75</b>	0.05	0.22	0.22	<b>0.80</b>	0.11	0.13	0.09
	Conventional/instrumental gestures	<b>0.51</b>	<b>0.54</b>	<b>0.44</b>	<b>0.53</b>	0.29	<b>0.43</b>	<b>0.51</b>	0.22	0.27	<b>0.43</b>	<b>0.53</b>	0.25	0.17	0.16
	Spontaneous imitation of actions	<b>0.53</b>	<b>0.35</b>	<b>0.48</b>	0.34	0.26	<b>0.52</b>	0.31	0.13	0.25	<b>0.52</b>	<b>0.35</b>	0.16	0.10	0.19
	Imaginative play	<b>0.69</b>	0.28	<b>0.65</b>	0.29	0.21	<b>0.70</b>	0.26	0.19	0.20	<b>0.71</b>	0.22	0.15	0.24	0.09
	Imitative social play	<b>0.62</b>	0.09	<b>0.64</b>	0.14	-0.03	<b>0.53</b>	0.12	<b>0.37</b>	-0.06	<b>0.53</b>	0.07	<b>0.35</b>	0.10	-0.12
Behaviour	Unusual preoccupations	0.03	0.09	-0.07	0.01	<b>0.42</b>	-0.01	0.02	-0.08	<b>0.43</b>	-0.01	0.07	-0.07	0.15	<b>0.39</b>
	Circumscribed interests	0.03	-0.13	-0.03	-0.20	0.31	-0.02	-0.20	-0.01	0.32	-0.03	-0.13	0.02	-0.01	<b>0.36</b>
	Compulsions/rituals	0.20	0.07	0.11	-0.01	<b>0.46</b>	0.08	-0.01	0.11	<b>0.45</b>	0.08	0.05	0.13	0.12	<b>0.41</b>
	Hand and finger mannerisms	0.25	0.20	0.19	0.16	0.30	0.11	0.16	0.20	0.28	0.11	0.09	0.13	<b>0.40</b>	0.15
	Other complex mannerisms or stereotyped body movements	0.20	0.12	0.15	0.10	0.18	0.08	0.11	0.18	0.16	0.08	0.01	0.10	<b>0.38</b>	0.04
	Repetitive use of objects or interest in parts of objects	0.30	0.26	0.20	0.21	<b>0.42</b>	0.17	0.21	0.15	<b>0.40</b>	0.18	0.15	0.08	<b>0.46</b>	0.26
	Unusual sensory interests	0.26	0.26	0.18	0.22	0.34	0.12	0.22	0.17	0.32	0.12	0.14	0.08	<b>0.50</b>	0.17

Note: Bold if loading  $\geq 0.35$ . ADI-R, Autism Diagnostic Interview-Revised.