Variance of IQ is partially dependent on deletion type among 1,427 22q11.2 deletion syndrome subjects

Human genetics

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Supplementary Table 2. Detailed grouping criterion for 21 study sites (no. of sample in parentheses)

Group of study site	Study site included
US and Canada	CHOP/U. Penn, PA(182); Duke U., Durham, NC(55); Emory U., Atlanta, GA(1); Upstate Medical Center, Syracuse, NY(137); UCLA, Los Angeles, CA(62); UC Davis, Davis, CA(58); Toronto, CA(101)
Northern Europe	Geneva, Switzerland(105); Leuven, Belgium(101); Maastricht, Netherlands(79); Utrecht, Netherlands(130)
Southern Europe	Marseille, France(24); Tel Aviv, Israel(81); Madrid, Spain(25); Mallorca, Spain(14); Rome, Italy(52); Santiago, Chile (60)
UK and Australia	Cardiff, Wales(75); Dublin, Ireland(53); London, England(11); Newcastle, Australia(21),

Supplementary Table 3. Multivariable linear regression analysis of IQ and deletion size with adjustment of sex and age stratified by group of study site

Study site	deletion type (No of subjects)	FSIQ		VIQ		PIQ	
		β	*P*	β	*P*	β	*P*
Canada &US	AD (reference,569)						
	AB(27)	1.46	0.247	1.77	0.246	1.3	0.363
Northern Europe	AD (reference,392)						
	AB(23)	5.09	1.59E-4	6.13	9.10E-5	4.9	4.24E-4
Southern Europe	AD (reference,238)						
	AB(18)	1.64	0.378	0.97	0.649	0.378	0.864
UK & Australia	AD (reference,154)						
	AB(6)	5.48	0.054	9.48	0.080	6.924	0.044

Supplementary Table 4. Statistical power (%) at α=0.05 under various differences in IQ measures between 22q11.2DS subjects with AD and AB deletions.

Difference (SD)	Power(%)
0.1	15
0.2	45
0.3	79
0.4	95

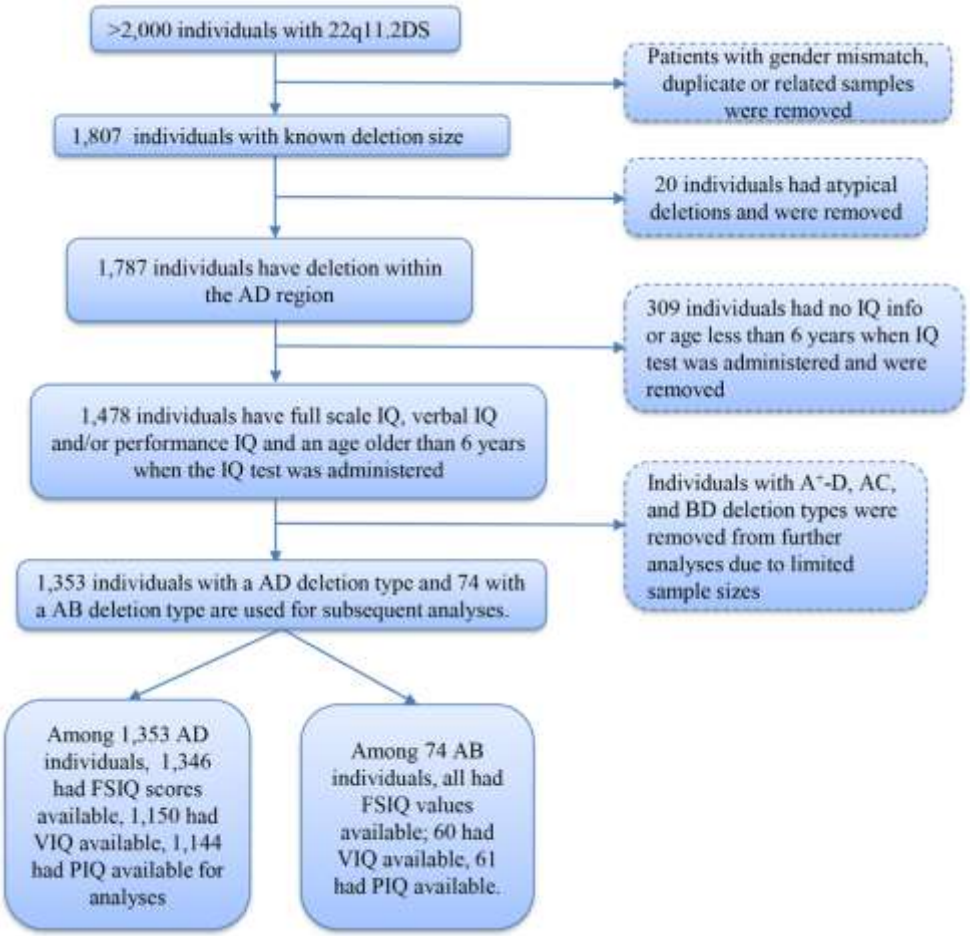
[a]Standard deviation (SD), PASS software (http://www.ncss.com/pass.html) was used for these calculations. In a design of an independent samples t-test, we have about 80% power to detect the IQ difference at 0.3 SD level when the sample size of AD equals to 1,270 and AB equals to 76, which are close to the top two largest deletion groups in our study.

Supplementary Table 5. Number of samples with missing values for each variable between AD and AB group and the distribution of each categorical variable between AD and AB group

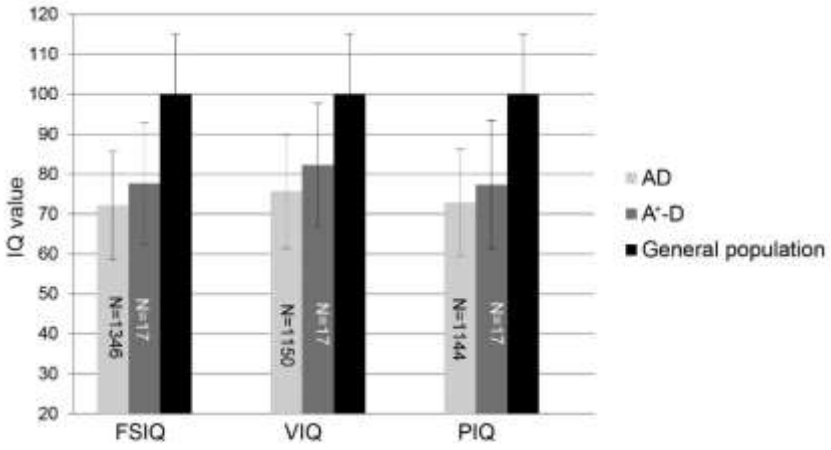
Total number=1427	AD	AB	*P* value
Sex			0.722[a]
Male	647	37	
Female	706	37	
Age	1330	74	
Missing	23	0	
CHD[c]			0.566[a]
Cases	286	17	
Controls	593	30	
Missing	474	26	
FSIQ[d]	1346	74	
Missing	7	0	
VIQ[e]	1150	60	
Missing	203	14	
PIQ[f]	1144	61	
Missing	209	13	
IQ test			0.460[b]
Wechsler	1306	73	
Non-Wechsler	39	3	
Unknown	8	1	
Study sites			0.381[a]
US&Canada	569	27	
North_Europe	392	23	
South_Europe	238	18	
UK&Australia	154	6	

[a]*P* values were calculated for categorical variables from Pearson chi-square software. [b]*P* value was calculated from fisher's exact test, [c]CHD, congenital heart disease, is defined as subjects with Tetralogy of Fallot (TOF), Persistent Truncus Arteriosus (PTA) or Interrupted Aortic Arch Type B (IAAB); [d]Full scale IQ; [e]Verbal IQ, [f]Performance IQ.

Supplementary Figures

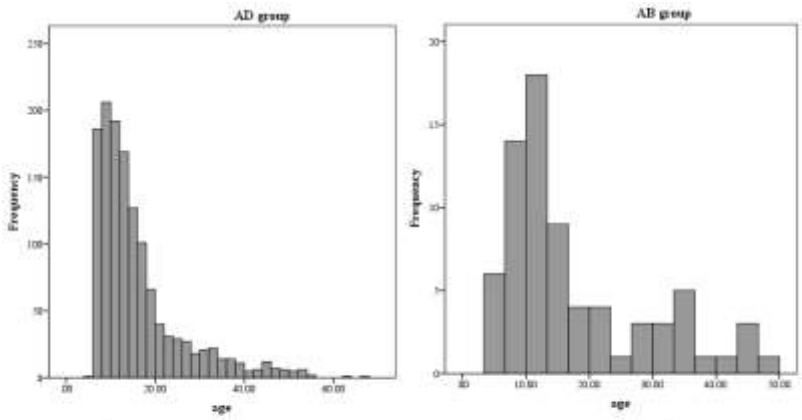


Supplementary Fig. 1 Flow diagram of selection steps of subjects with 22q11.2 deletion syndrome.



	FSIQ	VIQ	PIQ
AD	72.14±13.50	75.60±14.26	72.76±13.48
A^+-D	72.36±17.89	75.86±16.91	73.29±16.31

Supplementary Fig. 2. IQ differences between subjects with AD and nested A^+-D (2.8Mb) deletion types. IQ values are expressed as mean±SD. An independent-samples t-test was conducted to compare the mean IQ score in subjects carrying the AD deletion with those carrying A^+-D within the 22q11.2DS cohort. No significant differences were observed. Numbers in the bars denote samples size of each of the category, test for all three IQ scores have a $P > 0.05$



	AD group	AB group
Median ± SD	12.67±9.67	13.08±11.54

Supplementary Fig. 3. Distribution of age among subjects with 22q11.2DS with the AD deletion and AB deletion, respectively. The distributions of age in both AD (1,351 subjects) and AB (77 subjects) groups violate the normal distribution assumption according to the one-sample Kolmogorov- Smirnov test (both asymptotic P <0.05), while the distribution is the same between AD and AB groups (P>0.05 for Mann-Whitney U test). No significant differences were observed for the median ages as indicated by the independent-samples median test (P>0.05). Age is expressed as median ±SD

Supplementary Fig. 4. Genetic architecture of the 22q11.2 region based on the hg38 genome assembly**.** Coding genes, non-coding genes, miRNA, unknown genes and pseudogenes were aligned along the 3 Mb 22q11.2 region (chr22:18906222-21451463) spanning the four LCR22s (LCR22A-D), respectively. There are

49 coding genes, 18 non-coding RNAs, 7 miRNAs, 3 pseudogenes and 1 gene that is unclear whether it is a coding gene or pseudogene.