Detecting Cognitive Endophenotypes for Autism Using a General Population Twin Family Sample

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Background

Autism spectrum conditions (ASC) show an uneven cognitive profile:

- Relative peak performance on Block Design[1,2] and Embedded Figures[3].
- Poor performance on cognitive flexibility[4], language[2] and social cognition[5].

Studies of the Broader Autism Phenotype show that a similar uneven cognitive profile may also characterize first-degree relatives, suggesting familial influences[5].

Recent studies indicate that autistic traits are continuously distributed in the general population[6,7] and that individual differences in these traits show substantial heritability[8].

Objectives

I. To explore the association between autistic traits and performance on cognitive tests in a general population sample.

II. To examine whether this association is due to shared genetic or environmental influences.

A genetic link between certain cognitive abilities and autistic traits would point to these being promising endophenotypes for autism.

Methods I

Participants

18-year-old twin pairs (n = 197 pairs) and their siblings (n = 96; mean age 18.29 years, SD = 2.11) , who are all registered in the Netherlands Twin Register.

Methods II

Measures

The Autism-Spectrum Quotient (AQ): a quantitative measure of autistic traits[6,7] with 2 factors:

- Social Interaction (SOC, 40 items);
- Attention to Detail (ATT, 10 items).

Performance on an extensive cognitive test battery:

- 11 Wechsler intelligence scale subtests
- Stroop-interference
- California Verbal Learning Test
- Test of spatial short term memory (Corsi block tapping)
- Test of processing speed (Pi Inspection time)
- Test of working memory (N-Back)
- Phonological and semantic verbal fluency.

Statistics/genetic modelling

Stepwise backward regression analyses taking into account the genetic relatedness of the participants were conducted to study which cognitive abilities predicted variance in SOC and ATT scores. Genetic vs. environmental covariance was estimated using structural equation modelling in Mx.

Results I

Poor performance on the Wechsler Vocabulary subtest (VOC) and Semantic Verbal Fluency (SVF) predicted SOC difficulties ($\chi2 = 7.52$, df = 1, $p < .01$ and $\chi2 = 6.35$, df = 1, $p = .01$).

Performance on the Block Design (BD) and Information (INF) subtests of the Wechsler Intelligence scale both predicted ATT ($\chi2 = 5.41$, df = 1, $p = .02$ and $\chi2 = 6.25$, df = 1, $p = .01$).

Descriptives

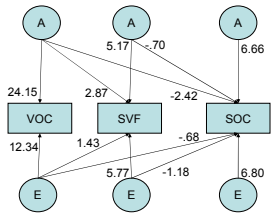
	N	Mean	SD	Sex effect	Age effect
AQ social interaction	470	80.00	10.01	M>F; p = .03	ns
AQ Attention to Detail	470	22.22	3.83	M>F; p = .01	ns
Vocabulary	455	10.18	2.71	ns	standardised
Semantic Verbal Fluency	453	.00	.86	ns	p < .001
Block Design	454	10.45	2.62	M>F; p = .04	standardised
Information	454	10.10	2.79	M>F; p<.001	standardised

Results II

Phenotypic correlations, familial resemblance and the genetic contribution to the (co)variance in and between traits

	VOC	SVF	SOC	VOC	SVF	SOC	VOC	SVF	SOC
	Phenotypic			MZ/ All 1st degree relatives			Genetic influences (%)		
VOC	1			.80/.38	.16	-.13	79		
SVF	.38	1		.30	.55/.19	-.10	80	50	
SOC	-.25	-.22	1	-.20	-.10	.50/.26	87	58	51
	BD	INF	ATT	BD	INF	ATT	BD	INF	ATT
	Phenotypic			MZ/ All 1st degree relatives			Genetic influences (%)		
BD	1			.68/.37	.15	.04	69		
INF	.38	1		.37	.84/.39	.02	95	83	
ATT	.16	.16	1	.08	.10	.49/.22	55	56	48

MZ = monozygotic twin correlation, All 1st degree relatives = correlation in dizygotic twins and twin-siblings



Correlations and cross correlations are higher in MZ twins than in 1st degree relatives.

Variance and covariance was explained by both genetic (A) influences and environmental effects unique to each family member (E). (The same model was applied to BD, INF and ATT).

Conclusions

General population autistic traits covary with the same cognitive strengths and weaknesses as observed in clinical ASC.

The relationship between autistic traits and the uneven cognitive profile is partly genetic, suggesting these could be used as endophenotypes for autism.

References

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