Published in final edited form as:
JAMA Psychiatry. 2014 September 1; 71(9): 1049–1057. doi:10.1001/jamapsychiatry.2014.994.

Consistent etiology of severe, frequent psychotic experiences and milder, less frequent manifestations: A twin study of specific psychotic experiences in adolescence

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Abstract

Context—The onset of psychosis is usually preceded by psychotic experiences, but little is known about their causes. The present study investigated the degree of genetic and environmental influences on specific psychotic experiences, assessed dimensionally, in adolescence in the community and in individuals with many, frequent experiences (defined using quantitative cut-offs). The degree of overlap in etiological influences between specific psychotic experiences was also investigated

Objective—Investigate degree of genetic and environmental influences on specific psychotic experiences, assessed dimensionally, in adolescence in the community and in individuals having

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Author contributions: Drs Zavos and Ronald had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Analysis and interpretation of data: Zavos, Ronald, Plomin.
Drafting of the manuscript: Zavos, Ronald.
Critical revision of the manuscript for important intellectual content: All authors.

Conflict of Interest Disclosures: None reported

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many, frequent experiences (defined using quantitative cut-offs). Test degree of overlap in etiological influences between specific psychotic experiences.

Design—Classic twin design. Structural equation model-fitting. Univariate and bivariate twin models, liability threshold models, DeFries-Fulker extremes analysis and the Cherny Method.

Setting—Representative community sample of twins from England and Wales.

Participants—5059 adolescent twin pairs (Mean age: 16.31 yrs, SD: 0.68 yrs).

Main outcome measure—Psychotic experiences assessed as quantitative traits (self-rated paranoia, hallucinations, cognitive disorganization, grandiosity, anhedonia; parent-rated negative symptoms).

Results—Genetic influences were apparent for all psychotic experiences (15-59%) with modest shared environment for hallucinations and negative symptoms (17-24%) and significant nonshared environment (49-64% for the self-rated scales, 17% for Parent-rated Negative Symptoms). Three different empirical approaches converged to suggest that the etiology in extreme groups (most extreme-scoring 5%, 10% and 15%) did not differ significantly from that of the whole distribution. There was no linear change in the heritability across the distribution of psychotic experiences, with the exception of a modest increase in heritability for increasing severity of parent-rated negative symptoms. Of the psychotic experiences that showed covariation, this appeared to be due to shared genetic influences (bivariate heritabilities = .54-.71).

Conclusions and Relevance—These findings are consistent with the concept of a psychosis continuum, suggesting that the same genetic and environmental factors influence both extreme, frequent psychotic experiences and milder, less frequent manifestations in adolescents. Individual psychotic experiences in adolescence, assessed quantitatively, have lower heritability estimates and higher estimates of nonshared environment than those for the liability to schizophrenia. Heritability varies by type of psychotic experience, being highest for paranoia and parent-rated negative symptoms, and lowest for hallucinations.

Introduction

The symptoms evident in people with psychotic disorders can also be experienced by people who are at increased risk of developing a psychotic disorder and in the general population (1). Across these populations, psychotic experiences appear to be associated with similar environmental factors (such as neighborhood deprivation and stressful life events) and to run in the same families (2, 3). Psychotic disorders typically begin in early adulthood, but psychotic experiences often first occur in adolescence (4). Individuals reporting psychotic experiences in childhood are at greater risk of psychotic disorders in adulthood (5, 6).

The last decade has seen increasing interest in the development of clinical interventions for individuals at high risk of psychosis(7). Understanding more about the causes of psychotic experiences in adolescence is one approach which might inform the development of such interventions. In adults, twin and adoption studies suggest that both genes and environment influence risk for psychotic disorders(8-10). However, these studies did not address the individual psychotic experiences as true dimensional quantitative traits.

In adolescence, there is limited understanding about the causes of psychotic experiences. Three reports on psychotic experiences (hallucinations and schizotypy traits) in adolescents (age 13-19) employing community twin samples of <600 pairs suggest that they are moderately heritable (33-57%) with the remaining variance explained by non-shared environment (environmental influences that make children growing up in the same family different) (11-13). Larger studies, using measures of the full range of positive, negative, and cognitive psychotic experiences, would make it possible to move beyond single heritability estimates to test whether etiological influences vary across the distribution of severity, with particular focus on the high scorers, and to test whether different psychotic experiences share the same etiological influences.

A symptom-specific approach to studying the etiology of psychotic experiences is encouraged in light of the multifactorial structure of psychotic experiences, as reported in numerous factor analytic studies e.g.(14, 15). A symptom-specific dimensional approach to studying the etiology of psychosis has also been championed by researchers using clinical samples(16-20).

The aim of the present study was to examine the degree of genetic and environmental influences on specific psychotic experiences in a community twin sample, and in subgroups defined by extreme levels of psychotic experiences (top 5%, 10% and 15%). Three empirical approaches were taken, one that categorized data to identify extreme scores and assumed an underlying liability (liability threshold model); one that used a group-based regression method (DeFries-Fulker extremes analysis); and one that tested whether there were any significant linear changes in the genetic and environmental estimates across the distribution (Cherny method).

Finally, where specific psychotic experiences co-varied, their relationship was decomposed to investigate the extent of overlap in genetic and environmental influences between different types of psychotic experiences.

Method

Participants

The Longitudinal Experiences And Perceptions (LEAP) study assessed psychotic experiences in adolescents (15) drawn from the Twins Early Development Study (TEDS), a general population sample of monozygotic (MZ) and dizygotic (DZ) twins born in England and Wales between 1994-1996 (21). TEDS has full ethical approval. TEDS originally contacted a sample of 16,302 families who had recently had twins in 1994-96, of whom 13,488 families responded with a written consent form. Families were not contacted for the LEAP study if they had withdrawn from TEDS, had never returned any data, had known address problems, or were special cases, most notably medical exclusions.

Initially, 10,874 TEDS families were contacted and invited to participate in LEAP. Of those contacted, 5076 (47%) parents provided data and 5059 (47%) twin pairs provided data (M = 16.32 years; SD = 0.68 years). Individuals were excluded (N = 876) if they did not provide consent at first contact (when TEDS was started) or for the present study, if they had severe

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medical disorder, if they had experienced severe perinatal complications or if their zygosity was unknown. The twin sample after exclusions (N = 4743 families) was 45% male. Participating and non-participating families were largely similar with regard to sex, zygosity, ethnicity and mother education level. Further details are provided in eTable 1. The non-participating families had higher scores on childhood psychopathology than the participating families. The difference of roughly 1 raw score between the participating and non-participating families however amounts only to an average of half a point difference on the measure (each item is rated 0-2 and even small differences are significant because of the large sample size).

Measures

Specific Psychotic Experiences Questionnaire (SPEQ)—The SPEQ(15) assesses six types of psychotic experiences in adolescents: Paranoia (15 items), Hallucinations (9 items), Cognitive Disorganization (11 items), Grandiosity (8 items), and Anhedonia (10 items) -- all via self report --, and Negative Symptoms via parent report (10 items). The SPEQ was developed by selecting and combining items from existing scales for adults and adapting wording when necessary to be age appropriate. Age appropriateness of items was ensured via obtaining expert clinical opinion (DF, AGC and PM) and via piloting on this age group (described in(15)). Subscales show good to excellent internal consistency (Cronbach's alpha = 0.77-0.93) and test-retest reliability across a nine-month interval (r = 0.65-0.74).

Construct validity was assessed in terms of the principal component analysis supporting the separation of the SPEQ subscale items (Ronald et al in press). Content validity was assessed via expert clinical opinion to judge the suitability of items for measuring adolescent psychotic experiences (by A.G.C., D.F., and P.M.). Validity was also assessed in terms of agreement with a second known measure of adolescent psychosis-like symptoms, the PLIKS (22). Individuals who reported "definitely" having any psychosis-like symptoms on the PLIKS had significantly more psychotic experiences on all the SPEQ subscales than individuals who did not report any definite psychosis-like symptoms (all significant at $p<.001$) with exception of Anhedonia which was not significant. The SPEQ positive and cognitive psychotic experiences subscales show significant positive correlations with the PLIKS quantitative score (Hallucinations r = .60, Paranoia r = .48, Cognitive Disorganization r = .41, Grandiosity r = .27, all $p<.001$). (15, 22). Finally, for all the SPEQ subscales except Anhedonia, individuals who reported a family history (having a first- or second- degree relative with schizophrenia or bipolar disorder) scored higher than individuals without a family history of psychosis (all $p<.05$ except Hallucinations which showed a trend in this direction).

Further information on how the scales were devised is provided in the Supplement.

Statistical analysis

The twin design—The rationale is to compare the degree of resemblance among MZ twins, who share 100% of their DNA sequence, with DZ twins, who share on average 50%. Relative differences in within-pair correlations are then used to estimate the following latent factors on the measures: additive genetic (A), shared environment (C), and non-shared

environment (E). Where correlations are higher for MZ as compared to DZ twins, genetic influence is inferred. Within-pair similarity that is not due to genetic factors is attributed to shared environmental influences (C), which is thus defined as aspects of the environment that contribute to resemblance between family members. Non-shared environment (E) accounts for individual specific factors that create differences among siblings from the same family. These are estimated from within-pair differences between MZ twins. Measurement error is included in this term.

Twin models in the whole sample—Statistical analysis was conducted in Mx(23). Variables were age and sex regressed as is standard practice for quantitative genetic model fitting(24). Twin correlations were estimated for each sex and zyosity group.

Univariate models examined the influences of A, C and E on psychotic experiences. Several models were tested and compared to a saturated model: 1) A full sex-limitation model allowing for quantitative and qualitative sex differences in addition to variance differences; 2) a model allowing for quantitative and variance sex differences; 3) a no sex differences model and finally; 4) a variance sex difference model (see 25 for more detail). Models were compared using χ^2 difference for nested models, and the Akaike information criterion (AIC), which is equal to χ^2 minus twice the *df (26)*, was used as an aid to selecting the best-fitting model on the grounds of parsimony and goodness of fit.

Analysis of the extremes—Comparisons of genetic and environmental influences across the distribution of psychotic experiences were made using three analytic techniques. As sex effects were not estimated, DZ opposite sex twins were excluded from these analyses.

Liability threshold modeling: Liability threshold models were used to estimate the etiology of categorically-defined extreme scores. These models assume that the joint distribution of twin pairs follows an underlying bivariate normal distribution(25). If the estimates of heritability and environmental influences of the liability of extreme psychotic experiences at various cut-offs (5%, 10% and 15%) are consistent, it would suggest that the etiology of the liability to psychotic experiences does not vary across severity.

DeFries-Fulker extremes analysis: DF extremes analysis investigates the genetic and environmental influences on the difference between the mean scores of extreme groups and the whole population(27). It is designed for proband-selected data where at least one twin has an extreme score and is based on regression of the co-twin to the mean of a quantitative trait score (for more detail see 27). A genetic link between extremes and the whole sample is implicated if significant group heritability estimates are found.

Cherny method: The Cherny method is an extension of the DF extremes model and examines whether the relative contributions of genes and environment change linearly across the full distribution. This is implemented by including interaction effects in a regression equation which allow for the estimation of the interaction between the heritability of a trait with the score on the trait (see 28).

Bivariate model-fitting of relationships between specific psychotic experiences in the whole sample

Bivariate twin models were used to assess the genetic and environmental influences on associations between specific psychotic experiences where within-person correlations between the different experiences were significant and greater than .20 (15). In bivariate analysis, MZ and DZ correlations are compared across traits, i.e. one twin's score on a trait is correlated with the co-twin's score on another trait(29).

A genetic correlation (rA) is derived from the model-fitting and can vary between 0 and 1, indicating the extent to which genetic influences on one variable overlap with a second phenotype. Correlations can similarly be estimated for shared and non-shared environmental factors. The extent to which genetic, shared and non-shared environmental factors contribute to the phenotypic correlations can also be calculated. For example, genetic influences on the correlation can be calculated by multiplying the square root of the heritability of each variable by the genetic correlation. Similar calculations can be done for shared and non-shared environmental influences.

Results

Univariate-model results for whole sample

There was some evidence of skew therefore variables were transformed (square root: cognitive disorganization, grandiosity, Hallucinations, paranoia; and log: Negative symptoms) as required to ensure skew statistics were between −1 and 1. Descriptive statistics are given in eTable 2. Twin correlations are given in Table 1. DZ correlations were all less than the MZ correlations, indicating additive genetic influences on all psychotic experiences. Shared environmental influences were also implicated for some psychotic experiences, for example Parent-rated Negative Symptoms, as DZ correlations were more than half the MZ correlation. As MZ correlations were less than 1, non-shared environmental influences were also implied. There was some indication of sex differences in the etiology, indicated by the different pattern of MZ and DZ correlations for male versus female and DZ same sex, and opposite sex pairs.

Univariate analyses are presented in Table 2. All ACE model fits were acceptable (i.e. not significantly worse than the saturated model). No qualitative or quantitative sex differences were evident in the genetic and environmental influences on the subscales with the exception of Hallucinations where heritability was higher in females compared to males (full details of model fit are shown in eTable 3). All subscales were moderately heritable, ranging from 32% for Hallucinations in females to 59% for Parent-rated Negative Symptoms, with the exception of Hallucinations in males which showed a low heritability (15%). Significant shared environmental influences were evident for Hallucinations (17% for males, 20% for females) as well as Parent-rated Negative Symptoms (24%). Non-shared environmental influences explained a significant proportion of the variance on all subscales (49%-64% for the self-rated scales, 17% for Parent-rated Negative Symptoms). The high genetic and shared environment estimates for Negative Symptoms may in part be explained shared

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method variance as parents are reporting on both twins within the pair which can inflate twin correlations.

Analysis of the extremes

Liability threshold models—Table 3 presents the extremes analyses. The liability threshold model results indicated genetic influences for all six types of extreme psychotic experiences, and point estimates were not significantly different across the quantitative extreme groups (5%, 10% and 15%) and were highly similar to the heritability estimates for the whole sample. Shared environmental influences showed the same pattern as for the whole sample, that is, being significant only for Hallucinations and parent-rated Negative Symptoms. Estimates of non-shared environment on the extreme groups were also highly consistent across extreme severity groups and closely resembled the whole sample estimates.

DF extremes analysis—Transformed co-twin means were calculated by dividing the co-twin scores by the proband mean for each zygosity group. The transformed co-twin means can be interpreted as twin 'group' correlations because they provide an indication of within pair similarity. They were generally higher in MZ twins than DZ twins suggesting additive genetic influences at the extremes (Table 3). Overall, the relationship between twins did not seem to vary substantially across the cut-off levels compared to whole sample twin correlations.

Group heritability estimates were consistent across the 5%, 10% and 15% extreme groups as indicated by similar point estimates and overlapping confidence intervals. The significant group heritability estimates indicate a genetic link between extreme psychotic experiences and variation in psychotic experiences in the whole sample. Group shared environment estimates also demonstrated consistency across the extremes.

Cherny analysis—Analysis using the regression-based Cherny method are presented in Table 4. There was significant linear change in heritability for only one of the psychotic experiences, suggesting in general that heritability does not differ across the distribution. The exception was parent-rated negative symptoms, which showed decreases in shared environmental influences and modest increases in genetic influences with increasing negative symptoms.

Full sample bivariate analyses between subscales

Bivariate genetic analyses were conducted in the full sample for relationships between psychotic experiences where phenotypic correlations were significant and above .20 (see eTable 4). Four relationships met this criterion (paranoia-hallucinations, paranoia-cognitive disorganization, hallucinations-cognitive disorganization, cognitive disorganization-parent-rated negative symptoms). Cross-twin cross-trait (CTCT) correlations are presented in Table 1. The majority of the MZ CTCT correlations were greater than their equivalent DZ CTCT correlation, suggesting genetic influences on the covariation. Similarly, for most comparisons, DZ CTCT correlations were greater than half the MZ CTCT correlations suggesting shared environmental influences on the covariation. Finally, MZ CTCT

correlations tended to be less than the relevant phenotypic correlation indicating that nonshared environment also contributed to the covariation.

Bivariate twin modelling, presented in Table 5, confirmed these observations (full model fits shown in eTable 5). High genetic correlations were evident between paranoia and hallucinations; paranoia and cognitive disorganisation; and hallucinations and cognitive disorganisation (rA = .61-.63). A moderate genetic correlation (rA=.27) was between cognitive disorganisation and parent-rated Negative Symptoms. The proportion of the covariation between each pair of variables was accounted for primarily by genetic influences; bivariate heritabilities ranged from 54% (cognitive disorganisation and negative symptoms) to 71% (paranoia and cognitive disorganisation). Shared environmental influences were important for the relationship between cognitive disorganisation and parent-rated negative symptoms only.

Moderate nonshared environmental correlations were evident between paranoia and hallucincations; paranoia and cognitive disorganisation; and hallucinations and cognitive disorganisation (rE = .24-.33) indicating some nonshared environmental influences are shared between different psychotic experiences. A lower nonshared environmental correlation (rE=.10) was evident between cognitive disorganisation and parent-rated Negative Symptoms. A significant proportion of the covariance between psychotic experiences was explained by nonshared environment (12-36%).

Discussion

This was the first time that individual psychotic experiences assessed dimensionally in adolescence have been examined for genetic and environmental contributions. Over 5000 twins were assessed on six spectra of psychotic experiences. We found that psychotic experiences in adolescence were moderately heritable, with Paranoia and parent-rated Negative Symptoms showing the highest heritability and hallucinations showing the lowest heritability. Non-shared environment played an important role in their etiology. Shared environment was only significant for hallucinations and negative symptoms. This is in line with previous research which has shown a number of environmental risk factors for psychosis which may be specific to the individual such as stressful life events, cannabis use and childhood trauma (30-32). The low heritability estimate for hallucinations is consistent with emerging research indicating the importance of early trauma for their occurrence(33). Indeed, the heritability estimates argue for a renewed interest in the contribution of the environment to risk for psychotic experiences.

The extremes analyses indicated that the heritability did not differ for individuals who reported the most severe and frequent psychotic experiences compared to the full sample (liability threshold model and Cherny method) and that there was a genetic link between the extreme group and the rest of the distribution (DeFries Fulker analysis). These findings add weight to the suggestion that psychosis exists on an etiological continuum with subclinical psychotic experiences (3). They have implications for genetic studies of psychotic disorders because if extreme, frequent psychotic experiences are part of the same construct as clinically diagnosed psychotic disorders (see e.g. (34, 35)), these findings are supportive of

the hypothesis that the same genes that influence symptoms within psychotic disorders also influence variation in psychotic experiences in the general population. So far, one study has been conducted, which tested whether a cumulative score of positive psychotic experiences in adolescence was associated with the same genetic variants as diagnosed schizophrenia as a whole (36).

Previous research suggests that psychotic experiences load onto separate components (including in this sample, (14, 15)); for this reason we analysed domains of psychotic experiences separately. The co-variation between psychotic experiences was found to be explained by shared genetic influences across domains. However, it is noted that not all domains correlated with one another and genetic correlations did not reach unity, suggesting there may be some etiological influences that are distinct across different psychotic experiences.

The twin design is based on several assumptions, including independence of the A, C and E latent factors, and ideally findings should be replicated across different study designs (see 37, 38). Self-report data of psychotic experiences has been shown to give higher means than interview data (39). It would have been advantageous to report the DF and LT models using even more extreme thresholds that more closely mirrored the prevalence of adult psychosis. The statistical power afforded with the etiological architecture of these scales (which involve modest amounts of A and in some cases C) was not high enough to estimate parameters accurately with more extreme (e.g. 1%) cut-offs. The 5% cut-off included here is similar to the prevalence of the at risk mental state (40) and a meta-analysis reported the median prevalence of adult psychotic experiences to be within the ranges of the extreme group cut offs, at 7.2% (41), but the 5% extreme cut-off does not mirror the prevalence of psychotic disorders. However it is noted that one of the other methods used for the extremes analysis, the Cherny method, was able to examine whether the relative contributions of genes and environment changed linearly across the full distribution of psychotic experiences, which incorporated all individuals, including at the very extreme. It is important to remember that nonshared environment estimates (E) include measurement error. However the E estimates were larger than the estimated error in each scale (calculated as 1 minus the Cronbach’s alpha or test-retest reliability statistic) suggesting E played an important role in specific psychotic experiences beyond measurement error, with the exception of the parent-rated negative symptoms scale, where error appeared to make up most of the E term.

The large sample enabled etiological sex differences to be tested and gave power to analyse the etiology of extreme groups. It was also advantageous that the full range of positive, negative and cognitive disorganisation experiences were included, using a reliable and validated measure in a narrow age range (15).

In conclusion, this study found significant heritability for all psychotic experiences, while also showing that environmental influences, particularly nonshared environment, play an important role and appear to have a more prominent role than suggested from twin studies on the liability of schizophrenia. Heritability varies by psychotic experience type, being highest for paranoia and parent-rated negative symptoms, and lowest for hallucinations.

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These findings suggest that the same genetic and environmental causal factors influence extreme, frequent, psychotic experiences and milder, less frequent manifestations in adolescents. A recognized challenge is to identify individuals at high risk of developing psychotic disorders prior to disease onset (42). To the extent that severe frequent psychotic experiences are indicators of risk for psychosis, these findings reveal their etiological architecture and can be used to guide molecular genetic and environmental risk factor investigations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the participants of TEDS for making this research possible. Special thanks to Andrew McMillan, Francesca Lewis, Louise Webster, Neil Harvey and Rachel Ogden, and to Peter McGuffin for help planning the study.

Funding/Support: Medical Research Council [G1100559 to A.R., G0901245; and previously G0500079 to R.P.]. DF is supported by a UK Medical Research Council Senior Clinical Fellowship [G0902308]. C.M.A.H. by the British Academy.

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Table 1

Twin Correlations with 95% confidence intervals

	MZM	DZM	MZF	DZF	DZOS
Cross-twin within trait correlations					
Paranoia	.47 (.41-.52)	.28 (.20-.34)	.55 (.51-.59)	.30 (.23-.35)	.24 (.19-.28)
Hallucinations	.37 (.30-.43)	.27 (.20-.34)	.48 (.43-.53)	.33 (.27-.39)	.23 (.18-.28)
Cognitive disorganisation	.40 (.34-.46)	.30 (.23-.37)	.50 (.45-.54)	.20 (.13-.26)	.24 (.19-.28)
Grandiosity	.48 (.42-.53)	.23 (.16-.30)	.49 (.45-.54)	.31 (.25-.37)	.24 (.19-.29)
Anhedonia	.47 (.41-.53)	.23 (.16-.30)	.49 (.44-.53)	.26 (.20-.32)	.19 (.14-.24)
Negative symptoms	.83 (.80-.85)	.53 (.47-.58)	.83 (.81-.85)	.59 (.55-.63)	.50 (.46-.54)
Cross-twin cross trait correlations					
Paranoia-hallucinations	.24 (.17-.31)	.13 (.05-.20)	.31 (.25-.36)	.19 (.17.25)	.15 (.10-.20)
Paranoia-cognitive disorganisation	.24 (.17-.31)	.17 (.09-.24)	.32 (.26-.37)	.18 (.11-.24)	.15 (.10-.20)
Hallucinations-cog disorganisation	.20 (.13-.27)	.25 (.17-.32)	.33 (.27-.38)	.22 (.16-.28)	.15 (.10-.20)
Cognitive disorganisation-negative symptoms	.23 (.16-.30)	.19 (.11-.26)	.22 (.16-.28)	.20 (.14-.26)	.15 (.10-.20)

Note: MZM=monozygotic males, DZM=Dizygotic males, MZF=monozygotic females, DZF=dizygotic females, DZOS=dizygotic opposite sex. Self-report data was available for 1400 MZ males, 1319 DZ males, 1995 MZ females, 1770 DZ females, 2998 DZ opposite-sex twin pairs. Parent-report data was available for 1410 MZ males, 1322 DZ males, 1994 MZ females, 1760 DZ females, 3024 DZ opposite-sex twin pairs

JAMA Psychiatry. Author manuscript; available in PMC 2015 March 01.

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Table 2

Full sample univariate parameter estimates for full ACE models (95% confidence intervals)

		N	A	C	E
Paranoia		9465	.50 (.41-.54)	.01 (.00-.09)	.49 (.46-.52)
Hallucinations	Male	4213	.15 (.00-.34)	.20 (.05-.34)	.64 (.58-.71)
	Female	5260	.32 (.18-.46)	.17 (.05-.29)	.51 (.47-.56)
Cognitive Disorganisation		9463	.43 (.33-.49)	.02 (.00-.10)	.55 (.51-.58)
Grandiosity		9467	.44 (.34-.51)	.04 (.00-.12)	.52 (.49-.55)
Anhedonia		9470	.47 (.41-.50)	.00 (.00-.05)	.53 (.50-.56)
Negative symptoms		9445	.59 (.54-.64)	.24 (.19-.29)	.17 (.16-.18)

Note. N = number of individuals; A = additive genetic influences; C = shared environmental infleucnes; E=non-shared environmental influences

Table 3

Extremes analysis

	Cut-off Level		
	>85%	**>90%**	**>95%**
Paranoia			
Co-twin means			
MZ	.48 (N=561)	.44 (N=367)	.42 (N=178)
DZ	.27 (N=495)	.22 (N=312)	.22 (N=156)
Proband Concordances			
MZ	.44	.32	.26
DZ	.30	.23	.18
Tetrachoric correlations			
MZ	.56 (.47-.63)	.47 (.36-.56)	.53 (.39-.65)
DZ	.34 (.24-.43)	.33 (.20-.47)	.38 (.21-.54)
DF Extremes			
hg^2	.42 (.24-.60)	.43 (.24-.61)	.41 (.20-.62)
cg^2	.05 (−.09-.20)	.01 (−.13-.16)	.01 (−.16-.18)
LT estimates			
h^2	.44 (.19-.63)	.27 (.00-.55)	.27 (.00-.63)
c^2	.12 (.00-.33)	.20 (.00-.45)	.25 (.00-.54)
e^2	.45 (.37-.53)	.53 (.44-.64)	.48 (.36-.62)
Hallucinations			
Co-twin means			
MZ	.45 (N=546)	.40 (N=383)	.38 (N=188)
DZ	.31 (N=493)	.27 (N=325)	.28 (N=167)
Proband Concordances			
MZ	.41	.32	.26
DZ	.33	.27	.20
Tetrachoric correlations			
MZ	.52 (.44-.60)	.47 (.36-.56)	.50 (.35-.62)
DZ	.39 (.29-.48)	.38 (.29-.49)	.41 (.25-.56)
DF Extremes			
hg^2	.21 (.07-.40)	.22 (.04-.39)	.19 (−.03-.40)
cg^2	.17 (−.25-.40)	.15 (−.21-.37)	.17 (−.24-.42)
LT estimates			
h^2	.27 (.02-.52)	.15 (.00-.45)	.15 (.00-.55)
c^2	.25 (.04-.46)	.32 (.06-.50)	.35 (.01-.55)
e^2	.48 (.40-.56)	.54 (.44-.64)	.51 (.38-.63)
Cognitive			
Disorganisation			
Co-Twin means			

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	Cut-off Level		
	>85%	**>90%**	**>95%**
MZ	.43 (N=681)	.34 (N=455)	.26 (N=258)
DZ	.33 (N=670)	.27 (N=431)	.18 (N=251)
Proband Concordances			
MZ	.43	.34	.23
DZ	.33	.27	.18
Tetrachoric correlations			
MZ	.46 (.39-.54)	.44 (.34-.53)	.37 (.24-.50)
DZ	.24 (.14-.33)	.30 (.19-.41)	.26 (.12-.41)
DF Extremes			
hg^2	.33 (.18-.49)	.30 (.13-.46)	.33 (.14-.52)
cg^2	.10 (−.02-.22)	.13 (−.00-.26)	.06 (−.10-.21)
LT estimates			
h^2	.45 (.23-.54)	.29 (.01-.53)	.22 (.00-.51)
c^2	.00 (.00-.20)	.15 (.00-.38)	.16 (.00-.40)
e^2	.53 (.46-.55)	.55 (.47-.65)	.62 (.50-.76)
Grandiosity			
Co-twin means			
MZ	.50 (N=571)	.49 (N=346)	.48 (N=214)
DZ	.25 (N=483)	.26 (N=377)	.27 (N=182)
Proband Concordances			
MZ	.48	.39	.32
DZ	.29	.25	.18
Tetrachoric correlations			
MZ	.62 (.55-.69)	.60 (.51-.68)	.57 (.45-.67)
DZ	.30 (.20-.42)	.32 (.21-.43)	.34 (.18-.49)
DF Extremes			
hg^2	.51 (.33-.68)	.46 (.28-.65)	.41 (.21-.61)
cg^2	−.01 (−.15-.13)	.07 (−.11-.17)	.08 (−.10-.22)
LT estimates			
h^2	.62 (.37-.68)	.58 (.29-.68)	.44 (.05-.67)
c^2	.00 (.00-.21)	.02 (.00-.25)	.13 (.00-.45)
e^2	.38 (.32-.46)	.40 (.32-.49)	.44 (.33-.56
Anhedonia			
Co-twin means			
MZ	.50 (N=514)	.49 (N=295)	.46 (N=202)
DZ	.29 (N=546)	.29 (N=277)	.30 (N=192)
Proband Concordances			
MZ	.42	.49	.27
DZ	.32	.26	.18

	Cut-off Level		
	>85%	**>90%**	**>95%**
Tetrachoric correlations			
MZ	.54 (.45-.61)	.51 (.40-.61)	.48 (.34-.60)
DZ	.29 (.16-.42)	.29 (.16-.42)	.28 (.11-.44)
DF Extremes			
hg^2	.41 (.24-.57)	.36 (.17-.55)	.32 (.11-.54)
cg^2	.09 (−.04-.23)	.11 (.00-.26)	.13 (−.04-.30)
LT estimates			
h^2	.51 (.25-.62)	.42 (.08-.61)	.41 (.00-.60)
c^2	.04 (.00-.25)	.08 (.00-.61)	.07 (.00-.42)
e^2	.46 (.38-.54)	.49 (.39-.61)	.52 (.40-.66)
Negative symptoms			
Co-twin means			
MZ	.80 (N=578)	.81 (N=433)	.77 (N=199)
DZ	.50 (N=525)	.44 (N=327)	.41 (N=175)
Proband Concordances			
MZ	.73	.73	.61
DZ	.51	.39	.30
Tetrachoric correlations			
MZ	.91 (.88-.94)	.91 (.88-.94)	.86 (.80-.91)
DZ	.60 (.51-.69)	.60 (.51-.69)	.57 (.44-.69)
DF Extremes			
hg^2	.62 (.43-.81)	.74 (.55-.94)	.71 (.49-.93)
cg^2	.19 (.03-.35)	.07 (−.09-.23)	.06 (−.12-.23)
LT estimates			
h^2	.44 (.30-.60)	.59 (.41-.79)	.58 (.33-.87)
c^2	.45 (.31-.58)	.32 (.13-.49)	.28 (.01-.51)
e^2	.11 (.08-.14)	.09 (.06-.12)	.14 (.09-.20)

Note. MZ=monozygotic, DZ=dizygotic, DF=DeFries-Faulker, hg^2=group heritability, cg^2=group shared environmental influences, LT=Liability threshold, h^2=heritability estimate, c^2=shared environmental estimate, e^2=non-shared environmental estimate

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Table 4

Cherny results: tests of linear changes in heritability across the distribution

	N	h^2	c^2	h^2 linear	c^2 linear
Paranoia	3214	.52 (.35/.69)**	.05 (−.04/.19)	−.06 (−.14/.02)	.00 (−.06/.07)
Hallucinations	3224	.15 (−.05/.36)	.27 (.11/.44)**	.06 (−.01/.13)	−.06 (−.13/.00)
Cognitive disorganisation	3216	.45 (.31/.58)**	.05 (−.06/.16)	−.07 (−.19/.05)	.02 (−.12/.23)
Grandiosity	3218	.49 (.33/.66)**	.05 (−.08/.19)	−.02 (−.11/.07)	.00 (−.07/.07)
Anhedonia	3218	.43 (.29/.56)**	.07 (−.03/18)	−.05 (−.14/.05)	.02 (−.05/.09)
Negative symptoms	3237	.38 (.21/.53)**	.49 (.36/.61)**	.09 (.04/.14)**	−.13 (−.17/-.09)**

* Note:<.05,

** p<01.

Significant h2 and c2 indicate significant genetic and shared environmental influences respectively. Significant linear effects suggest that genetic (h2 linear) or shared environmental (c2 linear) influence significantly increase/decrease at the extremes. Quadratic effects were tested but were not significant, results available from first author on request. N = Number of twin pairs.

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Table 5

Bivariate parameter estimates for best fitting models

						Proportion of rPh due to:		
	N	**rPh**	**rA**	**rC**	**rE**	**A**	**C**	**E**
Para-hall	9468	.47 (.46-.49)	.61 (.57-.65)	-	.33 (.30-.37)	.64 (.59-.69)	-	.36 (.31-.41)
Para-cog disorg	9463	.42 (.41-.43)	.62 (.57-.66)	-	.24 (.20-.27)	.71 (.66-.76)	-	.29 (.24-.34)
Hall-cog disorg	9468	.44 (.43-46)	.63 (.59-.68)	-	.28 (.24-.31)	.66 (.61-.71)	-	.34 (.29-.39)
Cog disorg-neg symp	9453	.25 (.23-.28)	.27 (.19-.36)	1.00 (.57-1.00)	.10 (.05-.15)	.54 (.35-.73)	.34 (.18-.50)	.12 (.07-.18)

Note. rPh=phenotypic correlation; rA=genetic correlation; rC=shared environmental correlaion; rE=non-shared environmental correlation. 95% confidence intervals in parentheses. N = number of individuals.