Evidence That the Impact of Childhood Trauma on IQ Is Substantial in Controls, Moderate in Siblings, and Absent in Patients With Psychotic Disorder

Jim van Os[*,1,2,5], **Anne Marsman**[1,5], **Daniela van Dam**[3,5], **and Claudia J. P. Simons**[1,4]; **GROUP Investigators**[†]

[1]Department of Psychiatry and Psychology, Maastricht University Medical Centre, PO BOX 616, 6200 MD Maastricht, the Netherlands; [2]Department of Psychosis Studies, Institute of Psychiatry, King's College London, King's Health Partners, London, UK; [3]Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; [4]GGzE, Institute for Mental Health Care Eindhoven and De Kempen, Eindhoven, The Netherlands

[5]These authors contributed equally to the article.

*To whom correspondence should be addressed; tel: +31-43-3875443, fax: +31-43-3875444, e-mail: j.vanos@maastrichtuniversity.nl

[†]The members of the GROUP investigators and their affiliations have been mentioned in Acknowledgments section.

Research suggests that childhood trauma is associated with cognitive alterations, but it is not known whether the cognitive alterations observed in patients with psychotic disorder, and their relatives, is trauma-related. Patients with a schizophrenia-spectrum diagnosis ($n = 1119$), siblings of patients ($n = 1059$) and healthy comparison subjects (HCS; $n = 586$) were interviewed 3 times over a period of 6 years. Repeated measures of IQ were analyzed as a function of childhood trauma and group, controlling for confounders. There were significant differences in the impact of childhood trauma on IQ across the 3 groups. Exposure in HCS was associated with a nearly 5-point reduction in IQ (-4.85; 95% confidence interval [CI]: -7.98 to -1.73, $P = .002$), a lesser reduction in siblings (-2.58; 95% CI: -4.69 to -0.46, $P = .017$) and no significant reduction in patients (-0.84; 95% CI: -2.78 to 1.10, $P = .398$). One-fourth of the sibling-control difference in IQ was reducible to childhood trauma, whereas for patients this was only 5%. Over the 6-year follow-up, those with trauma exposure showed significantly less learning effects with repeated cognitive assessments ($b = 1.36$, 95% CI: 0.80–1.92, $P < .001$) than the nonexposed ($b = 2.31$, 95% CI: 1.92–2.71, $P < .001$; P interaction = .001). Although childhood trauma impacts cognitive ability and learning in non-ill people at low and high genetic risk, its effect on the observed cognitive alterations in psychotic disorder may be minor. Twin and family studies on cognitive alterations in psychotic disorder need to take into account the differential impact of trauma on cognition across ill and non-ill, at risk groups.

Keywords: psychosis/trauma/cognition/genetics

Introduction

Childhood abuse and neglect has been found to impact many aspects of (social) cognition[1–8]; impairments that have been suggested to persist into adulthood.[9–11]

Both a history of childhood trauma and cognitive impairments are highly prevalent in patients with psychotic disorders.[12,13] Cognitive alterations are highly relevant clinically, impacting on community functioning, which may be mediated particularly by alterations in social cognition.[14] Although it has been suggested that childhood trauma may contribute to the neurocognitive impairments observed in patients with nonaffective psychotic disorders, findings have been inconsistent across cognitive domains, diagnostic, demographic, and genotype subgroups, and relatively small samples.[15–21] Sideli et al[22] reported an association between trauma and cognition in the controls, but not in patients, suggestive of a floor effect in patients, whose cognition already is substantially lower compared to controls. No studies to date had access to measures of cognition over time, in order to study not only any association between childhood trauma and cross-sectional measures of cognition, but also between childhood trauma and change of cognition over time.

In the current study, we attempted to study the link between childhood trauma and cognition taking into account the following issues: (1) adequate sample size to study main effects and test for moderation by group; (2) focus on schizophrenia spectrum diagnosis; (3) inclusion of endophenotypic measures of cognition in siblings of patients, in order to tease apart effects of aetiological and disease-related factors; and (4) repeated measures of the cognitive outcome over time.

We hypothesized (1) a main effect of childhood trauma on cross-sectional cognitive outcome, conform the findings by Sideli et al.,[22] and (2) moderation by group (healthy comparison subjects [HCS], patients, siblings of patients). In addition, we hypothesized that those with exposure to childhood trauma would show less prominent learning effects with repeated cognitive assessments over time. Given evidence that (1) most of the overall effect of a schizophrenia diagnosis on cognitive performance is mediated through a single common factor, indicating that a generalized cognitive deficit is a core underlying feature,[23] and (2) the effect of trauma on cognitive function is driven by deficits in general cognitive functioning[17] the analyses focused on IQ as a summary measure of cognitive performance.

Methods

GROUP Study

Full details of the GROUP study have been presented elsewhere.[24,25] In representative geographical areas in the Netherlands and Belgium, patients were identified through clinicians working in regional psychotic disorder services, whose caseload was screened for inclusion criteria. Subsequently, a group of patients presenting at these services either as out-patients or in-patients were recruited for the study. HCSs were selected through random mailings to addresses in the catchment areas of the cases. The GROUP study was not conducted in a geographically well-defined small area, as it in fact included the majority of mental health services in the Netherlands, and a substantial part of mental health services in Dutch-speaking Belgium. HCSs could not be representative in all aspects, as an exclusion criterion was absence of a family history of psychotic disorder. The goal was to collect a group of HCSs that (1) was collected from the same geographical area as the case in the relevant mental health service, (2) was sufficiently large to allow for chance variation, (3) was frequency-matched in age- and sex distribution to the siblings, and (4) had absence of family history of psychotic disorder.

Sample. The full GROUP sample at baseline consisted of 1119 patients with nonaffective psychotic disorder, 1059 siblings of these patients, 920 parents of the patients, and 586 unrelated HCSs. Inclusion criteria were: (1) age range 16–50 years and (2) good command of Dutch language. For patients, an additional inclusion criterion was the presence of a clinical diagnosis of nonaffective psychotic disorder. HCSs status was confirmed by using the Family Interview for Genetic studies[26] with the HCS as informant, to establish absence of first degree relatives with a psychotic disorder. Diagnosis was based on the Diagnostic and Statistical Manual of Mental Disorder-IV (DSM-IV) criteria,[27] assessed with the Comprehensive Assessment of Symptoms and History (CASH) interview[28] or Schedules for Clinical Assessment for Neuropsychiatry (SCAN 2.1).[29] The majority of patients had a DSM-IV diagnosis of schizophrenia (DSM-IV 295.x; *n* = 940, 84%). In the sibling and HCS groups, there were respectively, 154 (14%) and 59 (10%) participants with a history of a common mental disorder at baseline, the majority of whom had a mood disorder (DSM-IV 296.x).

The study was approved by the standing ethics committee, and all the subjects gave written informed consent in accordance with the committee's guidelines.

Follow-up. Patients, HCSs, and siblings were eligible for follow-up. Of the 586 HCSs and 1059 siblings at baseline, 78% (*n* = 1275) were assessed at 3-year follow-up (HCSs: 79%, *n* = 460; siblings: 77%, *n* = 815) and 67% (*n* = 1104) at 6-year follow-up (HCSs: 67%, *n* = 394; siblings: 67%, *n* = 710). Of the 1119 patients at baseline, 811 (73%) participated at 3-year follow-up and 662 (59%) at 6-year follow-up. Ratings of CASH, SCAN, and Community Assessment of Psychic Experiences (CAPE)[30] at follow-up reflected the period between baseline and first follow-up, and between first and second follow-up, respectively. Mean time to first follow-up was 3.3 years (SD = 0.4) and mean between first and second follow-up was 3.1 years (SD = 0.4).

Measures

CAPE. The Community Assessment of Psychic Experiences (CAPE; www.cape42.homestead.com) was developed in order to rate self-reports of lifetime psychotic experiences.[30] Items are modelled on patient experiences as contained in the PSE-9,[31] schedules assessing negative symptoms such as the Scale for the Assessment of Negative Symptoms (SANS)[32] and the Subjective Experience of Negative Symptoms (SENS),[33] and scales assessing depressive symptoms such as the Calgary Depression Scale.[34] Items are scored on a 4-point scale. In the current analyses, CAPE dimensions of frequency of positive experiences (20 items), negative experiences (14 items) and depressive experiences (8 items) were included (measured at baseline and 3-year follow-up), representing the person's perceived psychosis load over the lifetime (at baseline) or in the past 3 years (follow-up). A total score representing the mean of all items was calculated for each dimension.

IQ. At baseline and 3-year follow-up, IQ was estimated based on the 4-subtest version (Information, Block Design, Digit Symbol Coding and Arithmetic)[35] of the Wechsler Adult Intelligence Scale (WAIS-III).[36] At 6-year follow-up, IQ was estimated based on a short version of the WAIS-III short form: the Digit Symbol Coding subtest, uneven items of the Arithmetic subtest, uneven items of the Block Design subtest, every third item of the Information subtest.[37] Change in IQ over the follow-up period (hereafter: delta IQ) was defined as change in

IQ from baseline (T0) to T2 at 6 years or, in case T2 was missing, to T1 at 3 years.

Cannabis Use. Substance use was assessed repeatedly at baseline, 3-year follow-up (use over interval baseline and 3-year follow-up) and 6-year follow-up (use over interval 3- and 6-year follow-up), using the Composite International Diagnostic Interview (CIDI).[38] CIDI cannabis pattern of use during the lifetime period of heaviest use (hereafter: *cannabis frequency use*) was used in the analyses as the exposure variable, in agreement with previous work in this sample, and was scored as: none (0), less than weekly (1), weekly (2), and daily (3),[39,40] dichotomised in the analyses as "no use" (0) vs "any use" (1).

Childhood Trauma. Childhood trauma was assessed with the Dutch version of the Childhood Trauma Questionnaire (CTQ) 25-item Short Form,[41] with items rated on a 5-point Likert scale (1 = never true to 5 = very often true). Emotional, physical, and general abuse, and emotional and physical neglect were assessed, 5 items covering each trauma type.[41] The total trauma score represents the mean score of all 25 items. Childhood trauma was analyzed both as a continuous variable and as a dichotomous variable, around a cut-off representing the control group 80th percentile, conform previous analyses in this sample.[42]

Statistical Analyses

GROUP database version 5.0 was used for all analyses. In order to examine cross-sectional associations between childhood trauma and IQ, and differences herein as a function of group (controls, siblings, patients), random intercept multilevel regression models (given clustering of individuals within families as well as clustering of repeated measures within subjects) with IQ as dependent variable were fitted using the MIXED routine in the Stata program, version 14.[43] Independent variables were CTQ score, group and the interaction between CTQ and group. Analyses were corrected a priori for age, sex, ethnic group (white European vs other), educational level (continuous variable ranging from 0 [no education], 3–5 [school diploma] to 8 [university degree]), CAPE total score and binary cannabis use (hereafter: fully adjusted model).

In order to examine associations between childhood trauma and change in IQ, and differences in this association across group, random intercept multilevel regression models with IQ as dependent variable were fitted with CTQ, time (baseline, 3- and 6-year follow-up), group and the CTQ × time × group interaction. Analyses were corrected a priori for age, sex, ethnic group, educational level, CAPE total score, and binary cannabis use (hereafter: fully adjusted model).

Interactions between childhood trauma and group were fitted in the models of IQ and delta IQ, yielding 2 interaction terms (1 for siblings and 1 for patients); in the case of significant interaction, stratified values for HCSs, siblings, and patients were calculated from the model containing the interaction using the Stata MARGINS routine. Marginal effects and post-estimation contrasts were similarly calculated with the Stata MARGINS routine.

Associations are expressed as regression coefficients (b; change in *y* with one unit increase in *x*) from the multi-level random regression model.

Results

Sample Characteristics

Sample characteristics are displayed in table 1. The 3 groups were comparable in age, patients more often were of male sex. As reported before, siblings had values that were intermediate to HCSs and patients with regard to childhood trauma,[44] cannabis use,[45] and IQ.[46] All groups displayed increases in IQ over the 6-year follow-up.

Childhood Trauma and IQ

Table 2 displays IQ values at the 3 time points as a function of binary trauma exposure. Plotting IQ and continuous childhood trauma in the 3 groups suggested a negative association in HCSs, a weaker negative association in siblings and no associations in patients (figure 1). This was confirmed in the multilevel random regression analyses, which revealed a significant interaction between continuous childhood trauma and group in the model of IQ (unadjusted: siblings $P = .027$, patients $P < .001$; adjusted for age, sex, education and ethnic group: siblings $P = .007$, patients $P < .001$; adjusted for age, sex, education, ethnic group, CAPE total score and cannabis use: siblings $P = .005$, patients $P < .001$). The association between IQ and childhood trauma, stratified by group, calculated from the fully adjusted model was −8.09 (95% CI: −11.50 to −4.68, $P < .001$; HCSs) −2.27 (−4.57 to 0.02, $P = .052$; siblings) and −0.18 (−2.17 to 1.82, $P = .863$; patients). Using the binary trauma variable in the fully adjusted model, stratified effect sizes for trauma exposure across the 3 groups were: −4.85 for HCSs (95% CI: −7.98 to −1.73, $P < .001$); −2.58 for siblings (95% CI: −4.69 to −0.46, $P = .017$) and −0.84 for patients (95% CI: −2.78 to 1.10, $P = .398$).

In the fully adjusted model, the association between group and IQ, before entering continuous childhood trauma in the model, was −3.07 for siblings (95% CI: −4.57 to −1.57) and −9.66 for patients (95% CI: −11.24 to −8.07); after adding continuous childhood trauma to the model, this became −2.33 for siblings (95% CI: −3.97 to −0.69) and −9.15 for patients (95% CI: −10.93 to −7.38). Thus, in siblings, 24% of the sibling-HCS difference in IQ was thus reducible to childhood trauma, whereas for patients this was 5%.

Table 1. Sample Demographics and Measures of Childhood Trauma and IQ at Baseline (With the Exception of Delta IQ)

		Age	Education[a]	CTQ (Continuous)	Urbanicity Birth[b]	IQ	Delta IQ[c]	% CTQ Binary Exposure[d]	% Cannabis Use[e]	% Female	% Ethnic Minority
HCS	Mean	30.42	2.92	1.34	2.64	109.82	4.32	0.19	0.28	0.54	0.10
	SD	10.58	1.28	0.36	1.69	15.00	10.08				
	N	584	583	492	549	573	428	492	579	586	586
Sibling	Mean	27.83	2.56	1.41	2.66	102.87	6.44	0.25	0.38	0.54	0.17
	SD	8.27	1.47	0.41	1.67	15.49	9.52				
	N	1059	1039	816	969	1012	761	816	1047	1059	1059
Patient	Mean	27.57	1.95	1.61	2.76	96.08	3.72	0.44	0.63	0.24	0.23
	SD	7.95	1.36	0.50	1.68	15.32	10.20				
	N	1107	1086	755	981	1006	708	755	1094	1059	1119
Total	Mean	28.28	2.40	1.47	2.70	101.77	4.95	0.31	0.46	0.42	0.18
	SD	8.76	1.44	0.45	1.68	16.18	9.98				
	N	2750	2708	2063	2499	2591	1897	2063	2720	2764	2764

CTQ, childhood trauma questionnaire; HCS, healthy comparison subjects.
[a]Education (Verhage): range 0 (no education), 3–5 (school diploma), and 8 (university degree).
[b]Urbanicity: 1 ≤ 500/km²; 2 = 500–1000/km²; 3 = 1000–1500/km²; 4 = 1500–2500/km²; 5 = 2500+/km².
[c]Defined as change from baseline (T0) to T2 at 6 years or, in case T2 was missing, to T1 at 3 years.
[d]Exposure defined as CTQ value > 80th percentile of control CTQ value.
[e]Defined as CIDI cannabis pattern of use during the lifetime period of heaviest use, dichotomised as "no use" (0) vs "any use" (1).

Table 2. IQ as a Function of Trauma Exposure at Baseline, 3-Year and 6-Year Follow-up

		Baseline	3-Year Follow-up	6-Year Follow-up	Total
No trauma exposure[a]					
Healthy comparison subject	Mean	111.20	113.10	116.76	113.42
	SD	14.87	15.89	16.89	15.95
	N	395	222	284	901
Sibling	Mean	105.44	109.17	113.92	109.14
	SD	15.53	17.03	17.51	16.96
	N	591	425	455	1,471
Patient	Mean	97.47	99.76	102.96	99.84
	SD	15.00	16.26	17.34	16.27
	N	393	295	305	993
Total	Mean	104.82	107.15	111.49	107.54
	SD	16.06	17.32	18.17	17.31
	N	1,379	942	1,044	3,365
Trauma exposure[a]					
Healthy comparison subject	Mean	105.52	105.30	106.85	105.88
	SD	14.16	16.49	16.62	15.50
	N	90	53	65	208
Sibling	Mean	100.61	102.84	107.22	103.26
	SD	14.63	14.14	17.46	15.67
	N	197	120	144	461
Patient	Mean	96.84	97.96	99.98	98.06
	SD	15.90	16.54	16.42	16.26
	N	305	206	205	716
Total	Mean	99.42	100.53	103.58	100.96
	SD	15.52	16.04	17.15	16.25
	N	592	379	414	1,385

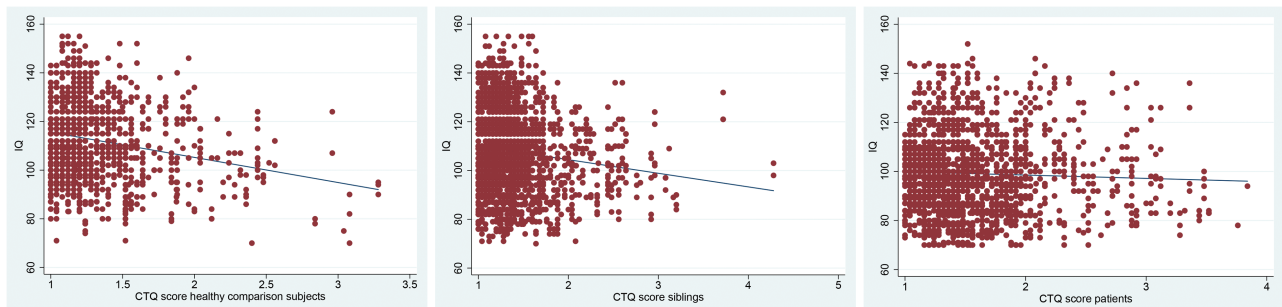[a]Defined dichotomously as CTQ value > 80th percentile of control CTQ value.

Fig. 1. Scatterplots with linear regression line of childhood trauma questionnaire (CTQ) score one the one hand, and IQ on the other in healthy comparison subjects, siblings, and patients.

Childhood Trauma and Delta IQ

Table 3 shows delta IQ for the 3 groups as a function of binary childhood trauma exposure. The results of the fully adjusted model with the 3-way interaction between time, binary childhood trauma and group revealed a marginal effect of time (linear effect $b = 2.03$, 95% CI: 1.67–2.39, $P < .001$) which differed as a function of binary childhood trauma (P interaction = .0013), exposed individuals showing less of an increase in IQ over time ($b = 1.36$, 95% CI: 0.80–1.92, $P < .001$) than the nonexposed ($b = 2.31$, 95% CI: 1.92–2.71, $P < .001$). The 3-way interaction between time, childhood trauma and group was not significant (siblings: $P = .393$; patients: $P = .820$), indicating that the moderating effect of childhood trauma on the

effect of time on IQ did not differ between HCSs, siblings, and patients.

Discussion

We found that childhood trauma impacted IQ in groups whose cognitive ability was not already compromised (HCSs) or only partially compromised (siblings of patients). Around a fourth of the sibling-HCS difference was attributable to childhood trauma, compared to only 5% of the case-healthy comparison difference. In addition, childhood trauma impacted on the course of IQ over time, in the sense of showing less learning effects of repeated cognitive assessments over time, regardless of group. The results suggest that childhood trauma impacts

Table 3. Change in IQ (Positive Value Indicates Increase Over Time), Defined as Change From Baseline (T0) to T2 at 6 Years or, in Case T2 was Missing, to T1 at 3 Years, as a Function of Group and Trauma Exposure

	Mean Delta IQ	SD	N
No trauma exposure			
Healthy comparison subject	4.76	10.33	335
Sibling	6.86	9.51	514
Patient	4.34	10.19	344
Total	5.54	10.00	1,193
Trauma exposure			
Healthy comparison subject	2.59	9.00	69
Sibling	5.09	9.71	161
Patient	2.33	9.51	245
Total	3.31	9.57	475

cognitive abilities and impedes learning; however, its impact on the observed cognitive alterations in psychotic disorder may be relatively small given smaller impact of childhood trauma on cognitive ability with progressively greater genetic risk for psychotic disorder.

Previous work indicates that the cognitive alterations observed in psychotic disorder are attributable to genetic liability underlying psychotic outcomes.[47] However, the findings suggest that the observation of familial clustering of cognitive alterations in patients with psychotic disorder and their siblings is confounded by the fact that the source of these alterations is different across groups. In siblings, 24% of the alterations of cognition respective to the healthy comparison group was reducible to childhood trauma, whereas in patients this was only 5%. This suggests that sibling and twin studies on cognition of schizophrenia focusing on genetic factors need to take into account the influence of childhood trauma for accurate results.

Given the large sample size, diagnostic homogeneity, adjustment for confounders, and the availability of repeated cognitive assessments over time, it is unlikely that the findings are due to chance or confounding. Several previous studies reported absence of association between childhood trauma main effects and cognitive outcomes in patients[16,19,21,22] and there is a body of work showing association between childhood trauma and cognitive outcome in non-ill groups.[1–11] Sideli et al.[22] reported findings that resembled the current report, in that an association between childhood trauma and cognitive outcomes was found in the control, but not the patient group. One likely explanation for the absence of an association between trauma and cognition in the patient group is a floor effect—ie, the impact of trauma is "trumped" by other sources that impact on cognitive alterations, eg, genetic effects,[47] the effects of current adversity,[48] or altered motivation to engage in neuropsychological testing.[49] Although childhood trauma did not show main effects, it can still interact with any of these factors to impact cognition; future work is required to investigate this

issue. The fact that childhood trauma impacted learning, regardless of group, does suggest that childhood trauma is not cognition-neutral in the patient group.

There is evidence that, contrary to the current findings on IQ—considered an indicator of altered neurodevelopment in psychotic disorder[50]—that psychopathology, particularly psychotic symptoms, is associated with childhood trauma in both patients and individuals in the general population.[12,51] Taken together, the results suggest that different aetiological influences may impact different psychopathological and neurodevelopmental domains in psychotic disorder. The focus of treatment related to exposure to childhood trauma may be more in the realm of treating the psychological effects of trauma rather than cognitive remediation of trauma-related cognitive alterations.[52–54]

Childhood trauma was associated with a decrease in the learning effect associated with repeated cognitive assessments. This impact did not differ between the different groups, including the patient group, suggesting that exposure to childhood trauma may have clinical relevance by moderating learning outcomes in patients with psychotic disorder. Although the effect was small, it may nevertheless be relevant in settings of rehabilitation and the application of cognitive remediation therapy.

Methodological Issues

Although the IQ assessment at second follow-up differed slightly, this cannot have impacted differential impact of childhood trauma across groups. Illness duration may be a factor in the patient group, potentially obscuring associations with childhood trauma. However, when modelling IQ in the patient group as a function of childhood trauma and the interaction with illness duration (years between baseline assessment and onset of first psychotic symptom), no interaction was present ($P = .110$), suggesting illness duration is not relevant for the association between IQ and childhood trauma. This finding is in agreement with the literature showing cognitive alterations in psychotic disorder are stable and not progressive.[55]

Funding

Acknowledgments

Genetic Risk and Outcome of Psychosis (GROUP) Investigators

GROUP investigators are: Berhooz Z. Alizadeh[a], Agna A. Bartels-Velthuis[a], Nico J. van Beveren[b,c,d], Richard Bruggeman[a], Wiepke Cahn[e], Lieuwe de Haan[f], Philippe Delespaul[g], Carin J. Meijer[f], Inez Myin-Germeys[h], Rene S. Kahn[e], Frederike Schirmbeck[f], Claudia J.P. Simons[g,i], Neeltje E. van Haren[e], Jim van Os[g,j], Ruud van Winkel[g,h]

[a]University of Groningen, University Medical Center Groningen, University Center for Psychiatry, Groningen, The Netherlands; Antes Center for Mental Health Care, Rotterdam, The Netherlands; [c]Erasmus MC, Department of Psychiatry, Rotterdam, The Netherlands; [d]Erasmus MC, Department of Neuroscience, Rotterdam, The Netherlands; [e]Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands; [f]Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; [g]Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University Medical Center, Maastricht, The Netherlands; [h]KU Leuven, Department of Neuroscience, Research Group Psychiatry, Center for Contextual Psychiatry, Leuven, Belgium; [i]GGzE, Institute for Mental Health Care Eindhoven and De Kempen, Eindhoven, The Netherlands; [j]Department of Psychosis Studies, Institute of Psychiatry, King's College London, King's Health Partners, London, United Kingdom

References

1. Cicchetti D, Rogosch FA, Maughan A, Toth SL, Bruce J. False belief understanding in maltreated children. *Dev Psychopathol*. 2003;15:1067–1091.
2. Pears KC, Fisher PA. Emotion understanding and theory of mind among maltreated children in foster care: evidence of deficits. *Dev Psychopathol*. 2005;17:47–65.
3. Colvert E, Rutter M, Kreppner J, et al. Do theory of mind and executive function deficits underlie the adverse outcomes associated with profound early deprivation? Findings from the English and Romanian adoptees study. *J Abnorm Child Psychol*. 2008;36:1057–1068.
4. Fonagy P, Gergely G, Target M. The parent-infant dyad and the construction of the subjective self. *J Child Psychol Psychiatry*. 2007;48:288–328.
5. Hoffman-Plotkin D, Twentyman CT. A multimodal assessment of behavioral and cognitive deficits in abused and neglected preschoolers. *Child Dev*. 1984;55:794–802.
6. Perna RB, Kiefner M. Long-term cognitive sequelae: abused children without PTSD. *Appl Neuropsychol Child*. 2013;2:1–5.
7. Bucker J, Kapczinski F, Post R, Cereser KM, Szobot C, Yatham LN, Kapczinski NS, Kauer-Sant'Anna M. Cognitive impairment in school-aged children with early trauma. *Compr Psychiatry*. 2012;53:758–764.
8. De Bellis MD, Hooper SR, Woolley DP, Shenk CE. Demographic, maltreatment, and neurobiological correlates of PTSD symptoms in children and adolescents. *J Pediatr Psychol*. 2010;35:570–577.
9. Majer M, Nater UM, Lin JM, Capuron L, Reeves WC. Association of childhood trauma with cognitive function in healthy adults: a pilot study. *BMC Neurol*. 2010;10:61.
10. Gould F, Clarke J, Heim C, Harvey PD, Majer M, Nemeroff CB. The effects of child abuse and neglect on cognitive functioning in adulthood. *J Psychiatr Res*. 2012;46:500–506.
11. Philip NS, Sweet LH, Tyrka AR, et al. Exposure to childhood trauma is associated with altered n-back activation and performance in healthy adults: implications for a commonly used working memory task. *Brain Imaging Behav*. 2016;10:124–135.
12. Varese F, Smeets F, Drukker M, et al. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophr Bull*. 2012;38:661–671.
13. Bora E, Yucel M, Pantelis C. Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study. *Br J Psychiatry*. 2009;195:475–482.
14. Fett AK, Viechtbauer W, Dominguez MD, Penn DL, van Os J, Krabbendam L. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neurosci Biobehav Rev*. 2011;35:573–588.
15. Lysaker PH, Meyer P, Evans JD, Marks KA. Neurocognitive and symptom correlates of self-reported childhood sexual abuse in schizophrenia spectrum disorders. *Ann Clin Psychiatry*. 2001;13:89–92.
16. Aas M, Dazzan P, Fisher HL, et al. Childhood trauma and cognitive function in first-episode affective and non-affective psychosis. *Schizophr Res*. 2011;129:12–19.
17. Aas M, Steen NE, Agartz I, et al. Is cognitive impairment following early life stress in severe mental disorders based on specific or general cognitive functioning? *Psychiatry Res*. 2012;198:495–500.

18. Shannon C, Douse K, McCusker C, Feeney L, Barrett S, Mulholland C. The association between childhood trauma and memory functioning in schizophrenia. *Schizophr Bull*. 2011;37:531–537.

19. McCabe KL, Maloney EA, Stain HJ, Loughland CM, Carr VJ. Relationship between childhood adversity and clinical and cognitive features in schizophrenia. *J Psychiatr Res*. 2012;46:600–607.

20. Schenkel LS, Spaulding WD, DiLillo D, Silverstein SM. Histories of childhood maltreatment in schizophrenia: relationships with premorbid functioning, symptomatology, and cognitive deficits. *Schizophr Res*. 2005;76:273–286.

21. Green MJ, Chia TY, Cairns MJ, et al., Australian Schizophrenia Research B. Catechol-O-methyltransferase (COMT) genotype moderates the effects of childhood trauma on cognition and symptoms in schizophrenia. *J Psychiatr Res*. 2014;49:43–50.

22. Sideli L, Fisher HL, Russo M, et al. Failure to find association between childhood abuse and cognition in first-episode psychosis patients. *Eur Psychiatry*. 2014;29:32–35.

23. Dickinson D, Iannone VN, Wilk CM, Gold JM. General and specific cognitive deficits in schizophrenia. *Biol Psychiatry*. 2004;55:826–833.

24. Korver N, Quee PJ, Boos HB, Simons CJ, de Haan L. Genetic Risk and Outcome of Psychosis (GROUP), a multi site longitudinal cohort study focused on gene-environment interaction: objectives, sample characteristics, recruitment and assessment methods. *Int J Methods Psychiatr Res*. 2012;21:205–221.

25. G.R.O.U.P. Evidence that familial liability for psychosis is expressed as differential sensitivity to cannabis: an analysis of patient-sibling and sibling-control pairs. *Arch Gen Psychiatry*. 2011;68:138–147.

26. NIMH Genetics Initiative. *Family Interview for Genetic Studies (FIGS)*. Rockville, MD: National Institute of Mental Health; 1992.

27. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed., text rev. ed. Washington, DC: APA; 2000.

28. Andreasen NC, Flaum M, Arndt S. The Comprehensive Assessment of Symptoms and History (CASH). An instrument for assessing diagnosis and psychopathology. *Arch Gen Psychiatry*. 1992;49:615–623.

29. Wing JK, Babor T, Brugha T, et al. SCAN. Schedules for Clinical Assessment in Neuropsychiatry. *Arch Gen Psychiatry*. 1990;47:589–593.

30. Konings M, Bak M, Hanssen M, van Os J, Krabbendam L. Validity and reliability of the CAPE: a self-report instrument for the measurement of psychotic experiences in the general population. *Acta Psychiatr Scand*. 2006;114:55–61.

31. Wing JK, Cooper JE, Sartorius N. *The Measurement and Classification of Psychiatric Symptoms*. London: Cambridge University Press; 1974.

32. Andreasen NC. Negative symptoms in schizophrenia. Definition and reliability. *Arch Gen Psychiatry*. 1982;39:784–788.

33. Selten JP, Sijben NE, van den Bosch RJ, Omloo Visser J, Warmerdam H. The subjective experience of negative symptoms: a self-rating scale. *Compr Psychiatry*. 1993;34:192–197.

34. Addington D, Addington J, Maticka-Tyndale E. Assessing depression in schizophrenia: the Calgary Depression Scale. *Br J Psychiatry Suppl*. 1993;22:39–44.

35. Blyler CR, Gold JM, Iannone VN, Buchanan RW. Short form of the WAIS-III for use with patients with schizophrenia. *Schizophr Res*. 2000;46:209–215.

36. Wechsler D. *WAIS-III: Wechsler Adult Intelligence Scale (3rd ed.) Administration and Scoring Manual*. San Antonio, TX: Psychological Corporation; 1997.

37. Velthorst E, Levine SZ, Henquet C, de Haan L, van Os J, Myin-Germeys I, Reichenberg A. To cut a short test even shorter: reliability and validity of a brief assessment of intellectual ability in schizophrenia—a control-case family study. *Cogn Neuropsychiatry*. 2013;18:574–593.

38. World Health Organisation. *Composite International Diagnostic Interview (CIDI) Version 1.0*. Geneva, Switzerland: World Health Organisation; 1990.

39. van Winkel R, Genetic Risk and Outcome of Psychosis (GROUP) Investigators. Family-based analysis of genetic variation underlying psychosis-inducing effects of cannabis: sibling analysis and proband follow-up. *Arch Gen Psychiatry*. 2011;68:148–157.

40. van Winkel R, van Beveren JM; Genetic Risk and Outcome of Psychosis (GROUP) Investigators. AKT1 moderation of cannabis-induced cognitive alterations in psychotic disorder. *Neuropsychopharmacology*. 2011;36:2529–2537.

41. Bernstein DP, Ahluvalia T, Pogge D, Handelsman L. Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *J Am Acad Child Adolesc Psychiatry*. 1997;36:340–348.

42. van Nierop M, Janssens M; Genetic Risk and Outcome of Psychosis (GROUP) Investigators. Evidence that transition from health to psychotic disorder can be traced to semi-ubiquitous environmental effects operating against background genetic risk. *PLoS One*. 2013;8:e76690.

43. StataCorp. *STATA Statistical Software: Release 14*. TX: College Station; 2015.

44. Heins M, Simons C, Lataster T, et al. Childhood trauma and psychosis: a case-control and case-sibling comparison across different levels of genetic liability, psychopathology, and type of trauma. *Am J Psychiatry*. 2011;168:1286–1294.

45. Genetic Risk and Outcome in Psychosis Investigators. Evidence that familial liability for psychosis is expressed as differential sensitivity to cannabis: an analysis of patient-sibling and sibling-control pairs. *Arch Gen Psychiatry*. 2011;68:138–147.

46. Verweij KH, Derks EM; Genetic Risk and Outcome of Psychosis (GROUP) Investigators. The association between intelligence scores and family history of psychiatric disorder in schizophrenia patients, their siblings and healthy controls. *PLoS One*. 2013;8:e77215.

47. Toulopoulou T, Picchioni M, Rijsdijk F, et al. Substantial genetic overlap between neurocognition and schizophrenia: genetic modeling in twin samples. *Arch Gen Psychiatry*. 2007;64:1348–1355.

48. Mani A, Mullainathan S, Shafir E, Zhao J. Poverty impedes cognitive function. *Science*. 2013;341:976–980.

49. Fervaha G, Zakzanis KK, Foussias G, Graff-Guerrero A, Agid O, Remington G. Motivational deficits and cognitive test performance in schizophrenia. *JAMA Psychiatry*. 2014;71:1058–1065.

50. Jones P, Rodgers B, Murray R, Marmot M. Child development risk factors for adult schizophrenia in the British 1946 birth cohort. *Lancet*. 1994;344:1398–1402.

51. van Dam DS, van Nierop M, Viechtbauer W, et al. Childhood abuse and neglect in relation to the presence and persistence of psychotic and depressive symptomatology. *Psychol Med*. 2015;45:1363–1377.

52. Mueser KT, Goodman LB, Trumbetta SL, et al. Trauma and posttraumatic stress disorder in severe mental illness. *J Consult Clin Psychol*. 1998;66:493–499.

53. Frueh BC, Grubaugh AL, Cusack KJ, Elhai JD. Disseminating evidence-based practices for adults with PTSD and severe mental illness in public-sector mental health agencies. *Behav Modif*. 2009;33:66–81.

54. Frueh BC, Grubaugh AL, Cusack KJ, Kimble MO, Elhai JD, Knapp RG. Exposure-based cognitive-behavioral treatment of PTSD in adults with schizophrenia or schizoaffective disorder: a pilot study. *J Anxiety Disord*. 2009;23:665–675.

55. Zipursky RB, Reilly TJ, Murray RM. The myth of schizophrenia as a progressive brain disease. *Schizophr Bull*. 2013;39:1363–1372.