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Childhood adversities and psychotic symptoms: The potential mediating or moderating role of neurocognition and social cognition

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ABSTRACT

Introduction: Childhood abuse and neglect are risk factors for psychotic symptoms. Early adversities may contribute to alterations in neuro/social cognition, which in turn is associated with psychosis. This study explored the possible mediating/moderating role of neuro/social cognition between childhood abuse and neglect on the one hand, and psychotic symptoms on the other.
Method: The sampling frame was 1.119 patients with a psychotic disorder. Childhood adversity was evaluated with the Dutch version of the Childhood Trauma Questionnaire. Psychotic symptoms were assessed with the Positive and Negative Syndrome Scale. Verbal learning-memory, attention-vigilance, working memory, information processing speed, reasoning-problem solving were evaluated as measures of neurocognition using the Word Learning Task, the Continuous Performance Test, the Wechsler Adult Intelligence Scale 3rd. Mentalization was evaluated as a measure of social cognition using the Hinting Task. Correlation, mediation, moderation, 95% Bias Corrected and accelerated (BCaCI) bootstrapped analyses were performed, considering possible sex differences.
Results: In male psychotic patients, attention and vigilance mediated the association between childhood neglect and negative symptoms (indirect effect: 0.18, BCaCI: 0.03–0.54), disorganization (indirect effect: 0.26, BCaCI: 0.05–0.61), excitement (indirect effect: 0.07, BCaCI: 0.004–0.23); mentalization mediated the association between childhood neglect and negative symptoms (indirect effect: 0.21, BCaCI: 0.02–0.51), excitement (indirect effect: 0.07, BCaCI: 0.01–0.20) disorganization (indirect effect: 0.29, BCaCI: 0.02–0.64); working memory mediated the association between childhood abuse and disorganization (indirect effect: 0.28, BCaCI: 0.05–0.57), excitement (indirect effect: 0.08, BCaCI: 0.01–0.20), emotional distress (indirect effect: 0.10, BCaCI: 0.01–0.27).
Discussion: In psychotic disorder, sex-specific mediation of neurocognition and mentalization may exist in the association between childhood adversity and psychotic symptoms.

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1. Introduction

The association between childhood adversities and psychosis is well known (Mansueto and Faravelli, 2017; Trotta et al., 2015; Varese et al., 2012a) with some evidence (Beards and Fisher, 2014; Bentall et al., 2014; Morgan and Gayer-Anderson, 2016) that specific subtypes of childhood adversities may predict later development of psychosis. Childhood abuse and childhood neglect may lead to a 2- to 3-fold increased risk of psychosis while childhood loss events may not (Ajnakina et al., 2016; Shevlin et al., 2015; Trauelsen et al., 2015; Varese et al., 2012a). Childhood adversities with intention to harm seem to be a stronger predictor of psychotic experiences than childhood adversities without intention to harm (van Nierop et al., 2014). Furthermore, childhood physical abuse increases the vulnerability to psychosis (Fisher et al., 2010) as does sexual abuse involving penetration (Cutajar et al., 2010).

It has been suggested that specific kinds of childhood adversities may lead to specific psychotic symptoms. Exposure to childhood abuse was found to be a strong predictor of positive symptoms (Aas et al., 2016; Ajnakina et al., 2016; Bentall et al., 2014; Chae et al., 2015; Cristóbal-Narváez et al., 2016; Gallagher and Jones, 2013; Heins et al., 2011; Lysaker et al., 2001; Schalinski et al., 2015; Shevlin et al., 2015; Sitko et al., 2014; Van Dam et al., 2015) while results on disorganization, excitement, and emotional distress are mixed (Aas et al., 2016; Chae et al., 2015; Schalinski et al., 2015). Experiences of childhood neglect have been associated with paranoia and negative symptoms (Bentall et al., 2014; Cristóbal-Narváez et al., 2016; Gallagher and Jones, 2013; Gibson et al., 2016; Sitko et al., 2014; Van Dam et al., 2015; Vogel et al., 2011) as well as with disorganization, excitement, and emotional distress (Aas et al., 2016; Chae et al., 2015; Schalinski et al., 2015).

Neurocognition (which involves attention, memory, processing speed, and executive functions) (de Gracia Dominguez et al., 2009) and social cognition (which involves perception, encoding, storage and regulation of information about people as well as the ability to think about and imagine mental states) (Fonagy et al., 2002; Green et al., 2015) may mediate in part the association between childhood adversities and psychosis (van Os et al., 2010; van Os et al., 2017).

Childhood adversities may induce a hypothalamic-pituitary-adrenal axis dysregulation that, through glucocorticoid receptors, diminishes hippocampal neurogenesis leading to altered neurocognition (Read et al., 2014). The exposure to childhood adversities may also cause deprivation of early social interactions, cognitive biases such as 'jumping to conclusions' and disrupted attachment, which in turn may affect the development of social cognitive abilities (Gibson et al., 2016; Jacobsen et al., 2015; van Os et al., 2010). Childhood adversity contributes to functional alterations of brain regions such as the temporoparietal junction (TPJ), the posterior cingulate cortex (PCC), and dorsomedial prefrontal cortex (dmPFC), which are essential for effective mental state inference (Quidé et al., 2017). Neurocognitive impairments were found in patients with psychotic disorder with a history of childhood abuse (Lysaker et al., 2001; Üçok et al., 2015) and poorer social cognition was observed in those exposed to childhood neglect if compared to those not exposed to childhood adversities (Garcia et al., 2016). In turn, impairments in neurocognition and social cognition were strongly associated with disorganization and negative symptoms, and were weakly associated with positive symptoms (de Gracia Dominguez et al., 2009; Fett et al., 2013; Ventura et al., 2013).

Guided by these findings, it may be hypothesized that patients with psychosis with early adversity may show poorer neuro- and social cognitive functioning which, in turn, is associated with psychotic symptoms. Mediation analyses, that attempt to identify the intermediary process between the independent (e.g. childhood adversities) and the dependent variables (e.g. psychotic symptoms) (Baron and Kenny, 1986; Muller et al., 2005) are a suitable model to evaluate whether neurocognition and social cognition represent a mediating factor between childhood adversities and psychotic symptoms. Moderation analysis (Baron and Kenny, 1986; Muller et al., 2005), in turn, may address the question to what degree neuro- and social cognitive functioning may enhance or reduce the susceptibility to psychotic symptoms in subjects who have been exposed to childhood adversities. Thus, the mediating and moderating role of neurocognition and social cognition in the association between childhood abuse/childhood neglect and psychotic symptoms were explored, using the Baron and Kenny (1986) criteria.

2. Methods

The present research is part of a 6-year longitudinal observational study called the 'Genetic Risk and Outcome of Psychosis Project (GROUP)' (Korver et al., 2012). The GROUP study includes a sample of patients with a diagnosis of non-affective psychotic disorder, their unaffected siblings, their unaffected parents, and healthy controls. The current analyses focus on the patients only. Patients were recruited from five university hospitals in the Netherlands and Belgium (i.e., Groningen, Amsterdam, Maastricht, Utrecht, Leuven) and their affiliated mental healthcare institutions. Patients were eligible for inclusion if they: (i) were aged 16–65 years; (ii) met the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) (APA, 2000) criteria for non-affective psychotic disorder; (iii) had their first contact with mental health care for psychosis < 10 years before; and (iv) were proficient in Dutch.

The GROUP study included three assessments: baseline, 3-year follow-up, and 6-year follow-up. The present analyses are based on the baseline assessment (n = 1119 patients).

The study protocol was approved centrally by the Ethical Review Board of the University Medical Centre Utrecht and by the local review boards of each participating institute. All subjects provided written informed consent.

2.1. Measures

Childhood adversities were assessed via the Dutch version of the Childhood Trauma Questionnaire (CTQ-SF; Bernstein et al., 2003), a 25-item retrospective self-report questionnaire rating on a Likert scale ranging from 1 (never true) to 5 (very often true) with good internal consistency, reliability, and validity (Thombs et al., 2009). The CTQ-SF measures physical abuse, physical neglect, sexual abuse, emotional abuse, and emotional neglect, all occurring before the age of 17 years.

Since the literature suggests that the phenomenology of psychosis can be adequately reduced to symptom dimensions (Ajnakina et al., 2016; Costello, 1992; van Os et al., 1999), we focused on psychotic symptoms using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). This is a 30-item interview-based scale rated on a 7-point Likert scale with good internal reliability and validity (Peralta and Cuesta, 1994).

Neurocognition encompassed the domains of verbal learning and memory, attention and vigilance, working memory, information processing speed, and reasoning and problem solving. Verbal learning and memory were assessed by means of the Word Learning Task (WLT) (Brand and Jolles, 1985). Outcome measures were immediate recall (i.e., number of words recalled over the three 15-word trials), retention rate (i.e., delayed free recall after 20 min divided by the maximum score of immediate recall trials 1–3). Lower scores of these outcomes variables reflect worse performance.

Attention and vigilance was assessed with the Continuous Performance Test (CPT-HQ) (Nuechterlein and Dawson, 1984; Wohlberg and Kornetsky, 1973), presenting a series of 300 white letters (on a laptop computer-controlled video monitor) at a rate of one per second in a randomized sequence. Subjects were instructed to press the space bar each time that the letter H was preceded by the letter Q (van Ommen et al., 2016). The CPT has shown good reliability and validity (Cornblatt and Keilp, 1994). Accuracy (i.e., proportion of correct

detections) was used as outcome measure; lower scores meant worse performance.

General cognitive abilities and achievement (i.e., IQ) were estimated with four subtests of the Wechsler Adult Intelligence Scale 3rd edition (WAIS-III) (Blyler et al., 2000; Wechsler, 1997). Working memory was assessed using the WAIS-III subtest Arithmetic; information processing speed was evaluated using the WAIS-III subtest Digit Symbol-Coding; reasoning and problem solving was assessed using the subtest WAIS-III Block Design; and the WAIS-III Information subtest was used as a measure of acquired knowledge.

Mentalizing abilities or Theory of Mind (ToM) was evaluated as a measure of social cognition (Fett et al., 2011; Green et al., 2015; van Os et al., 2010) using the Hinting Task (HT) (Corcoran et al., 1995; Fett et al., 2011) which assesses subjects' ability to infer real intentions behind indirect speech utterances. It comprises ten short passages presenting an interaction between two characters that ends with one of the characters dropping a hint. The subject is asked what the character really meant. Correctly identified hints were scored 2; in case of an incorrect response, a more obvious hint was added and the subsequent correct response was scored 1; incorrect responses were scored 0. The outcome measure was the sum of the scores of the ten items (range 0–20). The HT has shown good validity (Corcoran and Frith, 2003).

Frequency of cannabis use, during the lifetime period of heaviest use, was assessed with the short version of the Composite International Diagnostic Interview (CIDI) (Andrews and Peters, 1998) on a scale of 1 (less than weekly) to 3 (daily), using the Substance Abuse Module section L. Acceptability and reliability of the questions were found to be high (Cottler et al., 1989).

2.2. Statistic analyses

This study is a secondary analysis of data pertaining to a larger study with a different primary objective as described in Korver et al. (2012).

Some studies (Alemany et al., 2011; Kilian et al., 2017; Van Dam et al., 2015) considered abuse and neglect as separate childhood trauma dimensions showing a degree of specificity between these two types of early adversities and psychotic symptoms. To make present results comparable with previous studies (Alemany et al., 2011; Kilian et al., 2017; Van Dam et al., 2015), we grouped CTQ scores creating an abuse score (e.g. the sum of sexual abuse, physical abuse, emotional abuse scores) and a neglect score (e.g. the sum of physical neglect, and emotional neglect scores).

In order to discriminate patients with childhood adversity from those without childhood adversity, both childhood neglect and childhood abuse scores were dichotomized into high trauma and low trauma. We used as cut-off the 80th percentile of trauma scores as in previous studies (Heins et al., 2011; Van Dam et al., 2015; van Nierop et al., 2015) since having grouped CTQ scores to create a childhood abuse score and a neglect score, we could not use the cut-offs proposed by other authors (e.g., by Bernstein et al., 2003).

The five-factor of the PANSS including positive symptoms, negative symptoms, disorganization, excitement, and emotional distress, was used (van der Gaag et al., 2006a,b). This model may reflect the complex reality of schizophrenia and comorbid symptoms (Korver et al., 2012) and represents the dimensional structure of the PANSS (van der Gaag et al., 2006a,b; Wallwork et al., 2012) better than the original 3-factor model (Kay et al., 1987).

The Kolmogorov-Smirnov test was used to test normality of data (Ali and Bhaskar, 2016). *t*-Tests were performed to compare means of continuous variables. Chi-square tests were conducted to compare proportions. Analyses were performed with SPSS, version 21 (SPSS Inc.).

A correlation analysis was used to ensure that independent variables (IV) (i.e., childhood neglect or childhood abuse), dependent variables (DV) (i.e., psychotic symptoms), and hypothesized mediator (M)/moderator (MR) (i.e., neurocognition or social cognition) were associated (Baron and Kenny, 1986). Mediation models were tested when independent variables IV, DV, and M were associated; moderation models were tested when both IV and MR were significantly associated with the DV (Baron and Kenny, 1986). Mediation analyses and moderation analyses were performed using the Hayes PROCESS macro model 4 and the Hayes PROCESS macro model 1, respectively (Hayes, 2013; Preacher and Hayes, 2004).

To test the mediation models, three regression equations were run to verify the following conditions: (a) IV affects M; (b) IV affects DV; (c) M affects DV (Baron and Kenny, 1986). Fully mediating associations were considered when the association between IV and DV was not statistically significant after controlling for the effect of M; partial mediation was considered when, controlling for M, the direct effect of IV on DV was significant (Baron and Kenny, 1986). A bootstrapping procedure with n = 5000 bootstrap re-samples was used to assess indirect effects (Efron and Tibshirani, 1998; Kenny et al., 1998; MacKinnon et al., 2002; Preacher and Hayes, 2004). An indirect effect was considered significant if the 95% Bias Corrected and accelerated bootstrapped confidence interval (BCa CI) excluded zero.

Before testing the moderation models, both IV and MR were mean-centred (Dawson, 2014; Shieh, 2011) to mitigate the potential threat of multicollinearity between IV and the constructed cross-product term, thus facilitating the interpretation of the interaction effects (Shieh, 2011). To test moderation models, three regression equations were run and the following conditions verified: (a) IV affects DV; (b) MR affects DV; (c) the interaction effect between IV and MR affects DV (Baron and Kenny, 1986).

Mediation and moderation models were adjusted for the covariates age, sex, and lifetime cannabis use as a priori potential cofounders (Bäckman et al., 2006; Fisher et al., 2009; Green et al., 2015; Han et al., 2012; Ittig et al., 2015; Morgan et al., 2014; Sánchez-Torres et al., 2013; Pechtel and Pizzagalli, 2011; van Os et al., 2002; van Os et al., 2010).

Sex differences in cognition, clinical symptoms, and impact of early adversities, as well as a possible association between duration of psychotic illness, age, and cognitive functioning have been observed in previous studies (Bilder et al., 2000; Mendrek and Mancini-Marie, 2016; Üçok et al., 2015; Ventura et al., 2015). Thus the analyses of correlation, mediation, and moderation between childhood adversities, cognitive functioning and psychotic symptoms were run separately for men and women as well as for subgroups of patients on the basis of the duration of illness (recent onset vs non recent onset of psychotic disorder; recent onset was considered in the last 24 months) and age. According to Nakane et al. (1992), we considered the following 5 age groups: 15–19 years (n = 90); 20–24 (n = 207); 25–29 (n = 205); 30–34 (n = 116); 35–39 (n = 72); 40–44 (n = 57) 45–49 (n = 14); 50–54 (n = 3); 55–60 (n = 3). Given the lower number of subjects with ≥45 years, we excluded them from the analyses.

Release 5.0 of the GROUP database was used for the present study. The two-sided significance level was set at $p < .05$.

3. Results

3.1. Sample attrition

Of the 1.119 patients enrolled at baseline, 757 had data on childhood adversities.

Around 30% of the subjects did not or could not answer the childhood trauma questionnaire.

Comparing those who completed the childhood trauma questionnaire with those who did not, we found in the latter group: lower educational level (mean ± standard deviation no childhood adversity data vs childhood adversity: 3.75 ± 2.05 vs 4.18 ± 2.04; t = −3.21; p = .001); more severe symptoms: positive symptoms (mean ± standard deviation no childhood adversity data vs childhood adversity: 14.55 ± 6.54 vs 13.62 ± 6.58; t = 2.09; p = .03), negative symptoms (mean ± standard deviation no childhood adversity data vs childhood

adversity: 16.89 ± 7.25 vs 14.19 ± 6.19; t = 6.05; p < .001), disorganization (mean ± standard deviation no childhood adversity data vs childhood adversity: 18.17 ± 6.01 vs 16.16 ± 6.29; t = 4.75; p < .001), excitement (mean ± standard deviation no childhood adversity data vs childhood adversity: 12.87 ± 4.27 vs 11.70 ± 3.89; t = 4.27; p < .001), and emotional distress (mean ± standard deviation no childhood adversity data vs childhood adversity: 16.56 ± 5.82 vs 15.49 ± 5.65; t = 2.77; p = .01); lower score on neurocognitive tasks and social cognition: immediate recall (mean ± standard deviation no childhood adversity data vs childhood adversity: 22.17 ± 6.10 vs 23.28 ± 6.05; t = −2.71; p = .01), attention (mean ± standard deviation no childhood adversity data vs childhood adversity: 97.66 ± 7.99 vs 98.65 ± 3.85; t = −2.61 p = .01), processing speed (mean ± standard deviation no childhood adversity data vs childhood adversity: 8.96 ± 3.35 vs 9.87 ± 3.30; t = −4.09; p < .001), acquired knowledge (mean ± standard deviation no childhood adversity data vs childhood adversity: 10.14 ± 2.97 vs 10.83 ± 3.10; t = −3.37; p = .001), working memory (mean ± standard deviation no childhood adversity data vs childhood adversity: 9.13 ± 3.21 vs 9.62 ± 3.25; t = −2.25; p = .02), reasoning-problem solving (mean ± standard deviation no childhood adversity data vs childhood adversity: 97.43 ± 26.91 vs 104.29 ± 26.95; t = −3.79; p < .001) and mentalizing abilities (mean ± standard deviation no childhood adversity data vs childhood adversity: 17.13 ± 2.85 vs 17.71 ± 2.73; t = −3.08; p = .002).

For the other analyses, only participants with data on childhood adversity were included. For more details on descriptive analyses please see Table 1.

3.2. Childhood neglect

Patients with childhood neglect, compared with those without childhood neglect, showed more severe positive symptoms, disorganization, excitement, emotional distress, and lower scores on retention rate, and attention (Table 2). Childhood neglect was positively associated with psychotic symptoms and negatively associated with immediate recall, attention and vigilance, as well as with mentalizing abilities (Supplementary Table 3). Both neurocognitive functions and mentalizing abilities were negatively associated with psychotic symptoms (Supplementary Table 3).

Table 1
Descriptive analysis (n = 757).

Variables		n (%)
Gender (male)		568 (75%)
Variables		**Mean (SD); range**
Age		27.66 (7.60); 15–60
Educational level		4 (2.04); 0–8
CTQ	Childhood neglect	1.86 (0.63); 1–4.19
	Childhood abuse	1.43 (0.52); 1–3.73
PANSS	Positive symptoms	13.62 (6.58); 2–41
	Negative symptoms	14.19 (6.19); 3–39
	Disorganization	16.16 (6.29); 10–44
	Excitement	11.70 (3.89); 8–38
	Emotional distress	15.49 (5.63); 8–35
WLT	Immediate recall	23.28 (6.05); 7–41
	Retention rate	0.77 (0.20); 0.01–1.50
	Acquired knowledge	17.12 (5.48); 1–28
	Working memory	12.48 (4.77); 2–22
	Reasoning and problem solving	41.64 (16.7); 0–68
	Processing speed	66.18 (15.84); 13–120
CPT-HQ	Attention and vigilance	98.65 (3.85); 60–100
HT	Mentalizing abilities	17.71 (2.73); 3–20
CIDI	Cannabis use	0.64 (0.88); 0–3

CTQ: Childhood Trauma Questionnaire; PANSS: Positive and Negative Syndrome Scale; WLT: Word Learning Task; WAIS-III: Wechsler Adult Intelligence Scale III; CPT-HQ: Continuous Performance Test HQ (accuracy); HT: Hinting Task; CIDI: Composite International Diagnostic Interview 2.1.

Mediation models showed that lower immediate recall partially mediated the association between childhood neglect and disorganization (adjusted R-squared = 0.07, p ≤ .001; total effect: 1.20, BCa 95% CI: 0.46–1.94; indirect effect: 0.13, BCa 95% CI: 0.006–0.30) (Table 4). Moreover, mentalizing abilities partially mediated the association between childhood neglect and negative symptoms (adjusted R-squared = 0.07, p ≤ .001; total effect: 1.01, BCa 95% CI: 0.27–0.75; indirect effect: 0.17, BCa 95% CI: 0.02–0.40); childhood neglect and disorganization (adjusted R-squared = 0.11; p ≤ .001; total effect: 1.29, BCa 95% CI: 0.46–1.95; indirect effect: 0.23, BCa 95% CI: 0.03–0.49); and childhood neglect and excitement (adjusted R-squared = 0.055, p ≤ .001; total effect: 0.76, BCa 95% CI: 0.32–1.21; indirect effect: 0.05, BCa 95% CI: 0.009–0.14) (Table 4; Supplementary Fig. 1). Childhood neglect was not significantly associated with attention-vigilance, when adjusted for covariates (Table 4). Thus, mediation models between childhood neglect, attention-vigilance, and psychotic symptoms were not examined.

Moderation models showed that neither neurocognitive domains nor mentalizing abilities moderated the association between childhood neglect and psychotic symptoms (Table 5).

3.3. Childhood abuse

Patients with psychotic disorder with childhood abuse showed more severe psychotic symptoms than those without childhood abuse, while no statistically significant differences were found for neurocognition and social cognition (Table 2). Childhood abuse was positively associated with all psychotic dimensions except for negative symptoms and was negatively associated with working memory (Supplementary Table 3). Adjusting for age, sex, and lifetime cannabis use, the association between childhood abuse and working memory was no longer significant (B = −0.57, SE = 0.38, p = .10, BCa 95% CI: −0.10–0.11). Since the independent variable (i.e., childhood abuse) did not predict the hypothesized mediator variable (i.e., working memory) (Baron and Kenny, 1986), mediation models between childhood abuse, working memory, and psychotic symptoms were not run.

Moderation analyses showed that neither neurocognitive domains nor mentalizing abilities moderated the association between childhood abuse and psychotic symptoms (Table 6).

3.4. Mentalization and neurocognition

A positive association between mentalization and neurocognition scores was found. Mentalizing abilities were positively correlated with verbal learning and memory, attention and vigilance, working memory, processing speed, reasoning, and problem solving abilities (Supplementary Table 3).

3.5. Association between childhood adversities, cognitive functioning, and psychotic symptoms in male and female

3.5.1. Male psychotic patients

Childhood neglect was positively associated with all psychotic symptoms, and negatively associated with immediate recall, attention and vigilance, working memory and mentalizing abilities; both neurocognitive functions and mentalizing abilities were negatively associated with psychotic symptoms (Supplementary Table 7).

Attention and vigilance partially mediated the association between childhood neglect and negative symptoms (adjusted R-squared = 0.05, p ≤ .001; total effect: 1.22, BCa 95% CI: 0.29–2.14; indirect effect: 0.18, BCa 95% CI: 0.03–0.54), disorganization (adjusted R-squared = 0.06, p ≤ .001; total effect: 1.21, BCa 95% CI: 0.24–2.19; indirect effect: 0.26, BCa 95% CI: 0.05–0.61) and excitement (adjusted R-squared = 0.04, p = .001; total effect: 0.88, BCa 95% CI: 0.32–1.44; indirect effect: 0.07, BCa 95% CI: 0.004–0.23) (Supplementary Table 8). Mentalizing abilities: (a) partially mediated the association between childhood neglect and negative symptoms (adjusted R-squared = 0.06, p < .001;

Table 2
Comparison between patients with childhood adversity and patients without childhood adversity on cognition and psychotic symptoms. *t*-Tests for independent samples.

		No childhood neglect (n = 560)	Childhood neglect (n = 168)	p	No childhood abuse (n = 574)	Childhood abuse (n = 153)	p
		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
WLT	Immediate recall	23.48 ± 5.97	22.63 ± 6.28	.11	23.29 ± 6.02	23.25 ± 6.18	.93
	Retention rate	0.74 ± 0.21	0.74 ± 0.19	.005	0.78 ± 0.20	0.77 ± 0.19	.59
CTP-HQ	Attention/vigilance	98.90 ± 2.92	97.81 ± 5.95	.002	98.63 ± 3.86	98.74 ± 3.84	.77
	World knowledge	10.91 ± 3.04	10.60 ± 3.32	.25	10.80 ± 3.03	10.96 ± 3.36	.57
	Working memory	9.68 ± 3.22	9.43 ± 3.32	.39	9.72 ± 3.28	9.25 ± 3.08	.11
WAIS-III	Reasoning and problem solving	104.77 ± 26.41	102.69 ± 28.71	.38	104.53 ± 26.80	103.40 ± 27.61	.65
	Processing speed	9.74 ± 3.45	9.91 ± 3.25	.56	9.92 ± 3.29	9.69 ± 3.34	.44
HT	Mentalizing abilities	17.77 ± 2.56	17.51 ± 3.22	.29	17.67 ± 2.80	17.84 ± 2.47	.51
PANSS	Positive	15.32 ± 7.22	13.12 ± 6.30	<.001	12.98 ± 6.12	15.99 ± 7.63	<.001
	Negative	13.94 ± 5.88	14.99 ± 7.09	.05	14.20 ± 6.04	14.13 ± 6.75	.89
	Disorganization	15.73 ± 6.01	17.56 ± 6.99	.001	15.81 ± 6.03	17.45 ± 7.06	.005
	Excitement	11.42 ± 3.55	12.66 ± 4.75	<.001	11.41 ± 3.44	12.76 ± 5.10	.001
	Emotional distress	15.01 ± 5.33	17.12 ± 6.34	<.001	14.88 ± 5.34	17.73 ± 6.19	<.001

WLT: Word Learning Task; CPT-HQ: Subscale of Continuous Performance Test (accuracy); WAIS-III: Wechsler Adult Intelligence Scale III; HT: Hinting Task; PANSS: Positive and Negative Syndrome Scale. SD: standard deviation.

total effect: 1.29, BCa 95% CI: 0.39–2.18; indirect effect: 0.21, BCa 95% CI: 0.02–0.51); excitement (adjusted R-squared = 0.04, p < .001; total effect: 0.86, BCa 95% CI: 0.31–1.41; indirect effect: 0.07, BCa 95% CI: 0.01–0.20); (b) fully mediated the association between childhood neglect and disorganization (adjusted R-squared = 0.09, p < .001; total effect: 0.1.10, BCa 95% CI: 0.18–2.02; indirect effect: 0.29, BCa 95% CI:

Table 4
Mediating effect of neurocognitive domains and mentalizing abilities in the association between childhood neglect and psychotic symptoms, adjusted for age, gender, cannabis. Mediation analyses according to Baron and Kenny (1986) criteria and Bootstrapping.

		Step1				Step 2				Step 3			
		Cognitive function (DV); childhood neglect (IV)				Positive symptoms (DV); childhood neglect (IV)				Positive symptoms (DV); cognition (M)b; childhood neglect (IV)a			
		B	SE	p	95% BCa	B	SE	p	95% BCa CI	B	SE	p	95% BCa CI
HT	Mentalizing abilities	−0.38	0.16	.02	−0.71 to −0.05	1.48	0.38	<.001	0.71–2.24	a. 1.43 b. −0.13	0.39 1.94	.003 .14	0.66–2.20 −0.30–0.04

		Step1				Step 2				Step 3			
		Cognitive function (DV); childhood neglect (IV)				Negative symptoms (DV); childhood neglect (IV)				Negative symptoms (DV); cognition (M)b; childhood neglect (IV)a			
		B	SE	p	95% BCa	B	SE	p	95% BCa CI	B	SE	p	95% BCa CI
WLT	Immediate recall	−0.74	0.37	0.04	−1.46 to −0.01	1.01	0.37	.01	0.28–1.75	a 0.90 b −0.15	0.37 0.03	.01 <.001	0.17–1.63 −0.22 to −0.07
CPT-HQ	Attention and vigilance	−0.43	0.25	0.08	−0.93–0.06			–				–	
HT	Mentalizing abilities	−0.38	0.16	**0.02**	−0.71 to −0.06	1.01	0.37	**.007**	0.27–1.75	a 0.84 b. −0.45	0.37 0.08	**.02** <**.001**	0.11–1.56 −0.62 to −0.28

		Step1				Step 2				Step 3			
		Cognitive function (DV); childhood neglect (IV)				Disorganization (DV); childhood neglect (IV)				Disorganization (DV); cognition (M)b; childhood neglect (IV)a			
		B	SE	p	95% BCa	B	SE	p	95% BCa CI	B	SE	p	95% BCa CI
WLT	Immediate recall	−0.73	0.37	**0.04**	−1.46 to −0.01	1.20	0.37	**.001**	0.46–1.94	a 1.07 b −0.18	0.37 0.03	**.004** <**.001**	0.34–1.80 −0.25 to −0.10
CPT-HQ	Attention and vigilance	−0.43	0.25	0.08	−0.93–0.06			–				–	
HT	Mentalizing abilities	−0.38	0.16	**0.02**	−0.71 to −0.05	1.20	0.37	**.001**	0.46–1.95	a 0.97 b −0.61	0.36 −0.08	**.008** <**.001**	0.25–1.69 −0.78 to −0.45

		Step1				Step 2				Step 3			
		Cognitive function (DV); childhood neglect (IV)				Excitement (DV); childhood neglect (IV)				Excitement (DV); cognition (M)b; childhood neglect (IV)a			
		B	SE	p	95% BCa	B	SE	p	95% BCa CI	B	SE	p	95% BCa CI
WLT	Immediate recall	−0.73	0.37	0.04	−1.46 to −0.01	0.77	0.22	.001	0.32–1.21	a 0.74 b −0.04	0.22 0.02	.001 .08	0.29–1.18 −0.08–0.005
CPT-HQ	Attention and vigilance	−0.43	0.25	0.08	−0.92–0.05	–				–			
HT	Mentalizing abilities	−0.38	0.16	**0.02**	−0.71 to −0.06	0.76	0.22	**.0007**	0.32–1.21	a 0.70 b −0.14	0.22 0.05	**.002** **.004**	0.26–1.15 −0.25 to −0.04

IV = independent variable; DV = dependent variable; M = mediator. BCa = 95% Bias Corrected and Accelerated bootstrapped confidence interval. Significant mediation models (IV affect the M; IV affect the DV; M affect the DV) are evidenced in bold. Fully mediation: controlling for M, the direct effect of IV on DV was not significant; partial mediation: after controlling for M, the direct effect of IV on DV is significant (Baron and Kenny, 1986). WLT: Word Learning Task; CPT-HQ: Continuous Performance Test-HQ (accuracy); HT: Hinting Task.

Table 5
Moderating effect of neurocognitive domains and mentalizing capacity in the association between childhood neglect and psychotic symptoms, adjusted for age, gender, cannabis use. Moderation analyses according to Baron and Kenny's (1986) criteria.

	IV MR Interaction between IV and MR	Positive symptoms		Negative symptoms		Disorganization		Excitement		Emotional distress	
		B [95% CI]	p	B [95% CI]	p	B [95% CI]	p	B [95% CI]	p	B [95% CI]	p
CTQ	Childhood neglect			0.91 [0.17–1.63]	.01	1.08 [0.35–1.81]	.003	0.73 [0.29–1.18]	.001		
WLT	Immediate recall	Nc	Nc	−0.15 [−0.22 to −0.07]	.0001	−0.17 [−0.25–0.10]	<.001	−0.04 [−0.08–0.004]	.07	Nc	Nc
	Interaction			−0.003 [−0.12–11]	.95	1.08 [−0.16–0.06]	.39	–	–		
CTQ	Childhood neglect			0.95 [0.21–1.69]	.01						
WLT	Retention rate	Nc	Nc	−1.40 [−3.72–0.92]	.23	Nc	Nc	Nc	Nc	Nc	Nc
	Interaction			−1.46 [−5.29–2.36]	.45						
CTQ	Childhood neglect	1.37 [0.60–2.13]	.0005	0.89 [0.16–1.62]	.01	1.04 [0.33–1.76]	.004	0.75 [0.30–1.21]	.001	1.48 [0.82–2.15]	<.001
WLT	Processing speed	−0.09 [−0.26–0.06]	.06	−0.18 [−0.28 to −0.08]	.0002	−0.31 [−0.41 to −0.21]	<.001	−0.09 [−0.15 to −0.03]	.002	−0.11 [−0.20 to −0.03]	.008
	Interaction	–	–	−0.05 [−0.21–0.09]	.47	−0.03 [−0.18–0.12]	.69	0.75 [−0.09–0.10]	.94	0.03 [−0.10–17]	.64
CTQ	Childhood neglect	1.40 [0.63–2.17]	.003	0.99 [0.26–1.71]	.007	1.23 [0.51–1.95]	.0008	0.82 [0.36–1.27]	.0004	1.57 [0.91–2.24]	<.001
WAIS-III	Working memory	−0.03 [−0.06–0.001]	.06	−0.07 [−0.10 to −0.04]	<.001	−0.09 [−0.12 to −0.06]	<.001	−0.02 [−0.03 to −0.0005]	.04	−0.03 [−0.06 to −0.01]	.01
	Interaction	−0.02 [−0.07–0.02]	.26	0.02 [−0.02–0.06]	.39	0.005 [−0.04–0.05]	.83	0.002 [−0.03–0.03]	.88	0.01 [−0.02–0.05]	.45
CTQ	Childhood neglect	1.39 [0.63–2.16]	.0004	1.002 [0.27–1.73]	.007	1.17 [0.44–1.89]	.001	0.80 [0.34–1.25]	.005	1.53 [0.86–2.19]	<.001
WAIS-III	Reasoning-problem solving	−0.04 [−0.07 to −0.01]	.005	−0.03 [−0.6 to −0.006]	.01	−0.06 [−0.09 to −0.04]	<.001	−0.02 [−0.4–0.01]	.003	−0.02 [−0.05–0.001]	.04
	Interaction	−0.002	.91	−0.02 [−0.06–0.02]	.32	0.003 [−0.04–0.04]	.88	−0.007 [−0.03–0.02]	.61	0.005 [−0.03–0.04]	.78
CTQ	Childhood neglect	1.40 [0.63–2.16]	.0003	0.95 [0.22–1.68]	.01	1.09 [0.37–1.81]	.003	0.78 [0.32–1.23]	.005		
WAIS-III	Acquired knowledge	−0.06 [−0.15–0.02]	.14	−0.12 [−0.20 to −0.03]	.008	−0.24 [−0.33 to −16]	<.001	−0.05 [−0.10 to −0.001]	.04	Nc	Nc
	Interaction	–	–	−0.06 [−0.19–0.06]	.34	−0.02 [−0.16–0.10]	.65	0.002 [−0.08–08]	.94		
CTQ	Childhood neglect			0.88 [0.12–1.64]	.02	1.03 [0.25–1.79]	.008	0.75 [0.29–1.21]	.001		
CPT-HQ	Attention and vigilance	Nc	Nc	−0.24 [−0.37 to −0.12]	.001	−0.39 [−0.51 to −0.26]	<.001	−0.12 [−0.19 to −0.03]	.003	Nc	Nc
	Interaction			0.07 [−0.11–0.27]	.42	0.18 [−0.01–0.37]	.06	0.10 [−0.01–0.22]	.08		
CTQ	Childhood neglect	1.43 [0.67–2.02]	.003	0.84 [0.12–1.57]	.02	0.97 [0.25–1.69]	.008	0.71 [0.26–1.15]	.001	1.51 [0.84–2.18]	<.001
HT	Mentalizing abilities	−0.11 [−0.29–0.07]	.23	−0.42 [−0.59 to −0.25]	<.001	−0.61 [−0.78 to −0.44]	<.001	−0.13 [−0.23 to −0.02]	.01	−0.05 [−0.21–10]	.49
	Interaction	–	–	−0.19 [−0.44–0.06]	.13	−0.03 [−0.28–0.21]	.77	−0.10 [−0.25–0.05]	.19	–	–

IV = independent variable; DV = dependent variable; MR = moderator; nc: no significant correlation between variables. To test moderation models both IV and MR must be correlated with DV (Baron and Kenny, 1986), thus moderation analyses were not run among variables that were not significantly correlated each other. Moderation models were considered significant whether IV affects DV; MR affects DV; the interaction effect between IV and MR affects DV (Baron and Kenny, 1986). CTQ: childhood trauma questionnaire; WLT: Word Learning Task; CPT-HQ: Continuous Performance Test-HQ (accuracy); WAIS-III: Wechsler Adult Intelligence Scale III; HT: Hinting Task.

0.02–0.64) (Supplementary Table 8). When adjusted for covariates (e.g., age, cannabis), childhood neglect was not significantly associated with working memory (B = −0.38, p = .10, BCa 95% CI = −0.84–0.08) nor with immediate recall (B = −0.88.p = .05, BCa 95% CI = −1.74–0.002), thus, the mediating role of working memory and immediate recall were not examined. Neither neurocognition nor social cognition moderated the association between childhood neglect and psychotic symptoms (Supplementary Table 9).

Childhood abuse was positively associated with all psychotic dimensions, except negative symptoms; and negatively associated with attention and vigilance, working memory (Supplementary Table 7). Attention and vigilance did not mediate the association between childhood abuse and disorganization (indirect effect: 0.32, BCa 95% CI: −0.07–1.16), excitement (indirect effect: 0.07, BCa 95% CI: −0.02–0.40) (Supplementary Table 10). Working memory partially mediated the association between childhood abuse and disorganization (adjusted R-squared = 0.12; total effect: 3.34, BCa 95% CI: 2.19–4.49; indirect effect: 0.28, BCa 95% CI: 0.05–0.57), excitement (adjusted R-squared = 0.09; total effect: 2.36, BCa 95% CI: 1.68–3.05; indirect effect: 0.08, BCa: 0.01–0.20), emotional distress (adjusted R-squared = 0.11; total effect: 3.47, BCa: 2.47–4.48; indirect effect: 0.10, BCa 95% CI: 0.01–0.27) (Supplementary Table 10). Neither neurocognition nor social cognition moderated the association between childhood abuse and psychotic symptoms (Supplementary Table 11).

3.5.2. Female psychotic patients

Childhood adversity was correlated with psychotic symptoms, but not with neurocognition or mentalization (Supplementary Table 12). Thus, the mediating role of neurocognition and ToM in the association between childhood neglect, childhood abuse, and psychotic symptoms was not tested. Given that both neurocognition and mentalization were negatively associated only with disorganization, we tested its possible moderating role. Moderation analyses showed that neither neurocognition nor mentalization moderated the association between childhood neglect, abuse, and disorganization (Supplementary Table 13).

Table 6
Moderating effect of neurocognitive domains and mentalizing capacity in the association between childhood abuse and psychotic symptoms, adjusted for age, gender, cannabis. Moderation analyses according to Baron and Kenny's (1986) criteria.

	IV MR Interaction between IV and MR	Positive symptoms B [95% CI]	p	Disorganization B [95% CI]	p	Excitement B [95% CI]	p	Emotional distress B [95% CI]	p
CTQ	Childhood abuse			2.52 [1.62–3.41]	<.001	1.78 [1.25–2.31]	<.001		
WLT	Immediate recall	Nc	Nc	−0.17 [−0.25 to −0.10]	<.001	−0.03 [−0.08–0.005]	.08	Nc	Nc
	Interaction			−0.08 [−0.22–0.05]	.25	0.04 [−0.04–0.12]	.31		
CTQ	Childhood abuse			2.61 [1.71–3.52]	<.001				
WLT	Retention rate	Nc	Nc	−1.78 [−4.06–0.50]	.12	Nc	Nc	Nc	Nc
	Interaction			−1.89 [−6.57–2.79]	.42				
CTQ	Childhood abuse	3.56 [2.62–4.49]	<.001	2.55 [1.65–3.45]	<.001	1.97 [1.42–2.53]	<.001	3.12 [2.30–3.94]	<.001
WAIS-III	Working memory	−0.08 [−0.18–0.01]	.09	−0.31 [−0.40 to −0.21]	<.001	−0.08 [−0.14 to −0.03]	.004	−0.11 [−0.19 to −0.02]	.01
	Interaction	−0.01 [−0.22–0.19]	.87	−0.02 [−0.21–0.17]	.84	0.06 [−0.06–0.18]	.36	0.08 [−0.09–0.26]	.35
CTQ	Childhood abuse	3.58 [2.68–4.49]	<.001	2.65 [1.78–3.52]	<.001	1.96 [1.42–2.50]	<.001	3.11 [2.31–3.91]	<.001
WAIS-III	Processing speed	−0.02 [−0.05–0.002]	.07	−0.09 [−0.12 to −0.06]	<.001	−0.02 [−0.03–0.001]	.07	−0.03 [−0.05 to −0.004]	.02
	Interaction	−0.002 [−0.06–0.06]	.95	−0.04 [−0.09–0.02]	.28	0.01 [−0.03–0.05]	.59	0.03 [−0.02–0.09]	.19
CTQ	Childhood abuse	3.58 [2.68–4.49]	<.001	2.74 [1.85–3.64]	<.001	1.94 [1.39–2.48]	<.001	3.04 [2.23–3.85]	<.001
WAIS-III	Reasoning and problem solving	−0.04 [−0.06 to −0.01]	.008	−0.06 [−0.09 to −0.03]	<.001	−0.02 [−0.03 to −0.01]	.006	−0.02 [−0.04–0.001]	.06
	Interaction	−0.009 [−0.06–0.04]	.71	0.02 [−0.02–0.07]	.31	0.001 [−0.03–0.03]	.96	−0.005 [−0.05–0.04]	.83
CTQ	Childhood abuse	3.63 [2.72–4.53]	<.001	2.82 [1.95–3.69]	<.001	1.98 [1.44–2.52]	<.001		
WAIS-III	Acquired knowledge	−0.09 [−0.17 to −0.004]	.04	−0.26 [−0.34 to −0.18]	<.001	−0.06 [−0.11 to −0.01]	.01	Nc	Nc
	Interaction	−0.10 [−0.27–0.07]	.25	0.03 [−0.13–0.19]	.70	0.01 [−0.09–0.10]	.90		
CTQ	Childhood abuse			2.45 [1.49–3.40]	<.001	1.78 [1.23–2.34]	<.001		
CTP-HQ	Attention and vigilance	Nc	Nc	−0.36 [−0.48 to −0.23]	<.001	−0.09 [−0.16 to −0.02]	.01	Nc	Nc
	Interaction			0.05 [−0.08–0.18]	.43	0.01 [−0.06–0.09]	.73		
CTQ	Childhood Abuse	3.65 [2.74–4.56]	<.001	2.78 [1.91–3.40]	<.001	1.82 [1.29–2.35]	<.001		
HT	Mentalizing abilities	−0.16 [−0.34–0.002]	.05	−0.64 [−0.80 to −0.48]	<.001	−0.16 [−0.26 to −0.06]	.001	Nc	Nc
	Interaction	−0.02 [−0.38–0.33]	.89	0.009 [−0.33–0.34]	.95	−0.03 [−0.24–0.17]	.75		

IV = independent variable; DV = dependent variable; MR = moderator; nc: no significant correlation between variables. To test moderation models both IV and MR must be correlated with DV (Baron and Kenny, 1986), thus moderation analyses were not run among variables that were not significantly correlated each other. Moderation models were considered significant whether IV affects DV; MR affects DV; the interaction effect between IV and MR affects DV (Baron and Kenny, 1986).
CTQ: childhood trauma questionnaire; WLT: Word Learning Task; CPT-HQ: Continuous Performance Test-HQ (accuracy); WAIS-III: Wechsler Adult Intelligence Scale III; HT: Hinting Task.

3.6. Association between childhood adversities, cognitive functioning and psychotic symptoms according to the duration of psychotic disorder

Within subjects with recent onset of psychotic disorders (i.e., <24 months) neither neurocognition nor ToM correlated with psychotic symptoms (p-value range from .10 to .78), thus, the mediating or moderating role of cognitive functioning was not examined.

Within psychotic patients with late psychotic onset (≥24 months), neurocognitive scores were correlated with childhood abuse and psychotic symptoms (at $p < .01$). Adjusting the analyses for age, gender, and cannabis, problem solving (B = −0.02, 95% CI = −0.03 to −0.002, p = .03) moderated the relationship between childhood abuse (B = 3.18, 95% CI = 2.32–4.05, p ≤ .001) and emotional distress ($B_{\text{childhood abuse*problem solving}} = 0.03$, 95% CI = 0.001–0.06, p = .04) (adjusted r-square = 0.13, $p < .001$).

3.7. Association between childhood adversities, cognitive functioning and psychotic symptoms according to the age of subjects adjusted of covariates (e.g. age, gender, cannabis and duration of the illness)

Within subjects aged 15–19 years: (a) processing speed (B = −0.51, 95% CI = −0.93 to −0.09, p = .01) moderated the relationship between childhood abuse (B = 3.91, 95% CI = 1.10–6.72, p = .01) and positive symptoms ($B_{\text{childhood abuse*processing speed}} = -0.82$, 95% CI = −1.59 to −0.05, p = .03, adjusted r-square = 0.35, $p < .001$); (b) problem solving (B = −0.38, 95% CI = −0.67 to −0.09, p = .01) moderated the association between childhood abuse (B = 3.47, 95% CI = 1.89–5.05, p ≤ .001) and excitement ($B_{\text{childhood abuse*problem solving}} = -0.55$, 95% CI = −1.08 to −0.02, p = .04, adjusted r-square = 0.29, $p < .001$).

Within subjects aged 20–24 years, attention and vigilance (B = −0.82, 95% CI = −1.51 to −0.13, p = .01) moderated the association between childhood neglect (B = 2.37, 95% CI = 0.58–4.16, p = .01) and disorganization ($B_{\text{childhood neglect*attention and vigilance}} = -1.43$, 95% CI = −2.83 to −0.02, p = .04, adjusted r-square = 0.16, $p < .001$).

Within subjects aged 25–29 years: (a) immediate recall fully mediated the association between childhood neglect and disorganization: the path direct coefficient was significant (B = 1.90, 95% CI = 0.37–3.44, p = .01); childhood neglect predicted immediate recall (B = −1.46, 95% CI = −2.77 to −0.16, p = .02); immediate recall (B = −0.24, 95% CI = −0.43 to −0.09, p = .002) fully mediated the relationships between childhood neglect and disorganization (B = 1.52, 95% CI = −0.003–0.3.04, p = .05; adjusted R-squared = 0.11; p = .002; total effect: 1.90, BCa 95% CI: 0.37–3.44; indirect effect: 0.38, BCa 95% CI: 0.06–0.99).

No significant correlations were found between childhood adversities and cognitive functions, as well as between cognition and psychotic symptoms in those aged 35 and over. For this reason, mediation and moderation analyses were not tested.

4. Discussion

The present findings suggest that neurocognition and mentalization might be involved in the relationship between childhood adversities and psychotic symptoms, in particular in males.

In male patients with a psychotic disorder, lower mentalization, attention and vigilance appear to mediate the association between childhood neglect and negative symptoms, disorganization and excitement, while poor working memory appears to have a mediating role between childhood abuse and disorganization, excitement, and emotional distress. This finding supports previous findings suggesting that early experience of abuse or neglect might negatively impact the development of neurocognitive functions and mentalizing abilities, which may subsequently lead to psychotic symptoms (Colvert et al., 2008; Garcia et al., 2016; Jacobsen et al., 2015; Read et al., 2014) (Supplementary Fig. 2). Our results suggest that the intervening role of neurocognition or ToM in the association between childhood adversities and positive symptoms is not likely. Different pathways as for example dissociation (Varese et al., 2012b), affective dysregulation (Isvoranu et al., 2017) or temperament and character (Mansueto et al., 2018) may link early adversity with positive symptoms. Within female psychotic patients, cognition may not be involved in the association between childhood adversities and psychosis, consistently with studies in FEP and UHR samples showing a significant correlation between early adversities and cognitive impairments only in men (Aas et al., 2011; Üçok et al., 2015). These findings might in part be explained by sex differences in cognitive functioning in schizophrenia, impairments on neurocognition and mentalization abilities being more prominent in males than in females (Barajas et al., 2015; Mendrek and Mancini-Marie, 2016; Ochoa et al., 2012). In females, the association between early adversities and psychotic dimensions may be explained by mechanisms (Misiak et al., 2017) such as dissociation (Read et al., 2001). Our findings are not consistent with some studies (Mansueto et al., 2017; Palmier-Claus et al., 2016; Sideli et al., 2014). This discrepancy may be due to methodological features since neither specific type of childhood adversities nor sex differences were explored (Mansueto et al., 2017; Palmier-Claus et al., 2016; Sideli et al., 2014).

We found that the association between cognitive impairments and psychotic symptoms is significant within subjects with later onset of psychosis, but not among those with recent onset of illness. Previous studies suggested that the association between cognitive impairments and psychosis might be weaker during early onset of illness (Bilder et al., 2000; Daban et al., 2002; Ventura et al., 2015), suggesting that illness progression could change the relationship between psychotic symptoms and cognitive impairment (Daban et al., 2002). It is possible that acute psychotic symptoms may be influenced by factors other than cognitive deficits (Ventura et al., 2015) and that the association between cognitive impairments and psychosis dimensions might arise after acute episode effects have resolved (Daban et al., 2002; Ventura et al., 2015). Probably, in the association between childhood adversities and psychotic symptoms, cognitive impairments might influence mostly the severity and maintenance of psychotic symptoms rather than their onset. Furthermore, we observed that the association between early adversities, cognition, and psychosis is more apparent in younger subjects (e.g. 15–29 years old) compared to those aged 30 or over. These findings might be explained by age differences in the clinical presentation of psychosis, psychotic symptoms being less severe in older patients than in the younger ones (Folsom et al., 2006; Schultz et al., 1997).

Finally, we found that childhood abuse and childhood neglect were associated with more severe psychotic symptoms. This result is consistent with Heins et al. (2011) as well as with the literature according to which patients with psychotic disorder with a history of childhood adversities, compared to those not exposed to childhood adversities, have greater severity of psychopathology and greater degree of persistence of symptoms (Cotter et al., 2015; Faravelli et al., 2017; Trotta et al., 2015; van Nierop et al., 2016). This means that childhood adversities may have a 'pathoplastic effect' once the disorder is developed (Birnbaum, 1923; Furukawa et al., 1998). These findings may enrich the debate about the use of a stratified medicine approach (Kapur et al., 2012) in psychiatric research and in clinical practice.

Several methodological limitations should be considered. Although we assessed a broad range of neurocognitive functions, the assessments may not reflect the daily cognitive functioning of the patients; standard cognitive batteries may be insufficient to measure real-world functioning and a more ecological approach might be warranted (Burgess, 2000; Burgess et al., 2006; Chaytor and Schmitter-Edgecombe, 2003; Damasio, 1995; Lamberts et al., 2010). Recent findings showed that other aspects of social cognition, such as emotion recognition (Bilgi et al., 2017; Kilian et al., 2017), might be involved in the association between childhood adversities and psychosis. Unfortunately, we did not investigate these further aspects; future studies are warranted. Moreover, although we assessed psychotic symptoms according to the classification proposed by van der Gaag et al. (2006a,b), we did not focus on specific positive symptoms. Future investigations are warranted to explore the role of cognition in the relationship between early adversities and specific positive symptoms. Another limitation of our study is the large attrition rate (~30%). Patients with more severe impairments did not or could not answer the childhood trauma questionnaire. Thus, the present results should be interpreted with caution and generalized only to patients with mild or moderate psychosis. Moreover, childhood adversities were assessed using subjective retrospective report, thus recall may have influenced the results, although the research suggests a good reliability of retrospective childhood adversity assessment procedures (Fisher et al., 2011). Another limitation is that this is a cross-sectional study; correlational data allow evaluation of the association between early adversity, cognition, and psychosis, without causal inferences. On the basis of the literature (Read et al., 2014), the present findings allow to hypothesize that childhood adversity, cognitive, and psychotic domains correlate. Longitudinal studies (Berthelot et al., 2015) are warranted. We aim at using the follow-up data collected in the framework of the GROUP database to extend the present findings.

Strengths of the current study are: (a) the large sample size; (b) the focus on childhood neglect and abuse rather than the broader concept of childhood adversity, thus reducing interpretative biases; (c) the assessment of psychotic dimensions consistently with a 'symptoms approach' which, according to some authors, is preferable to operational diagnostic criteria (Ajnakina et al., 2016; Costello, 1992; van Os et al., 1999).

In conclusion, neurocognition and ToM might be involved in the association between childhood adversities and psychosis, although mostly within males. From a clinical point of view, some recommendations may be formulated. The possible mediating role of neurocognition and mentalizing abilities between childhood adversities and psychosis suggests that cognition may act as a protective factor mitigating the effect of childhood neglect and abuse on the persistence of psychotic symptoms, as reported earlier (Bartels-Velthuis et al., 2011). Thus, treatment aimed to improve neurocognitive and mentalizing abilities should be considered in male patients with a psychotic disorder with a history of childhood neglect and/or abuse. Future research should clarify the potential pathways linking childhood adversities to psychotic symptoms within females and in patients with a recent onset of psychotic disorder.

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Conflict of interest

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Giovanni Mansueto: Writing - original draft, Formal analysis. **Koen Schruers:** Supervision. **Fiammetta Cosci:** Writing - review & editing. **Jim van Os:** Supervision.

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