

Childhood Maltreatment and Its Association with Cognitive Ability in Young People Suspected to Be at Clinical High Risk of Psychosis

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Keywords

Physical abuse · Verbal memory · Processing speed · Clinical high risk for psychosis · Childhood maltreatment

Abstract

Introduction: Childhood maltreatment is associated with both reduced cognitive functioning and the development of psychotic symptoms. However, the specific relationship between childhood maltreatment, cognitive abilities and (pre) psychotic symptoms remains unclear. Therefore, the aim of this study was to investigate the association between childhood maltreatment and tasks of verbal memory and processing speed in a help-seeking sample of an early detection of psychosis service. **Methods:** A total of 274 participants consisting of 177 clinical high risk (CHR) for psychosis subjects and 97 clinical controls (CC) with subthreshold CHR underwent a battery of neurocognitive assessments measuring the latent variables verbal memory and processing speed. Additionally, the Trauma and Distress Scale (TADS) was administered to assess varying childhood maltreatment subtypes. Structural equation modeling (SEM) was used to examine associations between verbal memory, processing speed, and maltreatment subtypes. Other factors in the model were age, gender, clinical group (CHR or CC), and the presence of different CHR criteria. **Results:** Physical abuse

was associated with lower scores in verbal memory and processing speed. The explained variance in the SEM reached up to 9.5% for verbal memory and 24.9% for processing speed. Both latent variables were each associated with the presence of cognitive-perceptive basic symptoms. Lower verbal memory was additionally associated with the clinical high-risk group, and processing speed capacity was associated with higher age and female gender. **Conclusion:** Childhood physical abuse in particular was associated with poorer performance on verbal memory and processing speed across both groups of CHR and CC with subthreshold CHR symptoms. This adds to the current literature on reduced cognitive abilities when childhood maltreatment had occurred, albeit subtype dependent. Our findings, together with high prevalence rates of childhood maltreatment in patients with psychosis or CHR states, along with the presence of cognitive deficits in these patients, highlight the importance of not only assessing cognition but also childhood maltreatment in managing these patients. Future research should investigate the specific biological mechanisms of childhood maltreatment on verbal memory and processing speed in CHR subjects, as neurobiological alterations might explain the underlying mechanisms.

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Introduction

Interpersonal relationships are considered foundational to human existence. They have been found to improve health and well-being including reducing the risk of mortality, and act as a buffer against stress [1]. Conversely, interpersonal relationships can also have a negative impact on the individual, and this is particularly the case with childhood maltreatment [2]. In studies of psychological development, the child is seen not as an isolated unit, but as a social being, forming part of a network of relationships [3]. Typically, children interact daily with a variety of people including parents, siblings, and from time to time with relatives and friends, and these close relationships can have a significant impact over the life span [3–5]. However, most maltreatment for children begins at home and the vast majority of people (about 80%) responsible for child maltreatment are the child's own parents [6]. Childhood maltreatment can be subdivided into physical, emotional, or sexual abuse and emotional or physical neglect [7]. In a study from a German population, prevalence rates for physical abuse were 12.0%, emotional abuse 10.2%, sexual abuse 6.2%, emotional neglect 13.9%, and physical neglect 48.4% [8]. Childhood maltreatment is a serious issue for public health and society, with long-lasting consequences in several domains, such as mental and physical health [9–11].

According to Briere's (1996) self-trauma model, disruption to the child's development – including cognitive development – is a result of abusive experiences suffered by the child [2, 12]. In line with this model, research demonstrates that childhood maltreatment affects the individual's neurodevelopment, thereby decreasing brain function and size, leading to lower intelligence quotient and school performance [9]. More specifically, childhood maltreatment leads to poorer performance in memory, and executive and emotional functioning [13, 14], and trauma severity correlates with poorer general knowledge, lower processing speed, and impaired executive functions [15]. Further, verbal declarative memory has been found to be impaired in patients who experienced childhood maltreatment [16].

Moreover, specific neurodevelopmental effects from childhood maltreatment appear to be related to specific mental disorders, including psychosis. For example, semantic fluency, delayed visual recall, and visuospatial working memory were declined in a group of patients with first-episode psychosis with childhood maltreatment compared to a first-episode psychosis group without childhood maltreatment when controlled for pre-

morbid intelligence quotient [17]. Indeed, significant associations have been found between childhood abuse and psychosis, and various directions and mechanisms between maltreatment and psychosis have been posited [18, 19]. Traumatic experiences are found to be prevalent among patients with psychosis [20] and considered a risk factor for the development of a psychotic disorder [21–23].

Related findings with childhood maltreatment have been reported in subjects that are at clinical high risk (CHR) for psychosis, e.g., they have a higher risk of developing a full-threshold psychosis than subjects without a CHR state [24–28]. The majority of first-episode psychotic disorders are preceded by a prodromal phase in which a multitude of CHR symptoms, other mental health problems, psychosocial deficits, and neurobiological alterations associated with cognition may occur, and during which help may be sought [29–35]. In a review, a lifetime history of childhood maltreatment was found in up to 80% of youth with a CHR state [28], and in a meta-analysis, a mean prevalence rate of maltreatment was found in 87% of CHR subjects [27]. Further, adolescents with CHR symptoms demonstrated poor performance in tasks of verbal memory and processing speed compared to subjects without CHR symptoms [36–39]. Verbal memory and processing speed in particular have been shown to be useful in discriminating CHR from healthy controls [40–42] and were therefore chosen as the cognitive domains of focus for the current study.

Childhood maltreatment appears to impact cognitive functioning and is associated with the development of psychotic symptoms. However, the specific relationship between childhood maltreatment, cognitive abilities, and (pre)psychotic symptoms remains unclear. Therefore, the aim of this study was to investigate the association between childhood maltreatment and tasks of verbal memory and processing speed in subjects of an early detection of psychosis unit.

Materials and Methods

Participants

Subjects seeking help for mental problems at the Bern Early Recognition and Intervention Center for Mental Crisis (FETZ Bern; www.upd.ch/fetz; for further details see [43]) between November 2009 and October 2020 were included in the study. As required by the Local Ethics Committee, all participants and, in the case of minors, their legal guardians with the child's assent, gave written informed consent for their coded clinical data to be used in scientific analyses and publications (ID PB_2016-01991). Individuals with various psychiatric symptoms were admitted to the

FETZ Bern by physicians, psychosocial institutions or of their own initiative, whenever there was clinical suspicion for a developing psychotic disorder. The FETZ Bern is the only early detection and intervention center for psychosis in the Canton of Bern, Switzerland (1.035 mil population), screening approximately 80 patients per year (ages 8–40 years) according to the European Psychiatric Association (EPA) guidelines [34, 35]. The FETZ Bern targets help-seeking persons with putative psychotic symptoms or CHR symptoms between 8 and 40 years of age. Exclusion criteria are: (i) past clinical diagnosis of any psychotic disorder according to DSM and ICD; (ii) diagnosis of delirium, dementia, amnesic, or other neurological disorders; and (iii) general medical conditions affecting the central nervous system. After the diagnostics, the subjects of the current study were assigned to either the CHR group or the clinical controls (CC) group. Subjects of the CHR group fulfill at least one of the EPA criteria and CC might exhibit some CHR symptoms, but did not fulfill the onset and frequency requirements for CHR criteria. Subjects who already had a first-episode psychosis were excluded due to possible confounding with disease chronicity and medication affecting cognitive performance, and also because they were already beyond a CHR state.

Assessment

Participants were assessed as part of routine intake assessments by clinical psychologists using structured and semistructured interviews, questionnaires, and a cognitive test battery [43].

Measures

CHR Assessments

CHR symptoms and criteria according to the EPA [35] were employed as clinical interviews. UHR criteria [44] were evaluated with the Structured Interview for Psychosis-Risk Syndromes (SIPS) [45] and the early version of the Comprehensive Assessment of At-Risk Mental States (CAARMS) [46]. The SIPS/CAARMS assesses the presence of APS, B(L)IPS, and GRFD.

Basic symptom criteria [47] including cognitive-perceptive basic symptoms (COPER) and cognitive disturbances (COGDIS) were assessed using the Schizophrenia Proneness Instruments (SPI-A/SPI-CY) [48, 49]. The basic symptoms are self-experienced subclinical disturbances in thought, speech, and perception, which are barely perceived by others. The basic symptom criteria are 14 such disturbances that can be allocated to COGDIS and/or COPER.

All interviewers underwent intensive training for 3 months prior to diagnosing patients according to the respective criteria and underwent continued supervision of ratings during the diagnostic process. A detailed description of the interviews and the EPA guidelines can be found in online supplementary Table S1 and S2 (for all online suppl. material, see www.karger.com/doi/10.1159/000524947).

Trauma and Distress Scale

The Trauma and Distress Scale (TADS) is a self-report questionnaire with 43 questions for childhood maltreatment with the subscales physical abuse, emotional abuse, sexual abuse, emotional neglect, and physical neglect, ranging from 0 = “never,” 1 = “rarely,” 2 = “sometimes,” 3 = “often,” to 4 = “almost always” with a maximum value of 20 for each subscale [50]. The TADS was found to be a reliable ($\alpha = 0.94$) questionnaire [7].

Verbal Learning and Memory Test

To assess verbal memory, the Verbal Learning and Memory Test (VLMT) [51], a German version of the Auditory Verbal Learning Test [52], was used. The VLMT is a brief, easily administered, pencil-and-paper measure that assesses immediate memory span, learning capacity, susceptibility to interference, and recognition memory. The VLMT consists of 15 nouns (List A) that are read aloud for five consecutive trials (Trial 1: immediate memory span), and each trial is followed by a free-recall test. On completion of Trial 5 (Trials 1–5: learning capacity), an interference list of 15 words (List B) is presented, followed by a free-recall test of that list. Immediately after this, delayed recall of the first list is tested (Trial 6) without further presentation of the words. After a 20-min delay period, the participant was again required to recall words from List A (Trial 7). After this, a matrix array was tested, in which the individual must identify List A words from a list of 50 words (recognition memory) containing all items from List A and B and 20 words phonemically or semantically similar to those in List A and B. Correct answers are used as outcome variables (max. 15 in the Trials 1, 6, 7, List B, and recognition memory and max. 75 sum of Trials 1–5 [learning capacity]).

Trail Making Test

The Trail Making Test (TMT) is a paper-pencil test, which requires the subjects to connect randomly arranged numbers in a numerical order in part A, and numbers and letters in numerical and alphabetical orders in part B, alternating between numbers and letters. The outcome variables are the time for task completion in seconds [53].

Digit Symbol Substitution Test

The Digit Symbol Substitution Test (DSST) is a clinical tool in neuropsychology to measure processing speed [54]. Sometimes the DSST is also termed “coding” or “symbol coding,” and the test paradigm has survived with minor alterations to the most recent version found in the Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Intelligence Scale for Children (WISC). We used the DSST subtest from the WISC-IV [55] and WAIS-III [56] to assess processing speed. It is a paper-pencil test in which subjects match symbols to numbers according to a key from 1 to 9. The task is to draw the symbols in boxes under numbers as fast and as accurately as possible. The number of correct symbols after 120 s is counted. The maximum number of correct symbols can be 119 for children and 133 for adults.

Data Analysis

For interval-scaled variables to test for normal distribution, we used the Shapiro test, and for homogeneity of variance, we used Levene’s test. No homogeneity of variances was achieved. Therefore, a nonparametric test was used. Differences between groups were assessed using χ^2 tests for nominal data and Mann-Whitney U tests for the nonnormally distributed interval or ordinal data. Fisher’s exact tests were used when any cells from the χ^2 tests contained less than five observations. As nonparametric tests are distribution free, no data transformation techniques were used. No corrections for multiple comparisons were applied [57]. Further, we used structural equation modeling (SEM) that has several benefits over traditional multivariate techniques, such as the explicit assessment of measurement error and the estimation of latent (unobserved) variables, and model testing and data fitting [58]. Prior

Table 1. Sociodemographic and clinical characteristics of the sample

	Total N = 274	CHR n = 177	CC n = 97	Statistical values ^a
Age (mean ± SD, median, range)	18.2±4.6, 17.3, 08.9–37.6	17.9±4.2, 17.2, 09.5–36.4	18.9±5.1, 17.8, 08.9–37.6	U = 7,685, p = 0.152, r = 0.087
SOFAS score (mean ± SD)	61.4±12.3	60.4±12.0	63.5±12.7	U = 6,894, p = 0.073, r = 0.110
Gender, male, n, %	154	90	64	χ ² ₍₁₎ = 5.230, p = 0.022, V = 0.138
Nationality, Swiss, n, %	240	154	86	χ ² ₍₁₎ = 0.042, p = 0.837, V = 0.012
Highest ISCED score (3 ab), n, %	63	39	24	χ ² ₍₃₎ = 2.268, p = 0.484, V = 0.091
Currently employed or in training/school, n ^b , %	242	159	83	χ ² ₍₁₎ = 0.730, p = 0.393, V = 0.051
Current alcohol misuse, present, n, %	10	6	4	χ ² ₍₁₎ = 0.006, p = 0.738, V = 0.004
Current drug misuse, present, n, %	22	16	6	χ ² ₍₁₎ = 0.188, p = 0.664, V = 0.027
Any current axis-I disorder, n, %	141	104	37	χ ² ₍₁₎ = 9.849, p = 0.002, V = 0.189
Any affective disorder (F30–F39)	106	82	24	χ ² ₍₁₎ = 11.415, p ≤ 0.001, V = 0.204
Any anxiety disorder (F40–F41)	47	39	8	χ ² ₍₁₎ = 7.439, p = 0.006, V = 0.165
Any eating disorder (F50)	8	5	3	χ ² ₍₁₎ = 0.000, p = 1.000, V = 0.000
An obsessive-compulsive disorder (F42)	14	6	8	χ ² ₍₁₎ = 2.571, p = 0.109, V = 0.100
A posttraumatic stress disorder (F43.1)	4	4	0	χ ² ₍₁₎ = 0.819, p = 0.304, V = 0.057
UHR and BS, n, %				
APS		90		
B(L)IPS		6		
COPER		105		
COGDIS		63		
TADS score (mean ± SD)				
Physical abuse	2.2	2.4	1.8	U = 8,661, p = 0.069, r = 0.113
Emotional abuse	5.3	5.9	4.3	U = 9,149, p = 0.009, r = 0.163
Sexual abuse	1.1	1.2	0.8	U = 8,334, p = 0.077, r = 0.110
Emotional neglect	6.5	6.9	5.6	U = 8,871, p = 0.033, r = 0.133
Physical neglect	4.6	4.9	3.9	U = 9,069, p = 0.013, r = 0.155
Verbal memory correct answers (mean ± SD)				
VLMT recall Trial 1	7.4	7.2	7.9	U = 6,136, p = 0.020, r = 0.145
VLMT recall Trial 1–5	55.8	54.8	57.8	U = 6,174, p = 0.036, r = 0.131
VLMT recall interference (List B)	6.9	6.9	7.0	U = 7,066, p = 0.513, r = 0.041
VLMT recall Trial 6	12.1	12.1	12.3	U = 7,102, p = 0.555, r = 0.037
VLMT delayed recall Trial 7	12.3	12.2	12.5	U = 6,928, p = 0.366, r = 0.057
VLMT recognition	14.5	14.5	14.5	U = 7,300, p = 0.771, r = 0.018
Processing speed (mean ± SD)				
Trail Making Test A, s	25.9	26.5	24.8	U = 8,446, p = 0.104, r = 0.101
Trail Making Test B, s	59.9	62.6	54.8	U = 8,683, p = 0.027, r = 0.138
Digit Symbol Substitution Test (number correct)	69.9	69.1	71.4	U = 7,115, p = 0.478, r = 0.443

CHR, clinical high risk; CC, clinical controls; SOFAS, Social and Occupational Functioning Assessment Scale of DSM-IV; ISCED, International Standard Classification of Education; UHR, ultra-high risk; BS, basic symptoms; APS, attenuated positive symptoms; B(L)IPS, brief (limited) intermittent psychotic symptoms; COPER, cognitive-perceptive basic symptoms; COGDIS, cognitive disturbances; TADS, Trauma and Distress Scale, each subscale with a maximum of 20; VLMT, Verbal Learning and Memory Test, maximum of correct answers is 15 per trial. ^a Effect sizes reported as Cramer's V for χ² tests and Fisher's exact tests and r for Mann-Whitney U tests; 0.1 equals a small effect, 0.3 a medium effect, and 0.5 a large effect. ^b Includes sheltered employment, temporary employment, and regular full- and part-time employment (including schooling, academic studies, occupational training, full-time house work).

Table 2. Spearman correlation matrix between model variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1 Physical abuse	–																		
2 Emotional abuse	0.53***	–																	
3 Sexual abuse	0.35***	0.14*	–																
4 Emotional neglect	0.47***	0.71***	0.14*	–															
5 Physical neglect	0.50***	0.52***	0.06	0.66***	–														
6 VLMT recall Trial 1	–0.19**	0.04	–0.08	–0.02	–0.09	–													
7 VLMT recall Trials 1–5	–0.17**	0.02	–0.09	0.01	–0.03	0.77***	–												
8 VLMT recall interference list B	–0.14*	–0.01	–0.04	–0.04	–0.04	0.42***	0.53***	–											
9 VLMT recall Trial 6	–0.13*	0.00	–0.07	0.03	–0.05	0.51***	0.76***	0.40***	–										
10 VLMT delayed recall Trial 7	–0.10	0.02	–0.04	0.04	–0.06	0.56***	0.77***	0.46***	0.86***	–									
11 VLMT recognition	–0.10	–0.03	0.01	0.00	–0.07	0.28***	0.44***	0.24***	0.51***	0.54***	–								
12 Trail Making Test A	0.08	0.01	0.05	0.05	0.06	–0.22***	–0.24***	–0.16*	–0.16*	–0.13*	–0.08	–							
13 Trail Making Test B	0.13*	0.06	0.04	0.05	0.07	–0.13*	–0.21***	–0.07	–0.15*	–0.13*	–0.10	0.67***	–						
14 Digit Symbol Substitution Test	–0.19**	0.01	–0.01	–0.03	–0.09	0.35***	0.38***	0.26***	0.30***	0.28***	0.09	–0.32***	–0.21***	–					
15 Group	–0.11	–0.16**	–0.11	–0.13*	–0.16*	0.15*	0.13*	0.04	0.04	0.06	0.02	–0.10	–0.14*	0.04	–				
16 Age	–0.02	0.02	–0.01	0.06	0.04	0.15*	0.18**	0.05	0.18**	0.15*	–0.03	0.18**	0.25***	0.47***	0.09	–			
17 Gender	0.01	0.06	0.23***	0.02	–0.15*	0.05	0.07	0.06	0.15*	0.14*	0.07	0.01	0.00	0.15*	–0.15*	–0.10	–		
18 COGDIS	0.09	0.21***	0.09	0.22***	0.12	–0.10	–0.02	–0.10	0.09	0.01	0.05	0.13*	0.03	0.03	–0.39***	0.05	0.12	–	
19 COPER	0.14*	0.20**	0.07	0.25***	0.20**	–0.02	0.03	–0.05	0.06	0.01	0.04	0.08	0.03	0.09	–0.57***	0.06	0.03	0.53***	–
20 APS	–0.08	0.04	–0.03	0.04	–0.02	–0.14*	–0.09	0.01	0.01	0.01	–0.09	0.00	0.06	–0.01	–0.52***	–0.07	0.12*	0.33***	0.18**

VLMT, Verbal Learning and Memory Test; COGDIS, cognitive disturbances; COPER, cognitive-perceptive basic symptoms; APS, attenuated positive symptoms. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

to SEM and based on the previous literature on cognition in CHR states [40, 42, 59, 60], we defined the following latent variables: verbal memory consisting of the subtasks of the VLMT (correct words Trial 1, learning capacity in Trials 1–5, Trial 6, and recognition memory); processing speed consisting of the TMT-A, TMT-B, and DSST; and childhood maltreatment consisting of the TADS variables' physical abuse, emotional abuse, sexual abuse, emotional neglect, and physical neglect. We computed orthogonal confirmatory factor analyses with varimax rotation based on polychoric correlation matrices for processing speed, verbal memory, and childhood maltreatment. The explained variances for verbal memory and processing speed as latent variables and the model fit from the SEM were investigated from childhood maltreatment in the first step and then added with covariates [61]. Subsequent variables were included that were considered to have an impact on the cognitive latent variables, such as age, gender, clinical group (CHR or CC), the presence of APS, COPER, and COGDIS as dichotomous variables [62, 63]. Education was not used in the model, as it has been shown that it has little effect when age is already included as variable [64, 65].

We assessed the model fit with five indices: the χ^2 test, comparative fit index (CFI), Tucker-Lewis index (TLI), root-mean-square error of approximation (RMSEA) including 90%-confidence interval (90% CI), and standardized root mean square residual (SRMR). A nonsignificant χ^2 test, CFI ≥ 0.95 , TLI ≥ 0.95 , RMSEA ≤ 0.06 (90% CI should not contain 0.08), and SRMR ≤ 0.08 indicate a good model fit [66, 67]. We focused on CFI, TLI, RMSEA, SRMR, and RMSEA because the χ^2 test is sensitive to different conditions that can yield false significant results [61]. Analyses were conducted with RStudio Version 1.2.5042 and the lavaan package for R (R Core Team) [68].

Results

Participants ($N = 274$) were aged between 8 and 37 years (inclusive) with a mean age of 18.24 years (SD 4.57) and comprised 120 females (44%) and 154 males (56%). One hundred and seventy-seven participants were identified as CHR, and 97 as CC. Table 1 shows the sociodemographic and clinical characteristics of the sample as well as the means and standard deviations from the model variables, and Table 2 shows the bivariate correlations of the included variables for the model.

The initial model started with only the association of childhood maltreatment and verbal memory and processing speed as latent variables (online suppl. Fig. S1). The model fit indices were as follows: $\chi^2_{(74)} = 113.613$, $p = 0.002$; CFI = 0.971; TLI = 0.965; RMSEA = 0.047 (90% CI = 0.029–0.063); SRMR = 0.077, with explained variances for verbal memory of $R^2 = 0.4\%$ and processing speed of $R^2 = 2.6\%$. Childhood maltreatment was neither associated with verbal memory ($\beta = -0.060$, $p = 0.371$) nor processing speed ($\beta = -0.161$, $p = 0.099$).

However, when different forms of maltreatment (emotional neglect/abuse, physical neglect/abuse, sexual abuse) were separated and entered into the model, the bivariate correlations between the TADS and the VLMT, TMT-A/B, and DSST showed significant correlations for physical abuse (Table 2). Therefore, the nonsignificant childhood maltreatment variables were dropped and the next model yielded the following model fit indices: $\chi^2_{(33)} = 57.413$, $p = 0.005$; CFI = 0.976; TLI = 0.968; RMSEA = 0.055 (90% CI = 0.030–0.078); SRMR = 0.079, with explained variances for verbal memory of $R^2 = 3.1\%$ and processing speed of $R^2 = 4.0\%$ (online suppl. Fig. S2). Here, physical abuse was associated with verbal memory ($\beta = -0.177$, $p = 0.011$) and processing speed ($\beta = -0.200$, $p = 0.017$).

As the explained variance for verbal memory and processing speed was low with only physical abuse, age, gender, and clinical group, the dichotomous variables of APS, COPER, and COGDIS were added to the model. The model fit was as follows: $\chi^2_{(75)} = 143.817$, $p < 0.000$; CFI = 0.938; TLI = 0.918; RMSEA = 0.061 (90% CI = 0.046–0.076); SRMR = 0.073, with explained variances for verbal memory of $R^2 = 8.3\%$ and processing speed of $R^2 = 12.3\%$. Physical abuse was associated with verbal memory ($\beta = -0.172$, $p = 0.021$) and processing speed ($\beta = -0.191$, $p = 0.024$). With all the variables, the explained variance was higher for verbal memory and processing speed, but the model fit was not sufficient (online suppl. Fig. S3).

When removing the three nonsignificant variables (VLMT delayed recall, VLMT recognition, and TMT-A) with physical abuse (Table 2), the model fit yielded the following results: $\chi^2_{(36)} = 52.554$, $p = 0.037$; CFI = 0.972; TLI = 0.955; RMSEA = 0.043 (90% CI = 0.011–0.067); SRMR = 0.050, with explained variances for verbal memory of $R^2 = 9.5\%$ and processing speed of $R^2 = 24.9\%$. This model showed a better fit and explained a higher variance. Higher scores in verbal memory were associated with the presence of COPER ($\beta = 0.197$, $p = 0.020$) and less physical abuse ($\beta = -0.180$, $p = 0.012$) and lower scores with the CHR group ($\beta = 0.207$, $p = 0.024$). A better processing speed capacity was associated with the presence of COPER ($\beta = 0.238$, $p = 0.026$), less physical abuse ($\beta = -0.224$, $p = 0.010$), higher age ($\beta = 0.342$, $p = 0.004$), and female gender ($\beta = 0.209$, $p = 0.020$) (Fig. 1). The other variables COGDIS and APS were neither associated with verbal memory nor processing speed (online suppl. Fig. S4). Differences between groups were found in the distribution of gender (higher prevalence of males in the CC group compared to the CHR group) and the distribution of any current axis-I disorder – especially any

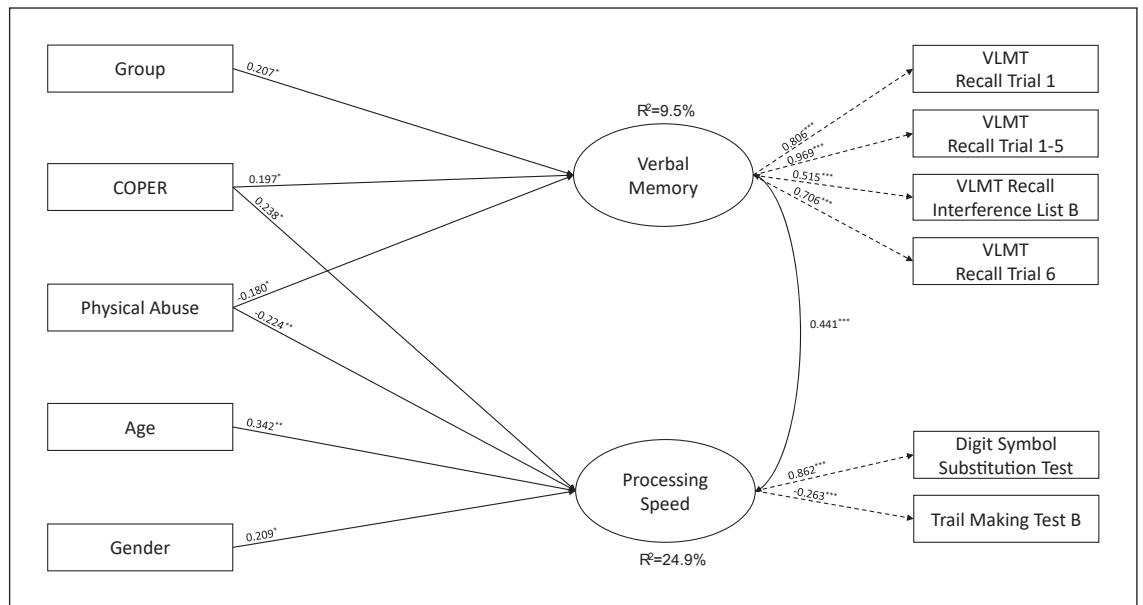


Fig. 1. Results of the model with non-significant associations removed ($n = 274$). Model fit indices: $\chi^2_{(36)} = 52.554$, $p = 0.037$; CFI = 0.972; TLI = 0.955; RMSEA = 0.043 (90% CI = 0.011–0.067); SRMR = 0.050. Explained variance (R^2) for each endogenous variable in *italics*. Note: rectangles represent observed variables; ovals represent unobserved latent variables; rounded arrows represent covariances; straight arrows represent regressions; black arrows represent significant; and dashed arrows represent factor loadings; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. VLMT, Verbal Learning and Memory Test; COPER, cognitive-perceptive basic symptoms.

affective and anxiety disorder – whereby the CHR group had higher prevalence of affective and anxiety disorders, compared to CC. Regarding childhood maltreatment, higher mean scores of emotional abuse, emotional neglect, and physical neglect were found for the CHR group compared to the CC group. Finally, the CHR group yielded fewer correct answers in the VLMT recall Trial 1 and recall Trials 1–5 and were slower in the TMT-B (i.e., higher mean time in seconds), compared to the CC group.

Discussion

The aim of this study was to investigate the association between childhood maltreatment and tasks of verbal memory and processing speed in subjects of an early detection of psychosis unit and thus, with symptoms suggesting a psychotic development. Childhood physical abuse explained variances of verbal memory and processing speed in help-seeking individuals defined as CHR subjects or CC. When the covariates age, gender, clinical group (CHR or CC), and the presence of APS, COPER, and COGDIS were included, the explained variance in

the SEM reached up to 9.5% for verbal memory and 24.9% for processing speed. Higher scores in verbal memory were associated with less physical abuse, the presence of COPER, and lower scores with the CHR group. A better processing speed capacity was associated with less physical abuse, the presence of COPER, higher age, and female gender.

Previous findings in patients across a range of various disorders, including psychosis, and healthy controls on reduced cognitive abilities when childhood maltreatment had occurred [13–17, 69] support our results for the subtype of childhood maltreatment physical abuse. Further, the current study revealed that being in a CHR state was associated with lower scores in verbal memory. This aligns with results for CHR subjects where cognitive impairments have been reported [36–39, 41, 62, 63]. Studies with healthy controls and patients with psychosis showed that patients demonstrated poorer cognitive performance when having had experienced childhood maltreatment and that more childhood maltreatment was associated with more cognitive impairments [70, 71]. Verbal memory in particular has previously been shown to be useful in discriminating CHR from healthy controls and pre-

dicted conversion to psychosis [40, 41, 62]. In addition, CHR subjects show more neurocognitive deficits than CC subjects, indicating that the risk status itself could already produce deficits [43] and this might help explain our current findings. A recently published meta-analysis found that CHR subjects performed worse than healthy controls on a variety of cognitive tasks, converters worse than non-converters, and patients with first-episode psychosis worse than CHR subjects [62], therefore leading to the assumption that more psychotic symptoms lead to more cognitive deficits.

Subtypes of Childhood Maltreatment

In this study, only physical abuse and none of the other abuse or neglect subtypes had an impact on verbal memory and processing speed, suggesting that not all forms of maltreatment affect cognitive ability equally. Subtypes of childhood maltreatment have been found to be associated differently with various psychiatric disorders [72]. More specifically, previous research revealed that the effects of childhood maltreatment subtypes manifest differently on cognitive abilities across patients with varying psychopathologies, including patients with schizophrenia spectrum disorders [13, 20]. Overall, the literature suggests that maltreatment is associated with cognitive impairment, albeit differently for varying cognitive domains and maltreatment subtypes, and this is reflected in the current findings for help-seeking patients with either CHR state or subthreshold symptoms (CC). However, we cannot yet determine why this particular combination of maltreatment subtype and cognitive domain was found.

Other Findings from the Model

Surprisingly, the presence of COPER was associated with higher scores in verbal memory and processing speed, but neither the presence of CODGIS nor APS showed any significant associations. Basic symptoms are generally experienced by the person in a subjective manner, with insight into both their previous standards of cognitive ability and the potential impact on current cognitive abilities [47], and patients often feel distressed by this perceived discrepancy. In an attempt to overcome this, they exert more effort into sustaining their previous cognitive abilities. Perhaps, due to the subjectively perceived cognitive-perceptual impairments of COPER, particularly as they must have been experienced for a longer period of time (COPER requires the presence of symptoms for >1 year), compensatory behavior might have set in whereby participants try to perform well on neurocognitive tasks.

Female gender and higher age were associated with better performance on tasks of processing speed. Females have frequently been found to have higher processing speed than males [73, 74], although opposite [75] and null findings [76] have also emerged. Previous research also shows that higher age leads to faster processing speed, until the age of 30 years [65, 77–79].

Possible Mechanisms Underlying the Childhood Maltreatment, Cognition, and CHR Relationship

The relationship of childhood maltreatment, cognitive ability, and psychotic symptoms is complex and multifaceted, and different mechanisms are involved in mediating the pathways [80–82]. To explain the underlying association of this relationship, several biological systems have been proposed [83–86]. First, the dopamine system in striatal regions might be affected through childhood maltreatment [84, 86], which has already been associated with psychosis and cognition [87–89]. Other systems include oxidation regulation processes, hippocampal volume loss, and alterations in frontal and parietal areas [83, 85]. The possibility of neurobiological alterations due to childhood maltreatment could act as a risk factor in the development of psychosis and lead to secular cognitive decline, and therefore, neuroimaging should be used to further understand these complex relationships.

Clinical Implications

The current study emphasizes the relationship between childhood maltreatment in CHR individuals and its association with verbal memory and processing speed in particular. Such cognitive deficits are associated with global functioning – a persistent problem even in those with (pre)psychotic symptom attenuation/remission [90–93]. In addition, associations have also been found with other cognitive tasks and psychosis, with childhood maltreatment even considered as a risk factor for its development [20, 21, 23], and symptom severity associated with less cognitive achievement [62]. The importance of assessing childhood maltreatment in managing CHR patients has already been emphasized previously [94], and taken together, these suggest that childhood maltreatment may have long-term and far-reaching consequences, and that the assessment of childhood maltreatment (including their subtypes) in CHR subjects is imperative in the early detection and intervention of psychotic disorders.

Strengths and Limitations

Naturally, the current study has various strengths and limitations. The sample size of the current study was large

and consisted of help-seeking subjects, adding to the overall strength. Additionally, the sample consisted of both subjects fulfilling the EPA criteria [35] and CC with subthreshold symptoms, allowing us to explore differences across symptomatic presentation. Clinical interviews and neurocognitive assessments were conducted by clinically trained psychologists, with regular supervision by experts in the field of CHR and early detection of psychosis, ensuring high data quality. The cross-sectional design of the study does not allow conclusions to be drawn regarding causality between childhood maltreatment and verbal memory and processing speed. Additionally, as no longitudinal data were included in the study, and thus no information on the risk of conversion of individual subjects, it might be that the findings are driven by those later converting to fully manifest psychosis. Therefore, our results should be considered preliminary findings. Furthermore, the age at which childhood maltreatment occurred was not assessed, and given that the age of childhood maltreatment modulates psychopathological symptoms [95], and younger subjects could additionally still be exposed to childhood maltreatment, future studies should aim to explore this. Self-rated questionnaires might pose the risk of memory distortion; however, the TADS was proven to be valid, reliable for assessing childhood maltreatment [7]. As it is unclear if subjects with COPER tried harder to perform well than other subjects, or if there is another reason for the finding that subjects with COPER performed better in processing speed and verbal memory, future studies should administer performance validity tests to disentangle this finding. Further, since performance was only assessed formally in two cognitive domains by three tests (DSST, TMT, and VLMT), with generally similar results, it is not clear that the tests emphasizing processing speed or memory actually reflect differential abilities in these domains or a more general type of cognitive response. Future studies should try to administer more tests being part of the same domains to shed some light on this. The somewhat exploratory use of the analysis could be viewed as a limitation because the data-driven approach restricts the generalizability of the results; however, this adaptive procedure is in line with the previous work using SEM [61, 96, 97].

Future Directions and Conclusion

This is the first study to concurrently explore associations between childhood maltreatment subtypes and cognitive abilities in a sample of help-seeking patients with suspected CHR for psychosis. Childhood physical abuse in particular was associated with poorer performance on

verbal memory and processing speed. Childhood maltreatment might have long-lasting, wide-ranging, and varying consequences in different cognitive domains, albeit depending on maltreatment subtype and on psychopathology. The high prevalence of childhood maltreatment in CHR subjects – over 80% – compared with general community prevalence (up to 48%), and the observed cognitive deficits associated with this highlight the importance of assessment of childhood maltreatment subtypes in the early detection of psychosis. Future research should endeavor to explore the specific neurobiological mechanisms of childhood maltreatment on verbal memory and processing speed, especially over longitudinal studies tracking psychosis converters and those who do not convert, but also the development of other severe psychopathological outcomes. This should include structural and functional neuroimaging, as well as information on frequency, severity, and when child maltreatment occurred, to clarify the outcome in the development.

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Statement of Ethics

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation, and with the Helsinki Declaration of 1975, as revised in 2013. This study protocol was reviewed and approved by the Human Research Ethics Committee of the Canton Bern, <https://www.gsi.be.ch/de/start/ueber-uns/kommissionen-gsi/ethikkommission.html>), approval number (ID PB_2016-01991). All participants gave written informed consent, and in minors, parental informed consent was provided.

Conflict of Interest Statement

Drs. Michel and Kindler, Prof. Kaess, and Ms. Bütiger (MSc) have declared no conflicts of interest in relation to the subject of this study.

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Author Contributions

Jessica R. Büetiger wrote the first draft of the manuscript and did the statistical analysis. Dr. Chantal Michel and Prof. Jochen Kindler rewrote sections of the manuscript. Prof. Michael Kaess provided meaningful contributions to the manuscript. All authors contributed to the article and approved the submitted version.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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