

Perceived Discrimination Moderates The Relationship Between Childhood Adversities and Cognitive Performance In Mental Illness

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Abstract

Childhood adversities and trauma (CAT) are linked to cognitive impairment, but their effects may vary across clinical profiles and in the presence of ongoing environmental stressors. We investigated CAT-cognition associations across recent-onset psychosis (ROP), clinical high risk for psychosis (CHR), recent-onset depression (ROD), and healthy controls (HC), and whether recent life events and perceived discrimination moderated these associations. We used baseline data from the PRONIA cohort (ROP: N = 150; CHR: N = 142; ROD: N = 148; HC: N = 282). Cognitive performance was assessed across social cognition, speed of processing, working and verbal memory, attention, and global cognition. Associations were tested using covariate-adjusted linear regression models based on HC-derived normative residualization, followed by moderation analyses. In ROP, higher CAT were associated with increased speed of processing ($\beta = 0.29$, $p_{\text{fdr}} = .046$). In CHR, CAT was associated with poorer social cognition, but higher attention and working memory scores ($b = -0.20$ to 0.44 , $p_{\text{fdr}} \leq .042$). In HC, increased physical neglect was associated with poorer attention ($b = -0.64$, $p_{\text{fdr}} < .001$). Perceived discrimination moderated associations between emotional abuse and attention in the ROP group ($\beta = -4.721$, 95% CI [-7.81, -1.63]), and between emotional abuse and social cognition in the ROD group ($\beta = 7.834$, 95% CI [2.430, 13.238]). CAT-cognition associations were heterogeneous across clinical groups, with perceived discrimination moderating specific associations. Relationships between CAT, particularly emotional neglect, and cognitive performance is not uniform but may vary depending on clinical context and ongoing psychosocial stressors.

Introduction

Childhood adversities and trauma (CAT), and burden of recent life events are highly prevalent among individuals with mental health disorders (1, 2). A large body of evidence indicates that CAT substantially increases the risk of developing psychosis (3), and predicts transition to psychosis specifically in individuals at clinical high risk (CHR) (2, 4). CAT has been widely implicated in cognitive functioning, suggesting a potential pathway through which it may affect cognitive outcomes in psychosis (5, 6), psychosis risk (7), and depression (8). However, findings vary according to trauma type, timing, and clinical population (5, 6). As compared with healthy controls (HC), who showed intact cognitive performance on average, individuals with mental disorders demonstrated a graded pattern of cognitive impairment, with relatively preserved performance in recent-onset depression (ROD), intermediate impairments in CHR groups, and the greatest impairments in recent-onset psychosis (ROP) across all cognitive domains (9).

Current evidence suggests that CAT exposure in individuals with psychosis is linked to reduced cognitive performance (10), especially in working memory (11), processing speed (6), executive functioning (12), and attention (13). While CAT is a well-established risk factor for the development of psychosis and is associated with poorer clinical outcome alongside cognitive, and neurobiological alterations in schizophrenia and individuals at ultra-high risk (14), burden of recent life events and perceived discrimination occurring later in life have additionally been linked to an increased risk of relapse in ROP

(15, 16), highlighting the potential role of later environmental stressors in interacting with earlier childhood adversity to influence cognitive functioning.

Reported findings regarding the association between CAT and cognition in CHR are mixed. Individuals at CHR for psychosis commonly demonstrate baseline cognitive impairments across several domains (7), which may interact with CAT to shape symptom expression and transition to psychosis (17, 18). For instance, some studies report that exposure to physical trauma is linked to markedly decreased performance in working memory and attention (19), whereas others suggests that individuals at CHR with histories of multiple CAT subtypes, especially emotional abuse and emotional neglect, may exhibit increased overall cognitive performance than those with no or minimal trauma exposure (20). Beyond childhood adversity, recent life events have also been implicated in cognitive and clinical outcomes. For example, a greater cumulative stress burden and increased negative symptoms compared with HC were present in an adolescent CHR sample (21). whereas, perceived discrimination (22) and burden of recent life events² have been associated with poorer cognitive performance.

CAT has also been strongly linked to the onset, severity, and recurrence of major depressive disorder (23). Beyond its association with psychopathology, CAT is also linked to cognitive functioning, as individuals with ROD exhibit impairments in processing speed, memory, executive functioning, verbal fluency, and general intelligence, with persistent deficits in verbal fluency even following remission (24). Similarly cognitive and biological models suggest that burden of recent life events may contribute to cognitive vulnerability in depression (25).

Associations between CAT and poorer cognitive performance have been reported in non-clinical populations, with HC samples demonstrating impairments in executive functioning, processing speed, and working memory (26). Furthermore, studies conducted in non-clinical populations showed that greater exposure to everyday discrimination and cumulative life stress was linked to poorer cognitive performance, particularly in working memory and cognitive flexibility (27–30).

CAT may shape long-term vulnerability in stress and cognitive processing systems, while later burden of recent life events and perceived discrimination may act as additional acute stressors that increase cognitive and emotional load, thereby amplifying attentional and cognitive control demands (5, 31–33). Therefore, individuals with a history of CAT may respond differently to recent stressors than individuals without such experiences. However, no studies have directly investigated whether the burden of recent life events and discriminatory experiences moderate the association between CAT and cognitive performance.

Yet, although CAT and recent adversities are each associated with cognitive impairment (34), little is known about whether burden of recent life events and discriminatory experiences possibly moderate the association between CAT and cognitive performance. This study aims to investigate potential moderation effects of burden of recent life events and discriminatory experiences between CAT and cognitive performance and how they differ between individuals with ROP, CHR, ROD, and HCs.

Methods

Sample

We used baseline data from the Personalised Prognostic Tools for Early Psychosis Management (PRONIA) Study, European Union the 7th Framework Programme. We included individuals with ROP (N = 150, mean age 25.5 ± 5.52 years, female/male = 60/90), individuals at CHR for psychosis (N = 142, 23.8 ± 4.98 years, 71/71), individuals with ROD (N = 148, 26.2 ± 6.17 years; 78/70), and HC (N = 282, 25.5 ± 6.38 years, 172/110). Information on demographic and clinical characteristics can be found in Supplementary Table 1.

Inclusion and Exclusion Criteria

Inclusion required age 15-40 years, and adequate language skills. General exclusion criteria were IQ < 70, relevant neurological or somatic illness, head trauma with >5-minute loss of consciousness, recent alcohol or polysubstance dependence, and any MRI contraindication. For HC participants, additional exclusion criteria were a current or past affective or non-affective psychotic disorder, having a first-degree relative with a psychotic spectrum disorder, the presence of other psychiatric conditions, psychotropic medications intake for more than 5 times/year and/or in the month before participation to the study.

CHR participants had to meet any of the adapted Ultra High Risk (UHR) criteria and/or the Cognitive Disturbances (COGDIS) criterion (35); treatment with any antipsychotic medication at or above the minimum dosage threshold defined by the DGPPN S3 Guidelines for the treatment of first-episode psychosis (36) for either more than 30 days or within the past 3 months before baseline assessment was an exclusion criterion for the CHR group.

The ROP group included participants who fulfilled the DSM-IV-TR (37) criteria for an affective or non-affective psychotic episode at any point in their lifetime, had experienced a psychotic episode within the past three months, and had an onset of the first episode of psychosis within the past 24 months. Exclusion criteria for the ROP group included treatment with antipsychotic medication for longer than 90 cumulative days at or above the minimum dosage for first-episode psychosis, as defined by the German Association for Psychiatry, Psychotherapy and Psychosomatics DGPPN S3 guideline (36).

For the ROD group exclusion criteria included: (1) any prior episode of major depression as defined by the DSM-IV-TR (37) before the current or most recent episode, and (2) a current depressive episode lasting longer than 24 months. RODs with an additional CHR status were included in the analysis as CHR.

All adult participants provided written informed consent before taking part in the study. For individuals under 18 years of age, written informed assent was obtained, along with written consent from their legal guardians. The study was registered with the German Clinical Trials Register (DRKS00005042) and approval was received from the respective local ethics committees at the seven study sites, Ludwig-

Maximilian University Munich (ethics ID: 351-13), University of Turku (ethics ID: 99/1810/2013), University of Birmingham (ethics ID: 14/WM/0019), University of Milan (ethics ID: N.PROT.0001885 | P | GEN/02), University of Basel (ethics ID: M12/99), University of Turku (ethics ID: 99/1810/2013), and University of Udine (ethics ID: 67172), in five European countries.

Measures

UHR status was assessed using the Structured Interview for Psychosis-Risk Syndromes (SIPS) (38), a semi-structured interview designed to identify psychosis-risk syndromes, including attenuated psychotic symptoms, brief intermittent psychotic symptoms, and genetic risk with functional deterioration. COGDIS was assessed using the Schizophrenia Proneness Instrument, Adult version (SPI-A) (35). Both clinical interviews were conducted by trained raters.

Cognition was assessed using the PRONIA Cognitive Battery (PCB) (9), based on previous literature (39, 40) including evaluation of attention, working memory, processing speed, social cognition, verbal learning and global cognitive score. Domain scores were derived from the raw task outcomes. Social cognition was represented by the number of correctly identified facial emotions on the Diagnostic Analysis of Nonverbal Accuracy (DANVA) (41). Working memory was calculated as the average of forward and backward digit span performance (42). Processing speed was computed as the mean of standardized semantic verbal fluency, Trail Making Test Part A (43), and Digit Symbol Substitution Test scores (42). Verbal learning was calculated as the sum of the five immediate recall trials of the Auditory Verbal Learning Test (44). Attention was defined as the difference between the number of correct responses and distracting errors on the Continuous Performance Test (CPTIP) (45). All domain scores were standardized across participants, and the global cognitive score was calculated as the mean of the five standardized cognitive domain scores, with higher scores indicating better cognitive performance.

CAT was measured using the Childhood Trauma Questionnaire (CTQ) (46). The CTQ is a 25-item self-report questionnaire that assesses 5 types of adversities prior to age of 17 including emotional, physical, and sexual abuse as well as emotional and physical neglect. In PRONIA, burden of life events was recorded with the Cologne Life Event List (CoLE) (47), which includes 117 events spanning 12 domains, such as education, partner, children, death. At each domain, up to ten events are recorded, with interviewers documenting their duration, category, subjective evaluation of burden, and controllability. Perceived discrimination was assessed by the total score of the Everyday Discrimination Scale (EDS) (48).

Statistical analyses

We performed all analyses using R, version 3.6.3 (49). Descriptive statistics comparing characteristics of HC with ROP, CHR, or ROD are presented in Supplementary Table 1. We computed Welch's two sample t-tests for parametric, and χ^2 -tests for categorical data. Raw cognitive test scores were z-standardized and combined into domain scores, which were then averaged to derive a global cognition score. For all analyses, confounding effects were controlled using a three-step residualization procedure (50). First, for

each cognitive outcome, a multifactorial linear regression model was estimated in the HC group, including sex, age and years of education covariates identified within each dataset. Second, this HC-based model was applied to the corresponding cognitive variables in the clinical datasets. Third, residualized scores reflecting deviation from normative cognitive performance were extracted and used in all subsequent analyses.

As cognitive variables were not normally distributed, all residualized scores were log-transformed prior to analysis. Three types of linear regression analyses were performed: (1) within-group analyses, conducted separately for each study group to estimate group-specific associations between CAT and cognitive outcomes; (2) between-group analyses, including an interaction term between CAT and study group to test whether these associations differed across groups; and (3) moderation analyses, including an interaction term between CAT and the moderators, burden of life events and perceived discrimination, to assess whether the association varied as a function of the moderator. P-values were adjusted for multiple comparisons across cognitive outcomes using the Benjamini-Hochberg false discovery rate (FDR) (51) procedure. Statistical significance was set at $p < .05$.

Results

All significant associations between CAT, and cognitive performance in CHR and HC are presented in Figure 1. In the ROP group, increased speed of processing performance was linked with increased emotional neglect ($\beta = 0.29$, $p_{\text{fdr}} = .046$). In the CHR group, poorer social cognition was associated with increased CTQ total scores ($\beta = -0.20$, $p_{\text{fdr}} = .038$), and with an increased rate of emotional neglect ($\beta = -0.17$, $p_{\text{fdr}} = .042$). Additionally, increased attention and working memory performances were associated with increased emotional neglect ($\beta = 0.44$, $p_{\text{fdr}} = .042$; $\beta = 0.18$, $p_{\text{fdr}} = .042$). In HC, poorer cognitive performance in the domain of attention was associated with increased physical neglect ($\beta = -0.64$, $p_{\text{fdr}} < .001$). In the ROD group, associations between CAT and cognitive performance were no longer significant after FDR correction (all $p > .05$). All associations can be found on Supplementary Table 2.

FIGURE 1 HERE

The associations of CAT with cognitive domains in HC compared to ROP, CHR, and ROD groups are presented in Figure 2. Significant interaction terms indicate that the association between CAT and cognition differed between the two groups. Compared with HC, the association between emotional neglect and attention differed in the ROP group ($\beta = 0.31$, $p_{\text{fdr}} = .025$). Similar interaction effects were observed for emotional neglect and processing speed ($\beta = 0.34$, $p_{\text{fdr}} = .014$), and global cognition ($\beta = 0.32$, $p_{\text{fdr}} = .014$), with higher emotional neglect associated with lower cognitive performance in HC but higher cognitive performance in the ROP group. An interaction was also observed between physical neglect and attention ($\beta = 0.39$, $p_{\text{fdr}} = .010$), higher physical neglect was associated with lower attention performance in HC, whereas no comparable association was observed in the ROP group. Compared with HC, the CHR group also showed different associations for total CAT and attention ($\beta = -0.39$, $p_{\text{fdr}} = .008$),

($\beta = -0.33$, $p_{\text{fdr}} = .019$), emotional neglect and working memory ($\beta = -0.29$, $p_{\text{fdr}} = .049$), and physical neglect and attention ($\beta = -0.56$, $p_{\text{fdr}} < .001$), with higher CAT associated with lower cognitive performance in HC but higher cognitive performance in CHR. Finally, the association between physical neglect and attention also differed between HC and ROD ($\beta = 0.38$, $p_{\text{fdr}} = .005$), that higher physical neglect was associated with lower attention performance in HC, whereas no comparable association was observed in the ROD group. All associations can be found on Supplementary Table 4.

FIGURE 2 HERE

The moderation of perceived discrimination on CAT and cognition associations are shown in Table 1. In the ROP group, perceived discrimination significantly moderated the association between emotional abuse and attention ($\beta = 7.834$, $p_{\text{fdr}} = .018$), that higher levels of perceived discrimination intensified the association between emotional abuse and attention. Further, in the ROD group, perceived discrimination significantly moderated the association between emotional abuse and social cognition ($\beta = -4.72$, $p_{\text{fdr}} = .003$), with the association becoming stronger at higher levels of perceived discrimination. No other moderations were found, including the burden of recent life events, or no longer significant after FDR correction (all $p > .05$). All associations can be found on Supplementary Table 6 and 8.

Table 1. Significant moderation of the association between childhood adversities and trauma and cognitive performance by perceived discrimination

Group	Childhood adversities and trauma	Cognitive domain	β	p	p_{fdr}
ROD	Emotional abuse	Social cognition	-6.385	0.001	0.003
ROP		Attention	5.242	0.003	0.018

Abbreviations: ROD = Recent-Onset Depression; ROP = Recent-Onset Psychosis

Discussion

To our knowledge, this is the first study to examine whether the association between childhood adversity and cognitive functioning differs across different clinical groups while considering the moderating role of ongoing environmental stressors. We found that the associations between CAT, particularly emotional neglect, and cognition differed between ROP and ROD. These associations were partly moderated by perceived discriminatory experiences, but not by the burden of recent life events in the past 12 months. Our results indicate that different types of environmental stressors may have distinct roles in the relationship between CAT and cognitive functioning.

Although CAT is often linked to cognitive impairment (4, 19, 24, 34), emerging developmental models suggest that its effects are not uniformly negative and may vary as a function of timing, illness stage, and contextual factors (52-57). CAT may contribute to cognitive vulnerability through stress-related neurodevelopmental alterations, but may engage adaptive processes that support functioning under challenging conditions (31). The observed associations may reflect stage-dependent compensatory processes that coexist with trauma-related vulnerability. Moreover, distinct neurocognitive subtypes in ROP (58, 59), may reflect underlying subgroup-specific resilience of the spared subtype. Finally, increasing exposure to CAT is associated with a decline in overall cognitive functioning among HC group than among those with psychotic disorders (6), suggesting that CAT related cognitive performance may manifest differently across the psychotic disorder in comparison to the participants without a mental health disorder.

Our findings indicate substantial heterogeneity in CAT-cognition associations across all groups, with increased overall CAT and emotional neglect associated with poorer social cognition in CHR (6, 60). In contrast, increased emotional neglect was associated with better attention and working memory in CHR, and better speed of processing in ROP. A recent study noted that CHR individuals exposed to multiple CAT types can show relatively preserved, or even enhanced, premorbid cognitive abilities, potentially reflecting compensatory or resilience-based mechanisms (20). Transdiagnostic models of risk and resilience (31) propose that CAT can influence cognitive functioning through both vulnerability pathways, such as stress sensitization leading to attentional disruptions, and resilience-oriented adaptations, including heightened threat monitoring or more efficient processing of salient cues. The positive associations observed in our sample may translate into faster reaction times and correctness as observed in the CPTIP, working memory, defined by the active maintenance and updating of information (61), and similarly shaped by such compensatory adaptations in executive control processes. CAT is associated with cognitive and perceptual biases, such as increased attention to threat, but also with alterations in working memory processes, given its reliance on the active maintenance and updating of information in order to guide behaviour (61). Notably, the negative association between physical neglect and attention observed in HC, but not in the diagnostic groups, may suggest that individual differences in resilience-related psychological processes, such as adaptive coping may contribute to these heterogeneous associations, potentially buffering the adverse effects of physical neglect on depression and social phobia in individuals at clinical high risk (62).

In contrast to attention and working memory, social cognition is especially sensitive to adverse social experiences in psychotic disorders (63, 64), and may therefore be particularly vulnerable to cumulative interpersonal stress. In our sample, ROP participants with a history of emotional abuse exhibited relatively higher attentional performance when they had reported higher levels of perceived discrimination while the ROD group was associated with a stronger relationship between emotional abuse and poorer social cognition, potentially reflecting the added burden of perceived discrimination as a chronic social stressor, thereby affecting social cognitive processing in individuals with a history of emotional abuse (32, 33). Notably, the burden of recent life events did not show significant moderating effects. This may suggest that chronic and socially evaluative stressors, such as perceived

discrimination, have a stronger and more sustained impact on cognitive and emotional functioning than discrete recent stressors (32, 33, 65).

The current findings need to be interpreted in the light of some limitations. As participants that experienced severe childhood trauma were relatively rare in the sample, the distribution was highly skewed, which may limit the precision of the estimates and the generalizability of the findings to populations with increased CAT exposure. Furthermore, the cross-sectional nature of the study does not allow for conclusions regarding directionality or causality between CAT, perceived discrimination, and cognitive functioning, which restricts interpretation in terms of developmental mechanisms. Moreover, since CAT was assessed retrospectively, current cognitive functioning or other unmeasured psychological factors may have influenced the appraisal and reporting of childhood adversity, particularly for experiences relying on subjective interpretation, such as emotional neglect (66).

Conclusion

Overall, the current study provides preliminary evidence that CAT may not be uniformly associated with cognitive impairment, but rather that its cognitive effects might differ depending on diagnostic status, CAT subtype, and exposure to recent environmental stressors. These findings suggest that CAT, in particular neglect, may interact with clinical status and current psychosocial experiences to contribute to distinct cognitive patterns. Future studies should investigate these mechanisms in larger samples with a broader range of CAT severity and more comprehensive assessments of resilience and environmental factors.

Declarations

Data Availability Statement

The data are not available due to agreements signed at the outset of the study.

Ethical standards

The authors assert that 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 2008.

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Conflicts of Interest

RU reports personal fees from Sunovion outside the submitted work, and RL personal fees by Boehringer Ingelheim outside the submitted work. NK and EM hold issued patent US20160192889A1 (“Adaptive pattern recognition for psychosis risk modelling”). NK reports grants from European Union during the conduct of the study. JK has served at the advisory board of Boehringer Ingelheim, Recordati Pharma GmbH, Jansen Pharmaceutica and Rovi GmbH. LKI has served at the advisory board of Boehringer Ingelheim and Recordati Pharma GmbH. Other authors report no conflict of interest. The authors have nothing to disclose.

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Figures

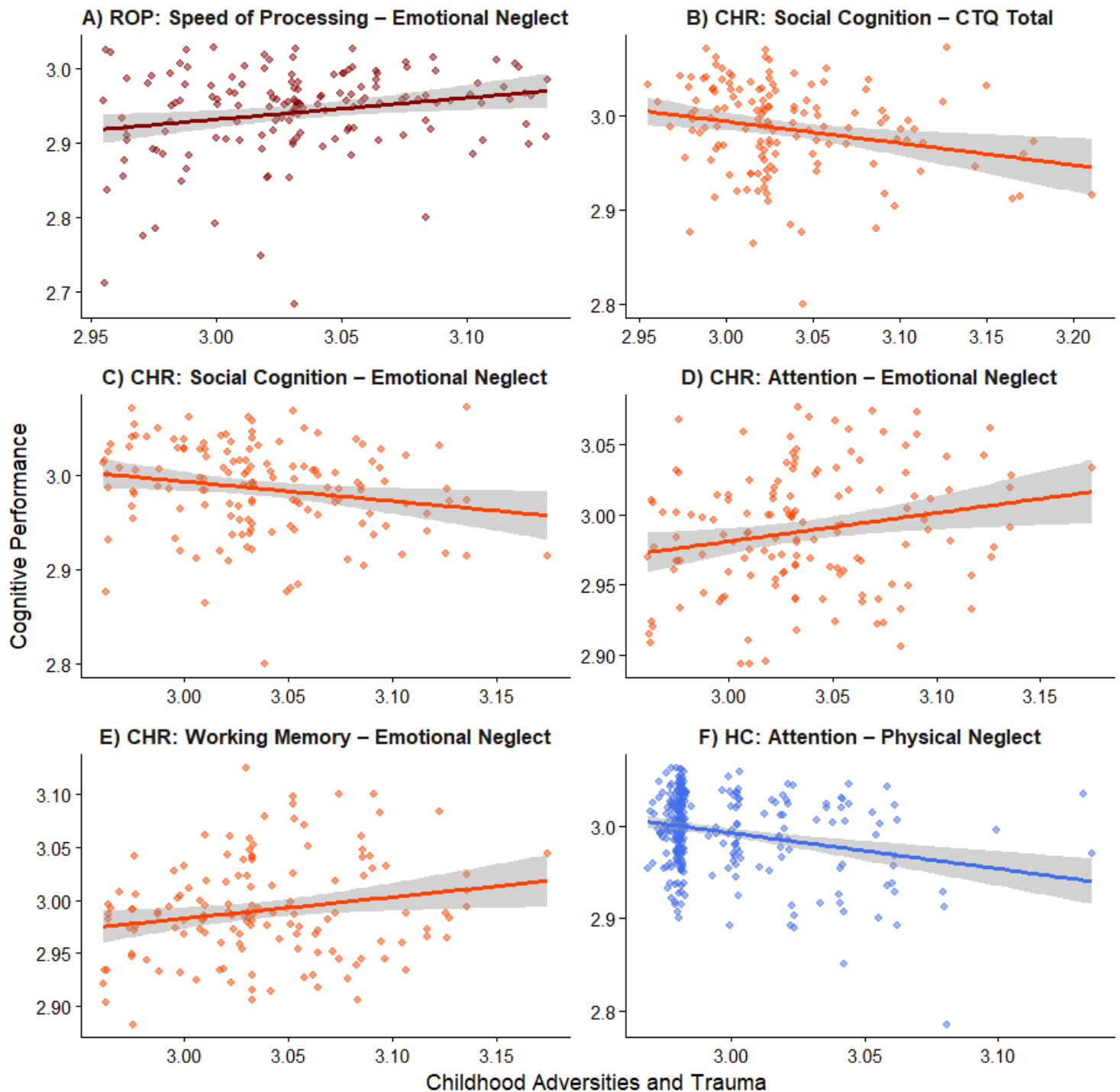


Figure 1

Significant associations between childhood adversities and trauma, and cognitive performance in ROP, CHR and HC

Note. Positive slopes indicate positive associations between childhood adversities and trauma and cognitive performance, whereas negative slopes indicate inverse associations. Each point represents an individual participant. Solid lines indicate fitted linear regression models, and shaded areas represent

95% confidence intervals. Abbreviations: HC = Healthy Controls; CHR = Clinical High Risk; ROP = Recent-Onset Psychosis; CTQ = Childhood Trauma Questionnaire.

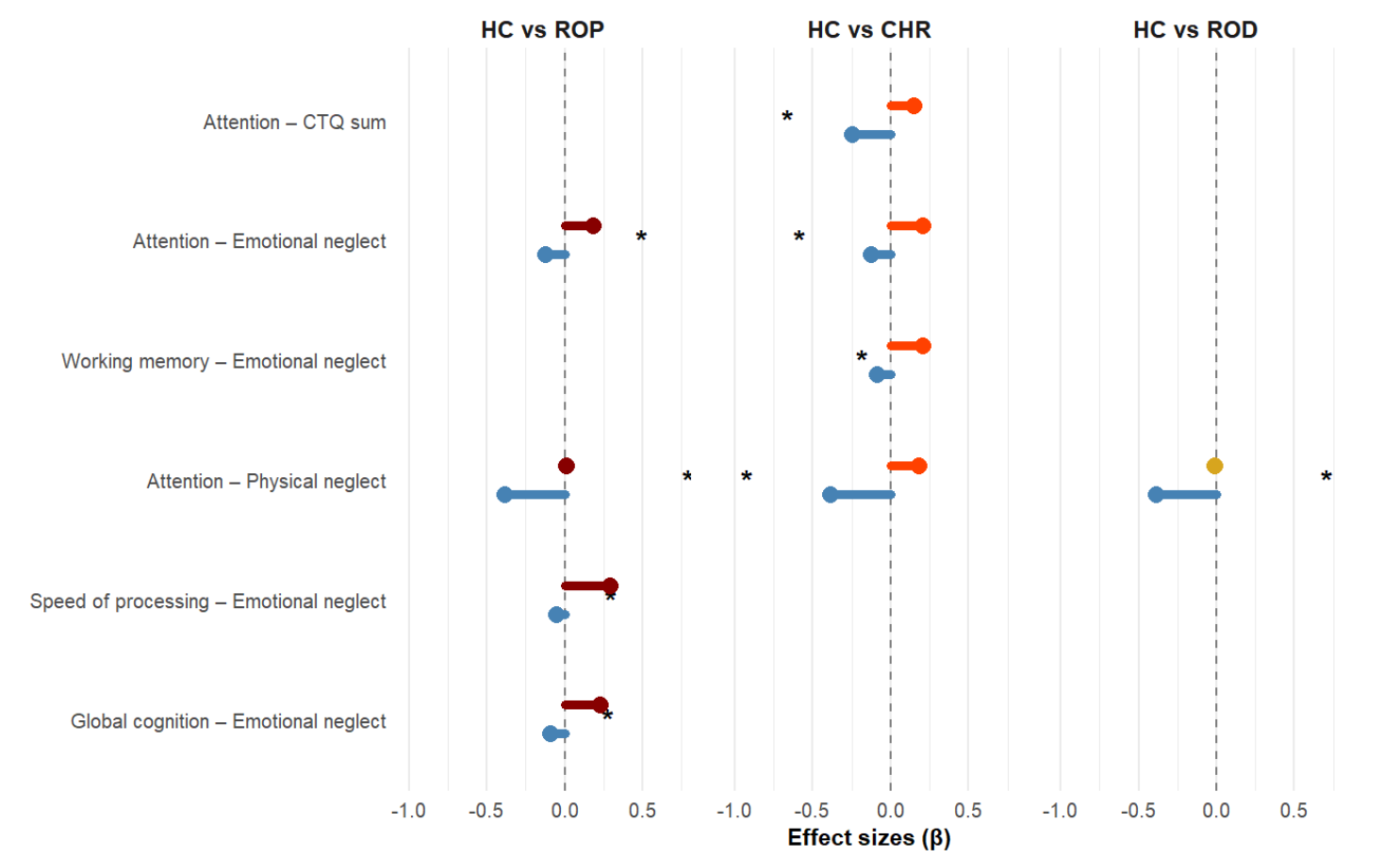


Figure 2

Differential associations of childhood adversities and trauma with cognitive performance in HC compared to ROP, CHR and ROD.

Note. Horizontal bars represent the standardized regression slopes (β) for healthy controls (HC; blue) and the respective clinical group (CHR, ROP, or ROD; colored) for each significant trauma–cognition association. Bars extending to the right indicate positive associations, whereas bars extending to the left indicate inverse associations. Asterisks denote significant differences in the trauma–cognition association between HC and the respective clinical group after FDR correction. Abbreviations: HC = Healthy Controls; CHR = Clinical High Risk; ROP = Recent-Onset Psychosis; ROD = Recent-Onset Depression; CTQ = Childhood Trauma Questionnaire; FDR = False Discovery Rate.

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