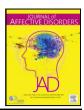


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Research paper

Complex post-traumatic stress disorder (CPTSD) of ICD-11 in youths with childhood maltreatment: Associations with age of exposure and clinical outcomes

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ABSTRACT

Background: Exposure to childhood maltreatment (CM) increases the risk of psychiatric morbidity in youths. The new Complex Post-Traumatic Stress Disorder (CPTSD) diagnosis captures the heterogeneity and complexity of clinical outcomes observed in youths exposed to CM. This study explores CPTSD symptomatology and its association with clinical outcomes, considering the impact of CM subtypes and age of exposure.

Methods: Exposure to CM and clinical outcomes were evaluated in 187 youths aged 7–17 (116 with psychiatric disorder; 71 healthy controls) following the Tools for Assessing the Severity of Situations in which Children are Vulnerable (TASSCV) structured interview criteria. CPTSD symptomatology was explored by confirmatory factor analysis, considering four subdomains: post-traumatic stress symptoms, emotion dysregulation, negative self-concept and interpersonal problems.

Results: Youths exposed to CM (with or without psychiatric disorders) showed greater internalizing, externalizing and other symptomatology, worse premorbid adjustment and poorer overall functioning. Youth with psychiatric disorder and exposed to CM reported more CPTSD symptomatology, psychiatric comorbidity and

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polypharmacy and earlier onset of cannabis use. Different subtypes of CM and the developmental stage of exposure differentially impact CPTSD subdomains.

Limitations: Small percentage of resilient youths was studied. It was not possible to explore specific interactions between diagnostic categories and CM. Direct inference cannot be assumed.

Conclusions: Gathering information on type and age of exposure to CM is clinically useful to understand the complexity of psychiatric symptoms observed in youths. Inclusion of the CPTSD diagnosis should increase the implementation of early specific interventions, improving youths' functioning and reducing the severity of clinical outcomes.

1. Introduction

Childhood maltreatment (CM) according to the definition of the World Health Organization (WHO) is the abuse and neglect that occurs to children under 18 years of age. Includes all types of physical and/or emotional abuse, sexual abuse, neglect and negligence, and commercial or other exploitation that results in actual or potential harm to the child's health, survival, development, or dignity in the context of a relationship of responsibility, trust or power (WHO, 2022).

Exposure to CM might increase vulnerability to different psychiatric disorders, soon after traumatic experiences but also throughout life (Heim et al., 2010; Scott et al., 2010; Teicher and Samson, 2013). Adverse childhood experiences (ACE) occur with the exposure during childhood or adolescence to environmental circumstances that are likely to require significant psychological, social, or neurobiological adaptation by an average child with trauma being one of the possible outcomes of exposure to adversity (McLaughlin, 2016). ACEs are associated with up to 45 % of all childhood onset psychiatric disorders and with around 30 % of later-onset non-specific psychiatric disorders (McLaughlin et al., 2010). Furthermore, evidence suggests that psychological outcomes may depend upon the nature, timing, chronicity and severity of the adverse experiences (Hughes et al., 2017; Jonson-Reid et al., 2012).

Although CM is considered a severe problem worldwide with high prevalence rates (Akmatov, 2011), an important proportion of cases remains unreported, since affected individuals are often reluctant to disclose their CM experiences (Radford et al., 2011). Additionally, clinicians often report not being sufficiently prepared to capture and adequately respond to these situations or revelations (Read et al., 2007). So, trauma histories can remain unnoticed for many years, leading to misdiagnoses that cause stress to affected individuals and impede integrative and holistic support and recovery.

Recent studies estimate that 70 % of the world's population has experienced at least one traumatic event (Kessler et al., 2017). Trauma occurs when a person perceives an event or set of circumstances as extremely frightening, harmful, or threatening-either emotionally, physically, or both (APA: American Psychiatric Association, 2013). After suffering or witnessing a traumatic event characterized as intense and acute (e.g., serious injury, sexual violence or witnessing death), some people experience post-traumatic stress symptoms, such as unwanted intrusive memories or flashbacks, avoidance of possible reminders of the event, various mood and functional impairments as well as alterations in arousal and reactivity (APA: American Psychiatric Association, 2013). However, clinicians have realized that diagnosing post-traumatic stress disorder (PTSD) does not explain the complex symptoms expressed by people exposed to severe, prolonged, multiple or repeated traumatic events (Van der Kolk and Najavits, 2013). So, "complex trauma" refers to multiple traumatic events of a long-lasting, invasive and primarily interpersonal nature, which it is difficult or impossible to escape from, since they usually result from close relationships (e.g., neglect, child abuse or intimate partner violence) (Cook et al., 2012). Complex trauma also interferes with children's ability to form secure attachments and thus alters many aspects of a child's development that rely on this primary source of safety, stability and the formation of a sense of self, with wide-ranging and long-lasting consequences (De Bellis and Zisk, 2014). However, after exposure to complex trauma, youth PTSD diagnoses are rare since most young patients meet the criteria for other diagnoses that may shadow the real contribution of PTSD (Jaffee, 2017).

The concept of Complex-PTSD (CPTSD) initially proposed by Herman (1992) and reformulated by Van der Kolk (2005) as Complex Developmental Trauma, refers to the particular effects of complex trauma in children, highlighting that these youths often receive inaccurate diagnoses. Although in recent decades trauma-related symptom research has elucidated different empirical CPTSD models (Cloitre et al., 2013; Karatzias et al., 2017; Knefel et al., 2015), this diagnosis was not recognized in the last version of DSM-5 (APA, 2013). However, the WHO has finally recognized CPTSD as a diagnostic entity distinct from the PTSD, and it now appears in the latest version of the ICD-11 manual (WHO, 2019). Briefly, CPTSD is defined by the presence of the three domains of classic PTSD (traumatic re-experiencing, avoidance of traumatic reminders and hypervigilance), along with three disturbances in self-organization (DSOs): emotional dysregulation, negative selfconcept and interpersonal problems (see Supplementary Material for details). Nevertheless, studies addressing CPTSD in child and adolescent populations are still scarce (Elliott et al., 2021; Haselgruber et al., 2021; Sachser et al., 2017; Villalta et al., 2020).

This new approach may improve diagnoses and treatment for individuals with a CM history, particularly those primarily treated for other comorbid psychiatric disorders with poor outcomes. Different studies show that adults with psychiatric disorders and a CM history have a distinct *ecophenotype* characterized by earlier onset, more severe symptoms and comorbidity, higher medication dosages and increased suicidal behaviour (Read et al., 2005; Teicher and Samson, 2013). It could be hypothesized that this worse prognosis is due to the DSOs described by CPTSD. Furthermore, it may be of great interest to explore whether the nature of CM (e.g., neglect versus abuse; physical versus emotional or sexual) and the developmental stage of exposure produce differential alterations to brain development and CPTSD subdomains. Elucidating such mechanisms may enhance the development of new targeted interventions for children and adolescents with mental health problems and a CM history.

This study is therefore designed to answer:

Aim I: Do youths with a CM history, regardless of whether they have a psychiatric diagnosis, show greater internalizing, externalizing and other symptomatology and worse global functioning? Do they display more severe symptomatology, higher diagnostic comorbidity, more pharmacological prescriptions, and earlier onset of substance use?

Aim II: Is the symptomology captured in the new CPTSD diagnosis present in children and adolescents with a CM history but with other psychiatric disorders? Specifically, (a) do all CM subtypes (emotional neglect, physical neglect, emotional abuse, physical abuse and sexual abuse) increase the symptomatology of CPTSD; and (b) is the developmental stage at which CM occurs relevant to the manifestation of each CPTSD subdomain?

2. Materials and methods

2.1. Participants

The sample was part of a cohort study exploring the psycho-neurobiological consequences of CM (EPI young stress project), from April 2016 to March 2020. The parent EPI-Young-Stress project is a multicenter study which aims to evaluate HPA-axis functioning, associated epigenetic signatures and immunological biomarkers involved in the association between CM and youth mental disorders (Marques-Feixa et al., 2022, 2021a, b).

Participants were 187 children and adolescents aged 7-17: 116 were diagnosed with a current psychiatric disorder recruited from six child and adolescent psychiatry departments in Spain (inpatients, outpatients and partial programmes) and 71 were healthy controls (HC) participants recruited via advertisements, primary healthcare centres, schools and other community facilities (see Table 1). Due to the complex and heterogeneous symptomatology observed in people exposed to trauma during nurture, our study adopted a transdiagnostic approach, including a wide range of mental health problems. The exclusion criteria for all participants included the diagnosis of an autism spectrum disorder, underweight anorexia nervosa, intellectual disability (IQ < 70), current drug dependence (not abuse), not being fluent in Spanish, extreme premature birth (<1500 g), head injury with loss of consciousness, and severe neurological or other pathological conditions (such as epilepsy, cancer or autoimmune diseases). The Ethical Review Board of each hospital and university involved in the project approved this study. Further details about the nature of the study have been described elsewhere (Marques-Feixa et al., 2021b).

Table 1 Sociodemographic, CM^a and $CPTSD^b$ symptoms of participants with and without current psychiatric disorders.

	Participants with	НС	t/χ^2	p	d/kappa
	psychiatric disorders n = 116 (62 %) n (%)/mean (sd) [range]	participants $n = 71$ (38 %) n (%)/mean (sd) [range]			
Developmental stage (adolescents)	63 (54 %)	30 (42 %)	2.561	0.110	-0.117
Age	13.8 (2.4) [7– 17]	13.4 (2.9) [7– 17]	1.052	0.270	-0.166
Sex (female)	68 (58 %)	40 (56 %)	0.094	0.759	-0.022
Family SES ^c	35.4 (17.7) [8– 66]	48.1 (15.4) [14–66]	-5.119	< 0.001	0.751
CM ^a history	79 (68 %)	15 (21 %)	38.879	< 0.001	-0.456
Emotional neglect	73 (63 %)	11 (16 %)	40.059	< 0.001	-0.463
Physical neglect	41 (34 %)	2 (3 %)	26.317	< 0.001	-0.375
Emotional abuse	43 (37 %)	6 (9 %)	18.654	< 0.001	-0.316
Physical abuse	42 (36 %)	8 (11 %)	13.984	< 0.001	-0.273
Sexual abuse	25 (22 %)	3 (4 %)	10.385	0.001	-0.236
CM-score ^d	13.9 (15.8) [0– 66]	2.3 (6.8) [0– 36]	6.926	< 0.001	-0.882
PTSD ^e score	10.2 (5.4) [0– 28]	2.5 (2.7) [0-13]	12.754	< 0.001	-1.669
Emotional dysregulation score	8.7 (3.7) [0–14]	4.2 (3.3) [0–12]	8.399	< 0.001	-1.274
Negative self- concept score	3.5 (2.3) [0–8]	1.1 (1.5) [0– 6]	8.691	< 0.001	-1.194
Disturbance relationships score	2.1 (1.8) [0–6]	0.4 (0.8) [0– 3]	9.061	< 0.001	-1.167

Note

- ^a CM: Childhood maltreatment.
- ^b CPTSD: Complex Post-traumatic Stress Disorder.
- ^c SES: socioeconomic status raw scores range from 8 to 66, with higher scores reflecting higher SES.
- $^{\rm d}$ CM-score: Childhood maltreatment scores were calculated adding (severity x frequency) for each CM subtype and range from 0 to 80.
- ^e PTSD: Post-Traumatic Stress Disorder.

2.2. Assessment measures

2.2.1. Sociodemographic and anthropometric

A clinical interview was conducted in order to collect basic demographic information, including socioeconomic status (SES), based on the Hollingshead Four-Factor Index of SES (Hollingshead, 1975). Developmental stage was assessed using the Tanner staging questionnaire (Morris and Udry, 1980); participants were classified as children (Tanner stages 1–3) or adolescents (stages 4–5).

2.2.2. Childhood maltreatment experiences

To assess features of CM, we used the TASSCV: a semi-structured interview validated by professionals working in child and adolescent care in Spain. This instrument is detailed elsewhere (Marques-Feixa et al., 2021b) and available online in Spanish (CARM, 2012). Data concerning five main CM subtypes were included: emotional neglect, physical neglect, emotional abuse, physical abuse and sexual abuse. As expected, for most subjects the different CM subtypes coexisted (see Fig. 1). The timing of exposure to each CM subtype was classified as absence/presence during early childhood (0–5 years), primary school age (6–12) or adolescence (13–17). To assess the CM history on a continuum spectrum for a more complete understanding of participants' complex trauma, a CM-score was created. Thus, for each CM subtype, reported severity (1 to 4) was multiplied by reported frequency (1 to 4), giving a final CM-score for each participant from 0 (absence of CM) to 80 (extreme and frequent CM in all subtypes) (see Fig. 1).

Additionally, adolescents who were older than 12 answered self-reports such as the short version of the Childhood Trauma Questionnaire (CTQ-SF) (Bernstein et al., 2003) and the Childhood Experience of Care and Abuse Questionnaire (CECA-Q2) (Bifulco et al., 2005) while participants aged 7–11 answered an adapted ad-hoc heteroadministered questionnaire (for details see Supplementary Material in Marques-Feixa et al., 2021b).

2.2.3. Internalizing and externalizing symptomatology

The Child Behavior Checklist 6–18 (CBCL) is a parent-reported inventory, which assesses competencies, and behavioural, emotional and social problems in children and adolescents aged 6 to 18 years (Achenbach and Rescorla, 2001; Lacalle Sistere et al., 2014). CBCL scores consist of several subscales. We included: Internalizing (Anxious/Depressed, Withdrawn, Somatic Complaints), Externalizing (Rule-Breaking Behaviour and Aggressive Behaviour) and other symptomatology (Social Problems, Thought Problems and Attention Problems), encompassed in a Total Problems score.

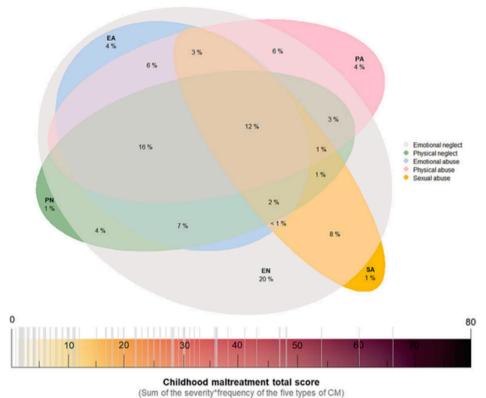
2.2.4. Premorbid adjustment and general functioning

The Premorbid Adjustment Scale (PAS) evaluates degree of achievement of different developmental goals, including scales for 5 domains of functioning: sociability and withdrawal, peer relationships, scholastic performance, adaptation to school and social–sexual aspects of life (Cannon-Spoor et al., 1982). The PAS included in the present study covers two periods of development: childhood (up to age 11) and early adolescence (12 to 15). PAS scores range from 0 to 30, with higher scores indicating worse global adjustment.

Global functioning and impairment was measured using the Children's Global Assessment Scale (CGAS) (Shaffer et al., 1983), providing a single score (1–100), between 1 'extremely impaired' to 100 'doing very well', based on a clinician's assessment of aspects related to a child's psychological and social functioning (adaptation at school and home, social life, hobbies, self-confidence, aggressiveness, autonomy, emotional distress, etc.).

2.2.5. Current psychiatric diagnostics and clinical outcomes

Present and lifetime psychopathology was ascertained using the Spanish version of the Kiddie-Schedule for Affective Disorders and



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 $\textbf{Fig. 1.} \ \ Overlap \ \ of \ \ CM \ subtypes \ \ in \ \ EPI_young_stress \ cohort.$

The most common CM subtype was emotional neglect (EN), present in 94 % of individuals. Noticeably, 74 % of individuals reported multiple forms of CM, while isolated forms were far less frequent. Specifically, isolated EN was present in 20 % of participants and only 6 % of subjects reported isolated physical neglect (PN), physical abuse (PA) or sexual abuse (SA). The CM-score is an index considering the severity, frequency and overlapping of different CM subtypes in the history (ranging from 0 to 80).

Schizophrenia for School-Age Children Version DSM-5 (K-SADS-PL-5) (APA, 2013; de la Peña et al., 2018).

Psychiatric diagnoses for each participant, both currently and throughout life, were reported by clinicians (or confirmed by caregivers in control subjects). The number of "lifetime psychiatric diagnoses": total number of different diagnoses received throughout life, was recorded (maximum number reported: 7).

The number of current psychiatric disorders for each participant was called "Psychiatric comorbidity" (maximum number: 5). Additionally, information about current prescribed psychiatric medication was collected (classified as: antipsychotics, antidepressants, anxiolytics, mood stabilizers, psychostimulants or others). Besides the dichotomized "use of psychiatric drugs" (absence/presence), the term "polypharmacy" considered as multimorbidity use of psychiatric drugs, calculated according to the sum of six types of psychotropic drugs prescribed daily (maximum number:4).

Moreover, age of first substance use was extracted from the K-SADS-PL5 interview. In our sample, only cannabis was the first substance used (at between age 9 and 16). There were insufficient affirmative controls to perform this analysis in this group.

2.2.6. Complex post-traumatic stress disorder symptomatology

Since CPTSD diagnosis has only recently been included in ICD-11 and, at the time of the current study, there was no valid and reliable CPTSD diagnosis instrument, additional analysis provided a proxy of this symptomatology (details in **supplementary material**). Briefly, following ICD-11 criteria, 28 items from two different measures were collected as a CPTSD proxy (14 items for PTSD and 14 items for DSOs). For detailed questionnaire and statistics information, see **supplementary material**. In short, to clarify the CPTSD multidimensional structure and examine the internal and external validity of the construct, a confirma-

tory factorial analysis was conducted using the statistical software package EQS. 6.1 (Bentler, 2006). Finally, an excellent fit was obtained with the 4-factor first-order model, including the domains: PTSD, emotional dysregulation, negative self-concept and interpersonal problems.

2.3. Statistical analysis

Statistical analyses were performed using SPSS version 26 (IBM, Chicago, IL, USA). Student's t-test for continuous and a chi-square test (χ^2) for categorical variables were performed to compare cases and controls regarding demographic variables, CM history and CPTSD symptomatology (Table 1).

To explore our first aim, hierarchical regression analyses were performed to study the impact of the CM-score on global functioning, symptomatology and clinical variables. Two levels were introduced as predictor variables: i) the first included: developmental stage, age, sex and SES, and ii) the second included the CM-score. Externally observed variables were considered as outcomes (PAS, CGAS, CBCL, lifetime psychiatric diagnoses, current psychiatric comorbidity, polypharmacy and first cannabis use age). To explore the differences in psychiatric drug prescription (absence/presence) predicted by CM-score, logistic regression analyses were conducted, also including as predictors the developmental stage, age, sex and SES.

To explore our second aim, an additional regression path was conducted to study the association between different CM subtypes, periods of exposure to each CM subtype, and CPTSD symptomatology. The four CPTSD domains (PTSD, emotional dysregulation, negative self-concept and interpersonal problems) were entered into the hierarchical regression analyses as outcomes. The predictive variables introduced in the first level were developmental stage, age, sex and SES. Then, the CM variables (CM-score and CM subtypes (absence/presence of physical ne-

glect, emotional neglect, emotional abuse, physical abuse, sexual abuse)) were introduced in the second regression level. Finally, we performed separate analyses introducing absence/presence of the different CM subtypes during each developmental stage (0–5 years, 6–12, and 13–17) in the second step. Due to the few CM experiences reported by control participants (n=15), the statistics of the impact of CM and the period of exposure on CPTSD symptomology for this subgroup are in the supplementary material.

3. Results

In our sample, 94 participants (50 %) reported CM. Fig. 1 shows the overlap of their CM subtypes. Participants with a current psychiatric disorder had lower SES, more CM experiences and increased CPTSD symptomatology than controls (Table 1).

3.1. Aim I: CM, symptomatology and poor clinical outcomes and functioning

Table 2 shows that participants with psychiatric disorder exposed to CM had worse premorbid adjustment before age 11, which was maintained through adolescence. However, HC participants with a CM history showed worse premorbid adjustment only in adolescence (12–15 years). The CGAS analysis indicated that participants with a severe CM history (both with and without current psychiatric disorders), showed worse global functioning.

Between 12 % and 15 % of the general symptomatology assessed by CBCL was directly explained by a CM history (see Table 2). Specifically, participants with psychiatric disorders exposed to CM showed statistically significantly increased internalizing, externalizing and other symptomatology (social, thought and attention problems) compared with those without CM. Interestingly, similar results were obtained in the HC group, revealing that, although they did not fulfill diagnostic criteria for mental disorders, those with a CM history showed statistically significantly increased internalizing, externalizing and other symptomatology.

Furthermore, youths with worse CM histories showed significantly more different lifetime psychiatric diagnoses (Table 2). Additionally, in participants with psychiatric disorder, a higher CM-score increased the number of current psychiatric comorbidities. Although CM had no effect on absence/presence of psychiatric drugs (Wald = 0.371, p=.54; Exp (B) = 1.010, 95 % CI (0.978, 1.044)), it did result in an increase of polypharmacy with youths exposed to CM, consuming up to four different families of psychotropics. We also observed earlier onset of cannabis use in participants with psychiatric disorder exposed to CM.

3.2. Aim II a: CPTSD symptomatology in participants exposed to CM with psychiatric disorders

The second regression analysis explores the impact of CM on CPTSD domains (Table 3; HC data reported in **supplementary material**). Participants with current psychiatric disorders and greater CM-scores obtained significantly higher scores in all CPTSD subdomains: PTSD symptoms, emotion dysregulation, negative self-concept and interpersonal problems. Particularly, all CM subtypes increased the probability of suffering from all CPTSD subdomains; except, physical neglect and sexual abuse did not increase emotional dysregulation (Table 3 and Fig. 2).

3.3. Aim II b: The impact of developmental stage at CM exposure on CPTSD symptomatology

The developmental stage (0–5 years, 6–12 or 13–17) at which CM subtypes occur might have an important effect in CPTSD subdomains (Table 3 and Fig. 2). The only CM subtype that constantly remains harmful, regardless of the developmental stage at which it occurs, is

emotional neglect. Moreover, physical neglect only affects the PTSD symptomatology subdomain if it occurs during the first 5 years of life. In contrast, although physical, emotional and sexual abuse have an effect in PTSD symptomatology during all developmental stages, physical abuse is especially harmful in the first 5 years of life, emotional abuse is especially critical during primary school age (6–12) and sexual abuse from age 6 to 17.

Regarding DSO subdomains, both emotional neglect and abuse, and physical abuse had a strong impact on emotional dysregulation, without any particular sensitivity to developmental stage; neither physical neglect nor sexual abuse had a significant impact on this domain. Secondly, regarding negative self-concept, all CM subtypes had a strong effect. Specifically, physical neglect was of greater risk during the first five years of life; however, no developmental stage of exposure to other CM subtypes (emotional neglect, emotional abuse, physical abuse and sexual abuse) had specific effects. Finally, all CM subtypes produced disturbances in interpersonal problems. Physical and emotional neglect produced interpersonal problems regardless of age of exposure, while physical abuse at 0–5 years had an especially strong effect, and emotional and sexual abuse when they occurred during primary school age (6–12 years).

4. Discussion

The present study demonstrates that CM experiences increase the expression of psychiatric symptomatology with a dose–response effect and worsen the global functioning of children and adolescents, independently of their current diagnostic status. Our findings also reinforce the new ICD-11 CPTSD diagnosis in youths with psychiatric disorders exposed to CM, as useful in detecting underlying DSOs of great relevance to prognosis and putative treatments.

Regarding our fist aim, this study shows that, both for cases and control subjects, CM is related with all types of symptomatology: internalizing (anxious-depressive, somatization), externalizing (behavioural disorders, aggressiveness, impulsiveness) and other symptoms (thought disturbances, social difficulties, attention problems). Thereby, CM might be a non-specific amplifying factor that "tips the balance" of inherited genetic susceptibilities to internalizing or externalizing spectra symptoms (Teicher and Samson, 2013).

This concurs with previous research supporting early maltreatment as a transdiagnostic risk factor that increases from 2- to 10-fold the risk of a wide range of mental disorders (Heim et al., 2010; Scott et al., 2010; Vachon et al., 2015). Furthermore, we detected an increase in the number of lifetime and current psychiatric diagnoses in all participants exposed to CM, highlighting the difficulties clinicians encounter when placing youths exposed to CM within conventional diagnostic boundaries. These findings also reveal that youths with a CM history who do not fulfil diagnostic criteria already show greater global symptomatology than their non-exposed peers, highlighting the importance of establishing preventive measures prior to psychiatric disorder onset.

Other authors indicate that individuals with psychiatric disorders and a CM history might be more resistant to conventional treatments and present worse outcomes (Lippard and Nemeroff, 2020; Teicher and Samson, 2013). Our study supports that this is indeed already the case in both child and adolescent populations, since youths with a CM history (especially those with greater overlapping, severity and chronicity) are characterized by earlier onset of worse premorbid adjustment, worse global functioning and greater current psychiatric comorbidity than those without a CM history. This agrees with the dose–response relationship between multiplicity of CM exposure and disease outcomes described previously (Anda et al., 2006; Janssen et al., 2004). Interestingly, our study also suggests that CM exposure does not correlate to use of psychiatric drugs during treatment but is associated with polypharmacy prescription. Thus, youth with a history of CM tend to be prescribed drugs from more different families than youth without a CM

Table 2
Regression analysis of childhood maltreatment score (CM-score) and premorbid adjustment, global functioning, psychiatric symptomatology, and other clinical outcomes (comorbidity, polypharmacy and onset of cannabis use).

Step	Effect	Participants with psychiatric disorders						HC participant					
			95 % CI						95 % CI				
		Beta	LL	UL	t	p	ΔR^{2} (*100)	Beta	LL	UL	t	p	ΔR^{2} (*100)
Drem	norbid adjustment 0–11 ye	pars1											
1	Developmental stage ^a	-0.316	-5.097	-0.379	2.303	0.023*	13.2 %**	-0.163	-2.498	1.123	0.758	0.451	6.5 %
	Age	0.028	-0.406	0.509	0.224	0.823		0.284	-0.100	0.508	1.339	0.185	
	Sex	0.103	-1.048	2.850	0.917	0.361		0.055	-0.798	1.263	0.450	0.654	
	Socioeconomic status	-0.295	-0.117	-0.026	3.097	0.003**		-0.177	-0.057	0.008	1.484	0.142	
2	CM-score	0.218	0.004	0.116	2.141	0.035*	3.8 %*	0.163	-0.036	0.136	1.164	0.249	1.9 %
Prem	norbid adjustment 12–15 y	ears ²											
1	Developmental stage ^a	-0.057	-4.688	3.096	0.407	0.685	12.2 %*	-0.262	-6.184	2.094	0.996	0.325	6.8 %
	Age	0.026	-0.896	1.106	0.209	0.835		0.256	-0.593	1.695	0.971	0.337	
	Sex	0.031	-3.054	3.906	0.244	0.808		-0.034	-2.651	2.119	0.225	0.823	
	Socioeconomic status	-0.345	-0.203	-0.048	3.221	0.002**		-0.208	-0.129	0.023	1.413	0.165	
2	CM-score	0.248	0.007	0.198	2.138	0.036*	4.7*	0.409	0.064	0.545	2.558	0.014*	12.6 %*
Curr	ent CGAS ³												
1	Developmental stage ^a	-0.166	-15.541	3.431	1.265	0.208	17.7 %***	0.054	-4.524	5.909	0.265	0.792	16.0 %*
	Age	-0.039	-2.130	1.534	0.323	0.747		0.006	-0.864	0.889	0.028	0.978	
	Sex	-0.036	-9.058	6.458	0.332	0.740		-0.124	-4.555	1.385	1.065	0.291	
	Socioeconomic status	0.325	0.151	0.517	3.617	< 0.001***		0.370	0.060	0.247	3.267	0.002**	
2	CM-score	-0.372	-0.644	-0.224	4.101	< 0.001***	11.4***	-0.361	-0.575	-0.102	2.859	0.006**	9.4 %**
CBCI	L total ⁴												
1	Developmental stage ^a	0.156	-7.582	27.372	1.123	0.264	10.4 %*	0.152	-8.004	18.249	0.779	0.439	23.7 %***
	Age	0.040	-2.823	3.885	0.314	0.754		-0.494	-5.059	-0.629	-2.564	0.013*	
	Sex	0.100	-8.120	20.858	0.872	0.385		0.113	-3.713	11.318	1.011	0.316	
	Socioeconomic status	-0.156	-0.613	0.059	1.635	0.105		-0.276	-0.537	-0.063	-2.532	0.014*	
2	CM-score	0.374	0.366	1.141	3.861	< 0.001***	11.5 %***	0.454	0.547	1.680	3.928	< 0.001***	14.8 %***
CBCI	L internalizing ⁴												
1	Developmental stage ^a	0.003	-5.380	5.493	0.020	0.984	26.4 %***	0.448	0.528	8.752	2.254	0.028*	20.5 %**
	Age	0.321	0.411	2.498	2.766	0.007**		-0.595	-1.746	-0.358	3.029	0.004**	
	Sex	0.261	1.210	10.224	2.516	0.013*		0.177	-0.519	4.190	1.557	0.124	
	Socioeconomic status	-0.068	-0.146	0.063	0.781	0.437		-0.224	-0.149	-0.001	2.019	0.048*	
2	CM-score	0.239	0.041	0.290	2.629	0.010**	4.7 %**	0.349	0.076	0.449	2.816	0.006**	8.8 %**
CBCI	L externalizing ⁴												
1	Developmental stage ^a	0.308	0.780	15.341	2.196	0.030*	8.3 %	0.067	-4.055	5.655	0.329	0.743	16.2 %*
	Age	-0.197	-2.471	0.323	1.525	0.130		-0.366	-1.563	0.075	1.813	0.074	
	Sex	-0.094	-8.508	3.564	0.812	0.418		0.106	-1.519	4.041	0.906	0.368	
	Socioeconomic status	-0.199	-0.286	-0.006	2.062	0.042*		-0.228	-0.175	0.000	1.997	0.050*	
2	CM-score	0.353	0.130	0.455	3.564	0.001***	10.2 %***	0.563	0.289	0.687	4.893	< 0.001***	22.8 %***
CBCI	L others ⁴												
1	Developmental stage ^a	0.058	-4.820	7.306	0.407	0.685	4.2 %	0.014	-4.328	4.664	0.074	0.941	26.1 %***
_	Age	0.029	-1.035	1.292	0.219	0.827		-0.421	-1.603	-0.086	2.224	0.030*	
	Sex	0.091	-3.082	6.970	0.767	0.445		-0.008	-2.669	2.479	0.073	0.942	
	Socioeconomic status	-0.115	-0.85	0.048	1.161	0.248		-0.277	-0.186	-0.024	2.583	0.012*	
2	CM-score	0.338	0.092	0.365	3.319	0.001***	9.4 %***	0.272	0.024	0.440	2.225	0.030*	5.3 %*
Lifet	ime psychiatric diagnoses	5											
1	Developmental stage ^a	-0.023	-0.945	0.794	0.173	0.863	9.6 %*	-0.035	-0.380	0.324	0.161	0.872	5.1 %
	Age	0.224	-0.018	0.322	1.771	0.079		0.153	-0.038	0.080	0.714	0.478	•
	Sex	0.039	-0.585	0.840	0.354	0.724		0.086	-0.131	0.270	0.695	0.489	
	Socioeconomic status	-0.172	-0.033	0.001	1.837	0.069		-0.157	-0.010	0.002	1.306	0.196	
2	CM-score	0.238	0.004	0.045	2.409	0.018*	4.7 %*	0.431	0.010	0.041	3.265	0.002**	13.4 %**
C11***	ent nevehiatrie comorbidia	-v6											
Curr 1	ent psychiatric comorbidit Developmental stage ^a	-0.085	-0.723	0.389	0.596	0.553	2.0 %	NA	NA	NA	NA	NA	NA
-	Age	0.147	-0.723	0.168	1.115	0.267		NA	NA	NA	NA	NA	
	Sex	0.147	-0.422	0.108	0.142	0.267		NA NA	NA NA	NA NA	NA NA	NA NA	
		-0.070	-0.015	0.007	0.710	0.479		NA	NA	NA	NA	NA	

(continued on next page)

Table 2 (continued)

Step	Effect	Participants with psychiatric disorders						HC participant					
			95 % CI	t	p 2	ΔR^{2} (*100)	Beta	95 % (95 % CI				
	Beta	LL	UL					LL	UL	t	p	ΔR^2 (*100)	
2	CM-score	0.234	0.002	0.028	2.246	0.027*	4.5 %*	NA	NA	NA	NA	NA	NA
Poly	pharmacy ⁷												
1	Developmental stage ^a	0.048	-0.469	0.670	0.349	0.727	9.3 %*	NA	NA	NA	NA	NA	NA
	Age	0.275	0.010	0.230	2.158	0.033*		NA	NA	NA	NA	NA	
	Sex	-0.059	-0.588	0.343	0.523	0.602		NA	NA	NA	NA	NA	
	Socioeconomic status	-0.063	-0.015	0.007	0.670	0.504		NA	NA	NA	NA	NA	
2	CM-score	0.201	0.000	0.027	2.000	0.048*	3.3 %*	NA	NA	NA	NA	NA	NA
Age	at first cannabis use ⁸												
1	Developmental stagea	0.023	-2.627	2.850	0.084	0.933	33.4 %*	NA	NA	NA	NA	NA	NA
	Age	0.455	0.117	0.939	2.660	0.014*		NA	NA	NA	NA	NA	
	Sex	-0.360	-3.653	0.768	1.350	0.190		NA	NA	NA	NA	NA	
	Socioeconomic status	-0.011	-0.041	0.039	0.061	0.952		NA	NA	NA	NA	NA	
2	CM-score	-0.457	-0.084	-0.005	2.325	0.030*	13.1 %*	NA	NA	NA	NA	NA	NA

Note: 95 % CI (95 % confidence interval, where LL is the lower limit and UL the upper limit).

- ¹ Premorbid adjustment scores for children range from 0 to 24, with higher scores indicating worse global adjustment.
- ² Premorbid adjustment scores range from 0 to 30, with higher scores indicating worse global adjustment.
- ³ CGAS: Children's Global Assessment Scale, provides a single score, between 1 'extremely impaired' to 100 'doing very well'.
- ⁴ CBCL: Child Behavioural Check-List scores include several subscales: Internalizing (Anxious/Depressed, Withdrawn, Somatic Complaints), Externalizing (Rule-Breaking Behaviour and Aggressive Behaviour) and Other symptomatology (Social Problems, Thought Problems and Attention Problems).
- ⁵ Lifetime psychiatric diagnoses: Total number of different diagnoses received throughout life (maximum number reported: 7).
- ⁶ Psychiatric comorbidity: Number of current psychiatric diagnosis (maximum number: 5).
- ⁷ Polypharmacy: considered as multimorbidity use of psychiatric drugs, calculated according to the sum of six types of psychotropic drugs prescribed daily (antipsychotics, antidepressants, anxiolytics, mood stabilizers, psychostimulants or others), maximum number: 4.
- ⁸ Age at first cannabis use: In our sample, cannabis was always the first drug used (at between age 9 and 16). Insufficient affirmative controls to perform this analysis in this group.

history, which is relevant in pediatric populations due to the possible consequences for their health (Horace and Ahmed, 2015). This polypharmacy is probably due to psychiatrists' difficulty treating the diverse and complex symptomatology expressed by youths exposed to CM, with no awareness that the serious symptoms may actually hide the origin of the suffering. This would also explain why pharmacological treatment often does not work with these patients, suggesting prioritization of re-processing complex trauma and associated DSOs, beyond the symptoms or forms that the expression of discomfort takes (Heim et al., 2010). Those results are in line with clinical treatment guidelines that recommend psychological interventions as first line treatments for CM (NICE, 2017; WHO, 2017).

The literature claims complex trauma creates a "perfect storm" that can result in youths being flooded with unwanted emotions, thoughts, and memories, which could lead to a wide range of dysfunctional avoidance or destructive behaviour: substance abuse, aggression, delinquency or suicidal behaviour (Briere and Scott, 2013; Herman, 1997; van der Kolk, 2005). Our study supports cannabis use appearing earlier in youths exposed to CM, perhaps as an attempt to cope with negative affect (Hogarth et al., 2019) or as a form of self-medication to "anesthetize" suffering and reduce global distress. Additionally, this supposes another risk factor for other serious psychopathological problems such as psychotic disorders (Forti et al., 2019), thus supporting a self-reinforcing cycle between CM, maladaptive personality traits and exposure to new stressors or risk factors for mental disorders (Marques-Feixa et al., 2021a).

Additionally, our study demonstrates that the four dimensions of the new CPTSD diagnosis are present in children and adolescents exposed to complex trauma who present a great variety of psychiatric disorders (behavioural, mood, anxious, psychotic, ADHD, etc.). These results support the literature on this topic, which highlights the wide-ranging and long-lasting consequences of complex trauma, as opposed to a single traumatic incident (Brewin et al., 2017; Redican et al., 2021). In fact, this new diagnosis may indicate that CM affects core personality do-

mains, as Self-Trauma Theory claims (Myers et al., 2002), altering how we perceive and interpret the world around us, consequently affecting how we respond to and manage future stressful situations (Allen et al., 2013). This set of symptoms (DSOs) affects essential aspects of living and adapting to society, which could underpin the worse global functioning previously reported in individuals with CM. The degree to which DSOs affect survivors' lives, more than PTSD itself, has a direct impact on clinical practice, since it facilitates diagnostic precision and more personalized and effective treatments (Cloitre, 2020).

Moreover, we aimed to examine whether the different CM subtypes have a differential impact on the alteration of CPTSD domains, or if this alteration depends on the developmental stage at exposure (Hughes et al., 2017; Jonson-Reid et al., 2012). In our sample, emotional neglect was the most prevalent CM subtype (Stoltenborgh et al., 2013) and contributed to all CPTSD subdomains throughout development. Taken together with the broader CM literature, our current findings support the notion that emotional trauma (neglect or abuse) is just as damaging, as other types of CM such as physical or sexual abuse, or even more so (e.g., McGee et al., 1997; Spinazzola et al., 2014).

Although post-traumatic stress symptomatology increased with all CM subtypes, a significant effect of physical neglect only appeared after exposure during infancy (0–5 years). Physical abuse seems to be detrimental throughout development, but also appears to be especially harmful when it occurs at 0–5 years, contrary to popular beliefs that events during early life are less important. Interestingly, emotional abuse seems to be the CM subtype that best explains the variability of PTSD symptoms (Hoeboer et al., 2021), contrary to the idea that this is sexual or physical abuse (Luthra et al., 2009). Furthermore, PTSD can particularly result from emotional abuse suffered at age six to 12, when language acquisition is already developed and children can understand the meaning of hurtful words; some studies also indicate sensitivity to intimate partner violence, considered a subtype of emotional abuse, at this developmental stage (Castro et al., 2017). Sexual abuse seems to be harmful and induce PTSD when occurs after age 5, as previously re-

Table 3
Regression analyses of the impact of CM¹ (each subtype and period of exposure) on CPTSD² symptomatology (PTSD³, emotional dysregulation, negative self-concept and interpersonal problems) in participants with a current psychiatric diagnosis.

Step	Effect	Cases	Cases						
			95 % CI	95 % CI					
		Beta	LL	UL	t	p	ΔR^2 (*100)		
Outcome	e: PTSD								
1	Developmental stage ^a	0.159	-0.994	4.444	1.258	0.211	23.8 %***		
	Age	0.200	-0.072	0.978	1.711	0.090			
	Sex	0.194	-0.107	4.340	1.887	0.062			
	Socioeconomic status	-0.089	-0.080	0.025	1.025	0.308			
2	CM-score	0.309	0.046	0.169	3.465	0.001***	7.8 %***		
2.1a	Physical neglect	0.103	-0.922	3.258	1.108	0.270	0.9 %		
2.1b	PN ⁴ 0–5 years	0.234	0.068	6.156	2.028	0.045*	7.1 %*		
	PN 6–12 years	0.029	-2.862	3.588	0.223	0.824			
	PN 13-17 years	-0.123	-5.157	1.150	1.260	0.211			
.2a	Emotional neglect	0.259	0.963	4.802	2.977	0.004**	5.9 %**		
.2b	EN ⁵ 0–5 years	0.048	-1.941	3.020	0.431	0.667	6.5 %*		
	EN 6–12 years	0.218	-0.393	5.110	1.700	0.092			
	EN 13-17 years	0.045	-2.012	3.009	0.394	0.695			
.3a	Emotional abuse	0.421	2.867	6.554	5.066	< 0.001***	15.0 %***		
.3b	EA ⁶ 0–5 years	-0.098	-4.152	1.461	0.951	0.344	13.9 %***		
	EA 6–12 years	0.488	2.752	8.418	3.909	< 0.001***			
	EA 13-17 years	-0.065	-3.539	1.830	0.631	0.529			
.4a	Physical abuse	0.290	1.437	5.079	3.547	0.001***	8.2 %***		
.4b	PA ⁷ 0–5 years	0.201	0.012	5.520	1.992	0.049*	9.8 %**		
	PA 6–12 years	0.157	-0.806	4.435	1.373	0.173			
	PA 13-17 years	0.013	-2.957	3.391	0.136	0.892			
.5a	Sexual abuse	0.350	2.386	6.925	4.068	< 0.001***	10.4 %***		
.5b	SA ⁸ 0–5 years	-0.141	-12.79	1.320	1.612	0.110	9.9 %**		
	SA 6–12 years	0.250	1.188	7.204	2.767	0.007**			
	SA 13-17 years	0.194	0.389	6.108	2.253	0.026*			
	e: emotional dysregulation								
	Developmental stage ^a	0.199	-0.567	3.417	1.419	0.159	6.2 %		
	Age	-0.217	-0.710	0.059	1.678	0.096			
	Sex	0.048	-1.287	1.971	0.416	0.678			
	Socioeconomic status	-0.176	-0.074	0.003	1.830	0.070			
	CM-score	0.225	00.005	0.098	2.206	0.030*	4.2 %*		
.1a	Physical neglect	0.169	-0.258	2.783	1.646	0.103	2.4 %		
.1b	PN 0–5 years	0.230	-0.274	4.324	1.747	0.084	3.4 %		
	PN 6–12 years	-0.091	-3.179	1.694	0.604	0.547			
	PN 13–17 years	0.009	-2.482	2.283	0.083	0.934			
.2a	Emotional neglect	0.200	0.036	2.909	2.033	0.045*	3.6 %*		
.2b	EN 0-5 years	0.059	-1.435	2.309	0.463	0.644	2.6 %		
	EN 6–12 years	-0.005	-2.116	2.038	0.037	0.971			
	EN 13–17 years	0.171	-0.647	3.143	1.306	0.194	400/#		
.3a	Emotional abuse	0.217	0.124	3.073	2.150	0.034*	4.0 %*		
.3b	EA 0–5 years	0.205 -0.044	-0.349	4.073	1.670	0.098 0.770	5.0 %		
	EA 6–12 years EA 13–17 years		-2.562 1.024	1.902	0.294				
40	EA 13–17 years Physical abuse	0.126 0.312	-1.024 0.974	3.206 3.652	1.023	0.309 0.001***	9.4 %***		
.4a .4b	Physical abuse PA 0–5 years	0.312	-0.691	3.436	3.426 1.319	0.001	9.4 %^^^ 8.2 %*		
טד.	PA 0-5 years PA 6-12 years	0.151	-0.691 -1.126	2.802	0.847	0.190	0.∠ %0		
	PA 0–12 years PA 13–17 years	0.110	-1.126 -1.029	3.728	1.125	0.263			
.5a	Sexual abuse	0.120	-0.920	2.641	0.958	0.340	0.8 %		
	SA 0–5 years	-0.064	-7.215	3.808	0.613	0.541	1.0 %		
2.5b	SA 6–12 years	0.109	-1.139	3.559	1.022	0.309	1.0 /0		
			-2.195	2.272	0.034	0.973			
		0.003		/-	0.001	3.270			
	SA 13–17 years	0.003							
		0.003							
outcome	SA 13–17 years e: negative self concept			1.554	0.549	0.584	13.3 %**		
outcome	SA 13–17 years e: negative self concept Developmental stage ^a	0.074	-0.880	1.554 0.394	0.549	0.584 0.184	13.3 %**		
Outcome	SA 13–17 years e: negative self concept Developmental stage ^a Age	0.074 0.166	-0.880 -0.076	0.394	1.338	0.184	13.3 %**		
Outcome	SA 13–17 years e: negative self concept Developmental stage ^a Age Sex	0.074 0.166 0.204	-0.880 -0.076 -0.063	0.394 1.856	1.338 1.928	0.184 0.066	13.3 %**		
Outcome	SA 13–17 years e: negative self concept Developmental stage ^a Age Sex Socioeconomic status	0.074 0.166 0.204 0.048	-0.880 -0.076 -0.063 -0.017	0.394 1.856 0.030	1.338 1.928 0.525	0.184 0.066 0.600			
Outcome L	SA 13–17 years e: negative self concept Developmental stage ^a Age Sex Socioeconomic status CM-score	0.074 0.166 0.204 0.048 0.340	-0.880 -0.076 -0.063 -0.017 0.022	0.394 1.856 0.030 0.077	1.338 1.928 0.525 3.600	0.184 0.066 0.600 <0.001***	9.5 %***		
Outcome	SA 13–17 years e: negative self concept Developmental stage ^a Age Sex Socioeconomic status	0.074 0.166 0.204 0.048	-0.880 -0.076 -0.063 -0.017	0.394 1.856 0.030	1.338 1.928 0.525	0.184 0.066 0.600			

(continued on next page)

Table 3 (continued)

Step	Effect	Cases							
			95 % CI						
		Beta	LL	UL	t	p	ΔR^2 (*100)		
	PN 13-17 years	-0.051	-1.764	1.075	0.481	0.631			
2.2a	Emotional neglect	0.268	0.392	2.115	2.885	0.005**	6.4 %**		
2.2b	EN 0-5 years	0.070	-0.794	1.459	0.585	0.560	5.0 %		
	EN 6–12 years	0.136	-0.631	1.868	0.982	0.328			
	EN 13-17 years	0.097	-0.693	1.588	0.779	0.438			
2.3a	Emotional abuse	0.309	0.574	2.327	3.280	0.001***	8.1 %***		
2.3b	EA 0–5 years	0.043	-1.079	1.572	0.368	0.713	7.7 %*		
	EA 6–12 years	0.234	-0.216	2.461	1.663	0.099			
	EA 13-17 years	0.059	-0.942	1.594	0.510	0.611			
2.4a	Physical abuse	0.289	0.543	2.186	3.294	0.001***	8.1 %***		
2.4b	PA 0-5 years	0.141	-0.443	2.080	1.287	0.201	7.6 %*		
	PA 6–12 years	0.109	-0.674	1.726	0.869	0.387			
	PA 13–17 years	0.122	-0.621	2.286	1.135	0.259			
2.5a	Sexual abuse	0.210	0.105	2.243	2.178	0.032*	3.7 %*		
2.5b	SA 0–5 years	-0.089	-4.820	1.802	0.904	0.368	3.9 %		
	SA 6–12 years	0.161	-0.277	2.545	1.593	0.114			
	SA 13-17 years	0.116	-0.528	2.156	1.203	0.232			
Outcome	e: interpersonal problems								
1	Developmental stage ^a	0.163	-0.386	1.541	1.189	0.237	10.6 %*		
	Age	0.037	-0.159	0.213	0.293	0.770			
	Sex	0.120	-0.359	1.217	1.080	0.283			
	Socioeconomic status	-0.131	-0.032	0.005	1.402	0.164			
2	CM-score	0.423	0.027	0.069	4.540	< 0.001***	14.7 %***		
2.1a	Physical neglect	0.206	0.031	1.491	2.066	0.041*	3.5 %*		
2.1b	PN 0-5 years	0.162	-0.394	1.807	1.274	0.206	5.0 %		
	PN 6-12 years	0.091	-0.795	1.537	0.631	0.529			
	PN 13-17 years	-0.087	-1.605	0.675	0.808	0.421			
2.2a	Emotional neglect	0.264	0.276	1.643	2.785	0.006**	6.1 %**		
2.2b	EN 0-5 years	-0.038	-1.029	0.749	0.313	0.755	5.7 %		
	EN 6–12 years	0.186	-0.327	1.645	1.325	0.188			
	EN 13-17 years	0.139	-0.398	1.401	1.106	0.271			
2.3a	Emotional abuse	0.407	0.821	2.159	4.417	< 0.001 ***	14.0 %***		
2.3b	EA 0-5 years	0.079	-0.666	1.381	0.693	0.490	11.9 %**		
	EA 6–12 years	0.314	0.142	2.208	2.256	0.026*			
	EA 13-17 years	0.003	-0.966	0.992	0.0236	0.979			
2.4a	Physical abuse	0.336	0.589	1.876	3.837	< 0.001 ***	11.0 %***		
2.4b	PA 0-5 years	0.246	0.131	2.089	2.249	0.027*	10.9 %**		
	PA 6–12 years	0.068	-0.675	1.188	0.547	0.586			
	PA 13-17 years	0.126	-0.456	1.800	1.182	0.240			
2.5a	Sexual abuse	0.272	0.351	2.019	2.818	0.006**	6.3 %**		
2.5b	SA 0-5 years	-0.067	-3.465	0.684	0.686	0.494	6.9 %*		
	SA 6-12 years	0.261	0.333	2.528	2.586	0.010**			
	SA 13-17 years	0.101	-0.487	1.600	1.058	0.292			

Note: Effects on participants without psychiatric disorders are reported in supplementary material.95 % CI (95 % confidence interval, where LL is the lower limit and UL the upper limit).

- ¹ CM: Childhood maltreatment.
- ² CPTSD: Complex Post-traumatic Stress Disorder.
- ³ PTSD: Post-Traumatic Stress Disorder.
- ⁴ PN: Physical Neglect.
- ⁵ EN: Emotional Neglect.
- ⁶ EA: Emotional Abuse.
- ⁷ PA: Physical Abuse.
- ⁸ SA: Sexual Abuse.

ported (Adams et al., 2018). These findings emphasize the importance of introducing the developmental stage of CM in clinical practice and future research.

We further observed that almost all CM subtypes seem to be associated with DSOs subdomains. For example, emotional trauma (both neglect and abuse) and physical abuse may affect the individual's ability to regulate emotions during all development (see Fig. 2). Youths might feel emotionally overwhelmed when trauma-related distress exceeds their ability to handle such situations, and they lack safe healthy role models to help them learn adaptive skills. In addition, physical abuse from abuser caregivers is often unpredictable and can induce feelings of

uncertainty, also generating greater emotional destabilization. This agrees with recent meta-analysis which showed a strong association between complex trauma and emotion regulation difficulties in children and adolescents (Villalta et al., 2020). Furthermore, difficulties with emotional regulation are associated with a wide range of both internalizing and externalizing disorders, increasing the risk of suffering other mental health problems (Turton et al., 2021). Meanwhile, negative self-concept and interpersonal problems seem to be affected by all forms of CM, modifying mental representations of oneself and others early on. Interestingly, physical neglect and abuse seem to be most damaging during the first 5 years of life, while emotional and sexual abuse are

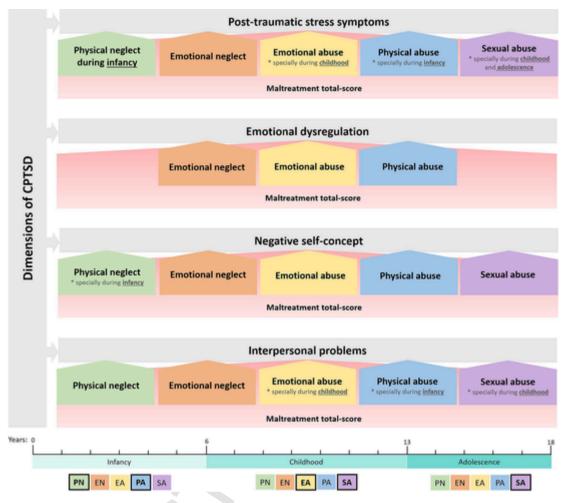


Fig. 2. The impact of CM^1 -score (in red) and CM subtypes (other colours) and the age of exposure on the different $CPTSD^2$ subdomains (in grey) in children and adolescents with current psychiatric disorders (n = 116).

How all CM subtypes contribute to CPTSD during all developmental stages is shown at the bottom of the figure. The bold boxes indicate the developmental stage at which each CM subtype has the greatest impact. PN: physical neglect, EN: emotional neglect, EA: emotional abuse, PA: physical abuse, SA: sexual abuse. ¹CM: Childhood maltreatment ²CPTSD: Complex Post-traumatic Stress Disorder. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

during primary school age (6–12). In summary, DSOs demonstrate that children can learn adaptations to cope with CM which are useful when physical or emotional threats are present, but can turn counterproductive as they grow up and encounter situations and relationships that are safe, producing interferences with the capacity to live, love, and be loved (Spinazzola et al., 2017).

Supported by considerable scientific evidence (Hyland et al., 2018; Yehuda and Wong, 2007), identification of CPTSD is important so that more complex consequences of traumatic experiences can be recognized and targeted intervention can be offered that avoids inaccurate and inadequate diagnoses and treatments (Karatzias et al., 2019). The inclusion of this new diagnosis may provide an opportunity to focus treatment on the processing of complex trauma, instead of having to rely on interventions focused on comorbid symptomatology that could hide the root of the problem (Briere and Hedges, 2010; Sachser et al., 2017). Timely quality interventions can make an important difference in shifting the balance between risk and protective factors (Chinitz et al., 2017).

To interpret the whole picture, we must consider that CM may alter brain architecture and dysregulate neurobiological mechanisms related to the stress response. This may influence self-concept and the ability to regulate emotions, resulting in reduced neurobiological resources to cope with new adverse experiences and respond effectively (Keding et al., 2021; Marques-Feixa et al., 2021b). However, genetic and environmental protective factors could also lead to resilience and explain why not everyone who experiences CM develops lifelong disabilities.

5. Limitations

The present study has some limitations. Firstly, the high percentage of psychiatric diagnoses in the sample means it was not possible to study specific interactions between specific diagnostic categories and CM history. In addition, there is a small percentage of resilient youths, defined as children with a history of CM but without current psychopathology. Exploring the presence of other biopsychological protective or risk factors, such as the relationship with the aggressor, genetics, the attachment to protective caregivers or the support received, could elucidate their contributions to mental health outcomes (Myers et al., 2002). This is a cross-sectional study, so direct inference cannot be assumed and longitudinal studies would be of great interest to assess the evolution of CPTSD symptomatology.

Moreover, the definition of CM is complex, while the methods available to evaluate it and the criteria for classifying victims differ greatly across cultures. For this reason, it is necessary to promote studies of CM based on child populations, when interventions are still possible. Furthermore, as childhood and adolescence are considered key develop-

mental stages for emotion regulation, self-concept and interpersonal abilities, developing a gold standard adapted to general young populations would be paramount. In this regard, Haselgruber et al. (2020) have recently validated the International Trauma Questionnaire (ITQ) to asses CPTSD in children and adolescents. However, deeper exploratory instruments should be designed to address complex trauma and CPTSD symptomatology in young populations.

6. Conclusions

CM is a highly complex phenomenon affecting individuals systemically and a major risk factor for dysfunctionality and a huge range of psychiatric disorders and comorbidity. The present study supports the clinical utility of gathering information on CM and adverse childhood experiences to help understand the complexity of psychiatric symptoms observed in children and adolescents exposed to complex trauma. The new diagnosis accepted by ICD-11, CPTSD, may help explain the worse clinical prognosis observed in patients exposed to CM, and may guide the development of more efficient preventive treatments and interventions focused on trauma, emotional dysregulation, negative self-concept and interpersonal problems, which are fundamental aspects during development.

Different subtypes of CM and the developmental stage of exposure differentially impact CPTSD subdomains. Specifically, emotional neglect was the most prevalent CM and contributed to all CPTSD subdomains throughout development. Although post-traumatic stress symptomatology increased with all CM subtypes, a significant effect of physical neglect only appeared after exposure during infancy (0–5 years). Physical abuse also appears to be especially harmful when it occurs at 0-5 years. Emotional abuse seems to be the CM subtype that best explains the variability of PTSD symptoms. PTSD can particularly result from emotional abuse suffered at age six to 12. Sexual abuse seems to be harmful and induce PTSD when occurs after age 5. Regarding DSOs subdomains, both emotional neglect and abuse, and physical abuse had a strong impact on emotional dysregulation. Negative self-concept and interpersonal problems seem to be affected by all CM subtypes. Specifically, physical neglect and abuse was of greater risk during the first 5 years of life, while emotional and sexual abuse were during primary school age (6-12 years).

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CRediT authorship contribution statement

Conceptualization, L.M-F., J.M.-H., S.R., P·S-P. and L.F.; methodology, L.M-F.; software, L.M-F. and J.M-H.; validation, L.M-F., J.M-H.; formal analysis, L.M-F. and J.M-H.; investigation, L.M-F., S.R., P·S.-P., MJ.M., E.A., A.M, M.M., and M.R.; resources, S.R., M.R., M.R.-C., I.Z., MJ.M., H·B-F., E.A. and L.F.; data curation, L.M-F.; writing—original draft preparation, L.M.-F. and J.M-H.; writing—review and editing, L.M-F., S.R., P.S-P., N.M-G., M.F-P., M.R.-C., H·B-F. and L.F.; visualization, L.M-F., J.M-H., S.R. and L.F.; supervision, L.M-F., J.M-H., S.R. and L.F.; funding acquisition, L.M-F., S.R., M.R.-C., I.Z. and L.F. The EPI-Young Stress GROUP members facilitate the study. All authors have read and agreed to the published version of the manuscript.

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.

Conflict of Interest

The authors declare no conflict of interest regarding the publication of this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.03.088.

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