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The relationship between childhood trauma and psychosis: The influence of a parental history of mental disorders

HOVEDOPPGAVE

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Forord

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Abstract

Childhood trauma (CT) has been reported as a risk factor for schizophrenia spectrum disorders (SSDs). Few studies have considered the possible influence of parental mental disorders on CT, though having parental mental disorders may increase both mental disorders and CT, including neglect. Understanding whether CT influences psychosis symptom severity independently of parental mental disorders has implications for prevention and treatment of SSDs. In this cross-sectional study, we aimed to examine whether the relation between overall CT, CT subtypes, and SSDs, was moderated by parental mental disorders. We hypothesized a positive association between CT and SSD symptoms, possibly moderated by parental mental disorders, and further that parental mental disorders would moderate the relation between childhood neglect and SSD symptoms. Patients with SSDs (N = 133) from the Bergen-Stavanger-Innsbruck-Trondheim (BeStInTro) study, were examined by means of multiple regression analysis with interaction term. Group differences were examined using independent sample t-tests or chi-square tests. SSD patients with CT experiences showed more psychosis symptoms compared to SSD patients with no CT. Regression analyses showed a dose-response relationship between CT and overall psychosis symptom severity and negative symptom severity. The association between CT and psychosis symptom severity was however independent, and not moderated by parental mental disorders. Prevention of CT is therefore important for SSDs, and trauma-related treatment for patients with SSDs may be warranted.

Keywords: Risk factors, psychosis, childhood trauma, parental mental disorders.

Sammendrag

Barndomstraumer (CT) har blitt rapportert som en risikofaktor for schizofrenia-spektrum lidelser (SSDs). Få studier har undersøkt innvirkningen foreldrenes psykiske lidelser kan ha på CT, til tross for at dette kan øke risikoen for både psykiske lidelser og CT, inkludert neglekt. Å forstå hvorvidt CT påvirker alvorlighetsgraden av psykosesymptomer uavhengig av foreldrenes psykiske lidelser har implikasjoner for forebygging og behandling av SSDs. Formålet med denne kryss-seksjonelle studien var å undersøke om sammenhengen mellom CT, CT subtyper og SSDs var moderert av foreldrenes psykiske lidelser. Vi predikerte en positiv sammenheng mellom CT og SSD symptomer, muligens moderert av foreldrenes psykiske vansker, og videre at foreldrenes psykiske vansker ville moderere sammenhengen mellom neglekt og SSD symptomer. Med et utvalg av SSD pasienter (N = 133) fra Bergen-Stavanger-Innsbruck-Trondheim (BeStInTro)-studien gjennomførte vi multiple regresjonsanalyser med interaksjonsledd for å undersøke sammenhengen. Gruppeforskjeller ble undersøkt ved hjelp av t-tester og chi-kvadrattester. SSD pasienter med CT-erfaringer rapporterte høyere nivå av psykotiske symptomer, sammenliknet med SSD pasientene uten CT-erfaringer. Regresjonsanalysene viste en dose-respons sammenheng mellom CT og overordnet grad av psykosesymptomer, samt grad av negative symptomer. Sammenhengen mellom CT og grad av psykosesymptomer var derimot uavhengig, derav ikke moderert av foreldrenes psykiske lidelser. Forebygging av CT er derfor viktig for SSDs, og trauma-relatert behandling for pasienter med SSDs kan være berettiget.

Nøkkelord: Risikofaktorer, psykose, barndomstraumer, psykisk lidelse hos foreldre

Table of contents

The relationship between childhood trauma and psychosis: The influence of a parental history of mental disorders

Psychosis and schizophrenia spectrum disorders (SSDs)

In the matter of both human suffering and social expenditure, schizophrenia is one of the costliest mental disorders (van Os & Kapur, 2009). Isolated, the estimated global lifetime prevalence of schizophrenia has varied between approximately 0.30 – 0.60% (Jongsma et al., 2019; Simeone et al., 2015; van Os & Kapur, 2009; World Health Organization [WHO], 2022b), whereas the estimation increases to approximately 2% if other psychotic disorders are included as a broader category (van Os & Kapur, 2009). Psychosis can be defined as a mental state in which the ability to distinguish between oneself and reality around oneself is affected, resulting in a partial or complete loss of reality (Johannessen & Joa, 2021). It is a symptom with multiple organic and psychological risk factors, as well as a core feature of schizophrenia spectrum disorders (SSDs; WHO, 2016). SSDs are often referred to as non-affective psychoses and include F20 Schizophrenia, F21 Schizotypal disorders, F22 Delusional disorders, F23 Brief psychotic disorders, F24 Shared psychotic disorders, F25 Schizoaffective disorders, F28 Other non-organic psychotic disorders, and F29 Unspecified non-organic psychosis in the International Classification of Disease, tenth edition (ICD-10; WHO, 2016).

SSDs are recognized by symptoms categorized as negative, positive, and disorganized, according to the ICD-10 (WHO, 2016). Negative symptoms involve a decline or absence of normal functioning regarding interest and motivation (e.g. social withdrawal, anhedonia, avolition) or expression (e.g. alogia, reduced affect), and positive symptoms reflect an excess of normal functioning such as hallucinations (of any sensory modality) or delusions (e.g. grandeur, control; Correll & Schooler, 2020). Disorganized symptoms may manifest through language (e.g., interrupted or disconnected speech), expression (incongruent affect) and behavior (e.g., catatonic, bizarre), and may reflect disorganized thinking (e.g., fast, slow or

interrupted thought flow; WHO, 2019). Other common symptoms include cognitive difficulties present before, during and/or after psychosis onset (Kahn & Keefe, 2013), as well as alterations in the sense of self (Moe & Docherty, 2014). Treatment of SSDs typically include a combination of evidence-based medical and psychological treatment, such as antipsychotic medication, cognitive behavioral therapy (CBT), and family interventions (Helsedirektoratet [HDIR], 2013; National Collaborating Centre for Mental Health [UK], 2014). Furthermore, the Norwegian national guidelines (HDIR, 2013) recommends the assessment of childhood trauma (CT) on people with psychosis, but does not at this stage recommend a specific treatment for trauma within psychosis treatment.

The development of psychosis and SSDs

Our understanding and conceptualization of schizophrenia and other psychotic disorders has changed over time (Valle, 2020). Traditionally mental disorders have been viewed categorically as different states with different etiology (Johannessen & Joa, 2021), however a more dimensional approach to psychopathology is growing (Chaiyachati & Gur, 2021), which acknowledges the significant overlap between different diagnostic groups (Johannessen & Joa, 2021). Psychosis is now understood as appearing on a continuum from a so-called "normal" thinking to a complete psychotic understanding of reality, in comparison to the previously categorical understanding (Johannessen & Joa, 2021). Research has shown that subthreshold psychotic experiences can be found in approximately 7% of the general population, with 80% of the psychotic experiences being transitory, 20% persistent, and 7% evolving into a psychotic disorder (Linscott & van Os, 2013), which further supports a dimensional thinking. People with psychotic symptoms vary where they appear on the spectrum, and the course of development for psychotic disorders such as schizophrenia usually happens gradually, but stagewise across the continuum (Häfner et al., 2003).

Another support for this transdiagnostic perspective is the observation of psychotic symptoms in several psychiatric disorders. This includes, but is not limited to, posttraumatic stress disorder (PTSD; Uldall et al., 2020), bipolar disorder (Aminoff et al., 2022), and autism (van Schalkwyk, 2017; van Schalkwyk et al., 2017). Furthermore, an increased prevalence of PTSD in patients with SSDs compared to the general population has been reported (van Os et al., 2003), with estimates of comorbidity ranging from 0 to 57% (Seow et al., 2016).

Multiple complex factors have been identified that contribute to the development of psychosis and SSDs (Chaiyachati & Gur, 2021). The presence of a biogenetic component of psychosis has been extensively studied (Husted et al., 2010; McGuffin et al., 1994). This is in part due to the observation of a familial clustering of psychotic disorders, where having a first-degree relative with a psychotic disorder statistically increases the risk for developing psychosis (Santesteban-Echarri et al., 2022). Several biological correlates for psychotic disorders have been reported, such as structural brain alterations and cognitive impairment, particularly with the use of magnetic resonance imaging (MRI). Meta-analyses consistently report reduced grey matter volume (GMV) in people with psychotic disorders (Haijma et al., 2013; Vita et al., 2015), as well as those with high familial risk or clinical high risk for psychotic disorders (Sprooten et al., 2013; van Lutterveld et al., 2014). Changes are especially apparent in frontal and temporal areas, as well as alterations in white matter integrity and their connections (Sommer & Kahn, 2015). Relatedly, cognitive impairment has been identified as both a vulnerability marker and a key component of schizophrenia, which may continue to decline after the onset of illness (Anda et al., 2019; Kahn & Keefe, 2013).

Furthering evidence of a biological component comes from the clinical effectiveness of antipsychotic medications targeting dopaminergic receptors in the brain (Howes & Kapur, 2009), suggesting a level of dopamine dysregulation in development of SSDs, commonly known as the dopamine hypothesis. There is also growing evidence for a vulnerability-stress-

inflammation model for schizophrenia, which proposes that genetic vulnerabilities interact with stress and results in inflammatory responses later in life, possibly also contributing to a dysregulation of dopaminergic neurons (Pedraz-Petrozzi et al., 2020). This is an extension of the stress-vulnerability model (Zubin & Spring, 1977), a renowned model which proposed that all individuals have a degree of biologically predisposed vulnerability which could result in a psychotic episode, given the right environmental circumstances (Zubin & Spring, 1977). Hence, it has been hypothesized that there is an interactive relationship between multiple genetic and non-genetic factors in the representation of psychosis (Husted et al., 2010), where environmental factors impact the expression of genes, without altering the DNA sequence itself (i.e. epigenetics; Gürel et al., 2020). Environmental factors may accentuate the already existing risk of certain vulnerability genes or interact with genes that, absent of the environmental factor, might not have posed a significant risk at all (Miller, 2022).

Several psychological and environmental risk factors and markers have been suggested in the development of psychosis. Known risk factors include childhood adversity (Varese et al., 2012), urbanicity (van Os et al., 2003), regular use of cannabis (Hasan et al., 2020; Marconi et al., 2016), as well as affective dysregulation and increased stress-reactivity (Radhakrishnan et al., 2019). Furthermore, insecure attachment style has been proposed as a psychological factor contributing to increased vulnerability for psychosis (Berry et al., 2017; Degnan et al., 2022; Gumley et al., 2014), as well as pre- and perinatal conditions such as maternal exposure to stressful or traumatic events, maternal inflammation markers, and maternal disease (Chaiyachati & Gur, 2021; De Matteis et al., 2020; Johannessen & Joa, 2021). The past decades, CT including sexual, physical, and emotional abuse as well as physical and emotional neglect, has received increased attention as research has shown associations of all CT subtypes to SSDs (Gil et al., 2009; Mørkved et al., 2020; Varese et al., 2012). Studies have suggested that these risk factors may have an accumulative effect to the overall risk of

psychosis (Cougnard et al., 2007), and there is also some support for an interplay between familial affective liability and environmental risks (Radhakrishnan et al., 2019). However, it is not known whether the relationship between CT and psychosis is due to a family liability for mental disorders impacting both the risk for psychosis and CT, or if trauma itself has an independent effect on psychosis.

CT and adverse childhood experiences

CT can be defined as adverse childhood experiences that entail harm, potential harm or threat of harm caused by commission or omission by the caregiver of the child (Sideli et al., 2012). This definition covers adverse childhood experiences such as physical abuse and neglect, emotional abuse and neglect, and sexual abuse (Bernstein et al., 2003). Bernstein et al. (2003) have provided definitions of these five subtypes of CT. They defined childhood physical abuse as "bodily assaults on a child by an adult or older person that posed a risk of or resulted in injury" (Bernstein et al., 2003), childhood physical neglect as "the failure of caretakers to provide for a child's basic physical needs, including food, shelter, clothing, safety, and health care" (Bernstein et al., 2003), childhood emotional neglect as "the failure of caretakers to meet children's basic emotional and psychological needs, including love, belonging, nurturance, and support" (Bernstein et al., 2003), childhood emotional abuse as "verbal assaults on a child's sense of worth or well-being or any humiliating or demeaning behavior directed toward a child by an adult or older person" (Bernstein et al., 2003), and childhood sexual abuse as "sexual contact or conduct between a child younger than 18 years of age and an adult or older person" (Bernstein et al., 2003). All these subtypes of CT have the potential to result in harm of health, development, survival, or dignity of the child (WHO, 2022a). CT is regarded as a global health problem that increase the risk of having negative physical and mental health consequences (Felitti et al., 1998; WHO, 2022a). Based on data from the World Health Organization world mental health survey, Kessler et al. (2010) found

that the prevalence of CT globally was high, where 8.0% reported physical abuse, 1.6% reported sexual abuse, and 4.4% reported neglect. In addition, they found that CT and other types of childhood adversities were highly interrelated, meaning one CT subtype was likely to co-occur with other subtypes (Kessler et al., 2010).

Child abuse and neglect are often used interchangeably under the terms childhood adversities or CT, moreover child abuse and neglect are predominantly regarded as traumatic experiences (Chaiyachati & Gur, 2021). It has been suggested that CT such as abuse and neglect could be particularly harmful due to the intentional nature of these traumatic experienced as compared to accidents during childhood (Arseneault et al., 2011). Norman et al. (2012) found that all forms of CT contributed to the burden of diseases globally and should be considered as important risk factors to negative health outcomes. CT often takes place in the context of a relationship of trust or power, such as, but not limited to, the parent-child relationship (WHO, 2022a). Kessler et al. (2010) found that CT and maladaptive family functioning such as parental mental illness, substance misuse, and domestic violence, was linked to a high risk of mental disorders. In addition, research indicates that some parental factors such as mental health problems, low income, misuse of alcohol or other substances, and a dysfunctional parent-child interaction may increase the risk of CT (Gilbert et al., 2009; Stith et al., 2008; WHO, 2022a).

CT as a risk factor for SSDs and other mental disorders

Felitti et al. (1998) conducted a landmark study of adverse childhood experiences which found a dose-response relationship between adverse childhood experiences, including having parents with mental disorders, and a range of negative adult physical and mental health outcomes. A dose-response relationship means that an increase of CT is associated with an increase of negative health outcomes such as an increased symptom load. Similarly, Kisely et al. (2018) found that exposure to multiple forms of CT elevates the risk of developing mental

disorders later in life. CT may impact physical health by immediate and direct injuries (Flaherty et al., 2014), insufficient access to medical care and child welfare (Szilagyi et al., 2015), risky behaviors such as high risk sexual behaviors (Norman et al., 2012), and long-term poor physical health outcomes (Felitti et al., 1998). Regarding mental health outcomes, research has found a link between CT and a range of mental disorders such as mood disorders, personality disorders, anxiety disorders, PTSD, dissociative disorders, and psychotic disorders (Carr et al., 2020; Gardner et al., 2019; Gilbert et al., 2009; Norman et al., 2012; Varese et al., 2012).

Research has shown that CT is associated with psychological, biological, neurological, and physiological consequences, which in turn are hypothesized as possible mechanisms that may explain the development of mental disorders (Baldwin et al., 2023; Chaiyachati & Gur, 2021). One suggested psychological mechanism associated with CT exposure is a heightened threat processing which may increase the vulnerability to mental health problems (McLaughlin & Lambert, 2017). CT is also associated with neurobiological changes and loss of GMV in specific brain regions related to stress regulation such as amygdala, hippocampus (Hoy et al., 2012; Paquola et al., 2016), and prefrontal cortex (De Bellis et al., 2002). Additionally, voxel-based analysis has showed that some variance in GMV in psychotic patients may be explained by a history of sexual abuse (Sheffield et al., 2013). Moreover, studies have found changes in complex higher order functions and changes more widely distributed across the cortex (Gehred et al., 2021). These neurobiological disturbances may decrease the brain's ability to regulate stress, and therefore increase the risk for psychopathology (Pechtel & Pizzagalli, 2011), including SSDs (Read et al., 2014).

The importance of CT as a risk factor for mental disorders (Baldwin et al., 2023) underlines the relevance of examining potential risk factors associated with CT exposure and the consequences of CT. For instance, people who report CT are more likely to have a

parental history of mental disorders (Gilbert et al., 2009; Santvoort et al., 2015; Sidebotham & Golding, 2001) and a genetic liability for mental disorders (Sallis et al., 2021). In addition, children of mentally ill parents have a higher risk at developing mental disorders compared to children of parents without mental disorders (Stracke et al., 2019), thus parental mental disorders may be an important factor to address in the association between CT and SSDs.

The relationship between CT and SSDs

A large body of research has found associations between CT and SSDs (Bonoldi et al., 2013; Matheson et al., 2013; Varese et al., 2012). It is important to note that not all individuals exposed to CT develop SSDs later in life, nor do all individuals with SSDs report CT exposure (Read et al., 2014). However, research has found a three-folded risk of reported CT in patients with SSDs as compared to healthy controls, suggesting evidence for a high prevalence of CT in SSD patients (Varese et al., 2012). Varese et al. (2012) conducted a meta-analysis which showed that CT is an environmental risk factor for SSDs and found that CT increased the risk for psychosis with an odds ratio of 2.8. Consequently, they estimated that a total prevention of CT would reduce SSDs by about 33%**,** if all other risk factors were held constant and assuming causality (Varese et al., 2012). Some studies have shown that the prevalence of CT may be even higher among patients with a psychotic disorder than other patient groups (Matheson et al., 2013; Mørkved et al., 2017).

CT may be of particular importance in SSDs as CT seems to worsen the prognosis of SSDs and increase treatment resistance, including a reduced response to antipsychotic medications (Hassan & De Luca, 2014; Misiak et al., 2017; Mørkved et al., 2022; Thomas et al., 2019). Moreover, research has found that CT is specifically associated with positive symptoms in SSDs, such as hallucinations and delusions (Scott et al., 2007; Shevlin et al., 2007). Research has also found that CT has been associated with psychotic experiences in healthy people, which might further emphasize the role of CT in the development of psychotic

symptoms (Sommer et al., 2010). In addition, Thompson et al. (2014) found that CT predicted the transition to psychosis from a state of ultra-high risk for psychosis. In sum, these findings may emphasize the importance of the potentially specific effects of CT in relation to SSDs.

Research has suggested a dose-response relationship between CT and SSDs, including symptom severity of SSDs (Şahin et al., 2013; Trauelsen et al., 2015; Varese et al., 2012). The dose-response relationship between CT and SSDs is of importance as one subtype of CT tends to co-occur with other subtypes of CT, thus increasing the consequences (Green et al., 2010; Varese et al., 2012). In addition, CT tends to be a chronic condition rather than one single experience (Gilbert et al., 2009), meaning CT often entails a high severity level and therefore the potentially harmful effects. These findings may be indicative of the dose-response relationship, which may both be of value in our understanding of the etiology, as well as for treatment and prevention of SSDs.

The relationship between CT subtypes and SSDs

Even though CT as a risk factor for SSDs is now widely accepted (Baldwin et al., 2023; Chaiyachati & Gur, 2021; Varese et al., 2012), the possible association between different types of CT and psychotic symptoms needs to be further investigated (Heins et al., 2011; Schalinski et al., 2019). The possible effects of neglect are still understudied, even though neglect is one of the most common forms of child maltreatment (De Bellis et al., 2009; Hornor, 2014; Stoltenborgh et al., 2013). Neglect entails growing up without the necessary care and protection, and the lack of positive stimulation that is essential for a normal brain development (Heins et al., 2011). Gilbert et al. (2009) found that neglect may increase the risk of negative health outcomes, at least in the same extent as physical and sexual abuse. Furthermore, it has been suggested that the absence of adequate care could disturb the normal brain development, and thus increase the risk for mental disorders (De Bellis et al., 2009).

There are some aspects of neglect that may emphasize possible specific effects of neglect on SSDs. Neglect is characterized by a chronic pattern of the caregiver not fulfilling the child's needs (Leeb et al., 2011), moreover neglect often co-occurs with other types of adversities such as parental substance abuse, poverty, and parental mental illness (Slack et al., 2011). The often chronic pattern of neglect and the additional adversities might increase the severity of CT, leading to more severe consequences in line with findings indicating a dose-response relationship between CT and SSDs (Green et al., 2010; Şahin et al., 2013; Varese et al., 2012). Research also indicates that neglect is specifically associated with different aspects of SSDs such as cognition, social cognition, and the development of SSDs (Kilian et al., 2018; Li et al., 2017; Mørkved et al., 2020; Schalinski et al., 2019). Regarding the association of neglect and specific symptoms in SSDs, Schalinski et al. (2019) found that neglect during the frontocortical development was associated with more severe positive psychotic symptoms. Neglect may thus be associated with specific aspects of SSDs and a worsening of psychotic symptoms possibly also due to an increase of CT exposures. Since parental mental disorders may affect neglect (Slack et al., 2011), it is important to examine how parental mental disorders influence the relationship between neglect and symptoms of SSDs.

On the other hand, studies have suggested specific effects of the other subtypes of CT on SSDs, such as sexual, physical, and emotional abuse (Trauelsen et al., 2015). This has been demonstrated by studies finding a stronger association of childhood abuse in comparison to childhood neglect on psychosis (Heins et al., 2011; Shevlin et al., 2007). Fisher et al. (2010) found that specifically physical abuse from the mother was the CT subtype strongest associated with psychosis, as the effect of childhood sexual abuse and maternal neglect disappeared when controlling for maternal physical abuse. Other authors have suggested that sexual abuse is specifically associated with auditory verbal hallucinations (Bentall et al., 2012).

Even though studies have suggested that the specific subtype of CT could be associated with specific aspects and symptoms of SSDs, research has in general shown mixed results regarding specificity of CT subtype on psychosis symptoms (Trauelsen et al., 2015). In addition, research has found that one subtype most often co-occurs with other subtypes, making the specific effect of one particular subtype on psychosis difficult to establish (DeRosse et al., 2014; Scher et al., 2004). A population study found that different types of abuse and neglect all were equally associated with delusions, paranoia and hallucinations when examining specific CT and psychotic outcome (van Nierop et al., 2014a). This may not be that surprising, considering that all subtypes of CT put the child at risk of psychological harm (De Bellis, 2001). Research into the mechanisms underlying the relation of CT and SSDs might give valuable knowledge of how they are connected, but also provide clues as to why it might be the overall harm of CTs and not specific subtypes that are the most important factor in the development of SSDs (Trauelsen et al., 2015).

Mechanisms potentially underlying the relationship between CT and SSDs

It is yet unknown how CT may increase the risk of SSDs, as the mechanisms potentially underlying the association between CT and SSDs are not straightforward and not fully understood (Chaiyachati & Gur, 2021). Research has found indications for a biopsychological model of psychosis, where both biological factors, such as genes, and adverse environmental exposures, such as CT, may impact the development and outcome of SSDs (Misiak et al., 2017). A better understanding of these mechanisms is deemed important as CT is arguably an important determinant of SSDs (Varese et al., 2012). This implies that finding preventive measures targeting not only SSDs directly, but also CT, might be an important step to decrease the risk of SSDs. As previously mentioned, research has estimated that the prevalence of SSDs would be reduced by about one third if CT was to be eliminated (Varese et al., 2012). In addition, there might be more risk factors associated with CT

exposure and SSDs that need to be further investigated (Baldwin et al., 2023), for instance one such risk factor might be parental mental disorders (Gilbert et al., 2009; Santvoort et al., 2015; Sidebotham & Golding, 2001). How and why parental mental disorders are associated with CT exposure and SSDs is not thoroughly examined in research.

When examining CT as a risk factor associated with SSDs, there are some important considerations regarding the direction and causality of how they are connected. Prospective studies have found that the reverse causation between CT and SSDs is unlikely, which means that it is unlikely that SSDs increases the risk of CT (van Winkel et al., 2013). There might be a causal effect of CT on SSDs (Lecei et al., 2019), however, studies that investigate possible confounders to better understand the mechanisms of the relationship are still needed (Baldwin et al., 2023; Chaiyachati & Gur, 2021). Research has suggested that CT might interact with genetic vulnerability and other environmental factors that are associated with biological alterations such as hypothalamic-pituitary-adrenal (HPA) axis dysregulation and structural brain alterations, in addition to psychological mechanisms such as affective dysregulation, insecure attachment, and dysfunctional cognitive schemas (Degnan et al., 2022; Misiak et al., 2017). Thus, it has been suggested that the mechanisms underlying the association between CT and SSDs may involve a genetic liability, neurobiological alterations, and additional environmental adversities (Chaiyachati & Gur, 2021; Collip et al., 2013; Fawzi et al., 2013).

CT may cause psychopathology directly, or alternatively interplay with other genetic and environmental risk factors confounding previously observed associations (Baldwin et al., 2023). It is important to note that the roles genes and environment play in the causation of mental disorders in general are not well understood (Norman et al., 2012). For instance, research has shown that CT tends to co-occur with family dysfunction, social deprivation, and additional environmental stressors which all are related to mental illness (Norman et al., 2012), making causality hard to establish. However, van Os et al. (2010) suggested that there

is a synergistic interplay between neurobiological and environmental factors in the development of SSDs. Furthermore, some models have emphasized how stressful life events may have harmful impacts on the brain during critical time of the development, which could both trigger the onset of SSDs as well as worsen the long term-term outcomes in SSDs (Misiak et al., 2014).

One proposed model for explaining the underlying mechanisms is the traumagenic model of schizophrenia (Read et al., 2001). The traumagenic neurodevelopmental model attempts to integrate biological and psychological processes as a part of the explanation of the link between CT and SSDs. The model suggests that the observed heightened sensitivity to stress and dysregulation of stress regulation mechanisms in SSDs could be due to neurodevelopmental changes in the brain caused by CT (Read et al., 2014). The neurodevelopmental changes associated with CT are seen in the HPA axis and the dopaminergic system, and these changes are also seen in SSDs (Read et al., 2014). In line with the hypothesis of CT making the individual more vulnerable to stressors, it has been suggested that the link between CT and SSDs could be explained by an increased vulnerability to the harmful effects of additional trauma or even daily life stressors (Lardinois et al., 2011). Lardinois et al. (2011) found that a history of CT in patients with SSDs was associated with an increased stress reactivity later in life, meaning an increased emotional and psychotic reaction to stressors. Thus, the disturbances of the stress regulative mechanisms and the increased reactivity to stress due to CT are suggested links to the development SSDs.

Several psychological mechanisms for the relation of CT and SSDs have been suggested (Misiak et al., 2017), including affective dysregulation as an underlying mechanism (Myin-Germeys & van Os, 2007). For instance, delusions in SSD patients have been associated with an increased tendency to perceive neutral stimuli as of negative value, moreover, a greater level of affective dysregulation has been linked to clinically relevant

psychotic experiences (van Rossum et al., 2011). Kramer et al. (2014) found evidence for an interaction of negative affect and feelings of paranoia, and that the mechanisms underlying the relation of CT and SSDs was due to the increased stress reactivity subsequent CT. Cognitive models have also proposed mechanisms underlying the association of CT and SSDs, and Gracie et al. (2007) found that the relation of CT and SSDs was moderated by negative beliefs about oneself and others. Lastly, attachment style has been proposed as a mediating, psychological factor in the relationship between CT and psychosis (Berry et al., 2017), where internalized CT is theorized to contribute to insecure attachment patterns (Fuchshuber et al., 2019).

Genetic factors predisposing to SSDs may also impact the association between CT and SSDs (van Winkel et al., 2013). Some authors have proposed that the association between CT and SSD could be due to gene-environment correlation, meaning that there may be a common underlying genetic factor that increases the risk for both CT and SSDs (van Winkel et al., 2013). However, a case-control and case-sibling comparison study found that a gene-environment correlation seemed unlikely (Heins et al., 2011). Furthermore, Lecei et al. (2019) studied monozygotic twins and found that a gene-environment correlation cannot fully explain the association between CT and SSD, because CT exposure was associated with SSDs within the twin pairs.

Rather than a gene-environment correlation, research has suggested that the mechanisms underlying the association between CT and SSDs could be due to a gene-environment interaction (Fisher et al., 2014; Morgan & Fisher, 2007; Pinckaers et al., 2019; van Winkel et al., 2013). This means that there might be underlying genetic risk that either increases the risk at being exposed to CT or increases the sensitivity of the harmful impact of CT. Indeed, a gene-environment interaction could explain why not all individuals exposed to CT develop SSDs (Fisher et al., 2014). Epigenetic mechanisms that shape the gene expression

has been a suggested underlying mechanism for the interaction of genes and CT that contributes to elevate the risk of SSDs (Babenko et al., 2015; Brietzke et al., 2012). Moreover, a recent study found indications of a synergistic effect where genes and CT may have a stronger effect when both are present (Aas et al., 2021).

Research examining the possible interactions between genetic risk factors and CT in relation to SSDs has been somewhat inconclusive (Pinckaers et al., 2019; van Winkel et al., 2013). Studies have found a significant and strong association between CT and SSDs also when controlling for genetic risk (van Winkel et al., 2013). One study found that childhood physical abuse was associated with the same level of risk of developing SSDs, regardless of parental psychosis as a measure of genetic risk (Fisher et al., 2014), while another study found indications for an interaction between CT and genetic liability (Pinckaers et al., 2019). It has further been suggested that the risk associated with having parents with mental disorders is not only genetic but may also be environmentally influenced, possibly due to a more unstable and unsafe upbringing (Fisher et al., 2014). Additive risk factors associated with CT might include environmental adversities and genetic liability, and more research into identifying specific risk factors is needed (Baldwin et al., 2023). For instance, parental mental disorders might both be a measure of genetic liability and environmental adversity (Fisher et al., 2014). Considering the proposed underlying mechanisms for the relationship between CT and SSDs, parental mental disorders could hypothetically affect the association between CT and SSDs in multiple ways; by increasing the genetic vulnerability (Sallis et al., 2021), increasing the risk of CT (Gilbert et al., 2009; Santvoort et al., 2015; Sidebotham & Golding, 2001), or perhaps by increasing the risk of harmful effects of CT exposures by being an additional stressor (Lardinois et al., 2011). Parental mental disorders may thus be a possible moderator worth examining in the association between CT and SSDs.

Even though research has shown that CT triples the risk of SSDs (Varese et al., 2012), it is still not fully understood why, or how they are connected (Aas et al., 2021). Research into identifying and better understanding risk factors and the nature of the relationship between CT and SSDs has both prognostic value as well as being an important preventive measure. Research regarding SSDs has tended to focus on genetic and not environmental confounders, thus more studies on environmental confounders are needed to avoid a biological bias (Read et al., 2009). One rarely examined factor is whether having parents with mental disorders may moderate the association found for CT and SSDs. Several studies have reported a dose-response relationship between CT and SSDs (Şahin et al., 2013; Trauelsen et al., 2015; Varese et al., 2012). However, few have examined the association of CT severity and psychosis symptom severity in SSDs while also considering the possible moderating influence or interaction of CT and parental mental disorders, which is quite prevalent in patients with SSDs (Sidebotham & Golding, 2001; WHO, 2022a). Parents who struggle with their mental health may also struggle in taking care of their children, possibly contributing to experiences related to childhood neglect (Slack et al., 2011). If this is indeed the case, it could have an impact on our understanding of how CT is related to SSDs, and possibly shed light on the association of parental mental disorders and childhood neglect in relation to SSDs. This might have implications for treatment of SSDs, as well as implications for prevention of CT and SSDs. A better understanding of parental mental disorders and CT on SSDs is therefore important both experimentally and clinically.

Aims

The primary aim of this study was to examine the interaction of parental mental disorders (i.e., bipolar disorder, schizophrenia, suicide attempts, alcohol use/dependence, substance use/dependence, other: specified) and CT in relation to psychosis symptom severity (i.e., total, positive, negative, and general psychopathology symptoms) in SSDs. The

secondary aim was to examine the interaction of the same parental mental disorders and CT subtypes (i.e., physical, sexual, and emotional abuse, and physical and emotional neglect) in relation to severity of the same psychosis symptoms in SSDs. It was hypothesized that there would be a positive association between CT severity and psychosis symptom severity in SSDs. Secondly, it was predicted that parental mental disorders would moderate the effect of neglect on psychosis symptom severity in SSDs.

Methods

Background

The present study was based on cross-sectional data from the Bergen-Stavanger-Innsbruck-Trondheim (BeSt InTro) study, which was a rater-blind, randomized, controlled trial in Bergen, Trondheim and Stavanger, Norway, and Innsbruck, Austria, see Johnsen et al. (2020) for details. The BeSt InTro study aimed to compare the effectiveness and safety of amisulpride, aripiprazole, and olanzapine in a head-to-head pragmatic trial (Johnsen et al., 2020). The patients included in the current study were 18 years or older, diagnosed within the schizophrenia spectrum according to the ICD-10 diagnoses F20-29 (WHO, 2016), and gave informed, written consent to participate. The further exclusion criteria in the study were pregnancy and breastfeeding, prolactin dependent tumors, hypersensitivity to the ingredients in the study drugs, concomitant use of medications that could induce torsade de pointes, phaechromocytoma, known risk of narrow angle glaucoma, and use of levodopa (Johnsen et al., 2020). Patients who were not able to understand the written and spoken native language were also excluded from the study (Johnsen et al., 2020). The BeSt InTro study was approved by Regional Committees for Medical and Health Research Ethics in Norway, and by the Etikkommission der Medizinische Universität Innsbruck and the Austrian Federal Office for Safety in Health Care in Austria. The present study was approved by Regional Committees

for Medical and Health Research Ethics in Norway (REK vest) in Western Norway (#2010/3387).

Sample

The sample in the present study consisted of 133 adult patients from the BeSt InTro study. See Table 1 for details on clinical and demographic characteristics. The mean age of the patients was 30.1 years (*SD* = 12.2) and 83 (62.4%) of the total sample were males. The diagnoses in the sample were as following: F20 Schizophrenia (*n* = 61), F21 Schizotypal disorder (*n* = 2), F22 Delusional disorder (*n* = 15), F23 Brief psychotic disorders (*n* = 17), F25 Schizoaffective disorder (*n* = 8), F28 Other non-organic psychotic disorders (*n* = 1), F29, and Unspecified nonorganic psychosis (*n* = 10). Patients diagnosed with organic psychosis or psychosis due to substance use were excluded. The assessment of the diagnoses was done through the administration of the Structural Clinical Interview for DSM-IV axis 1 disorders (Spitzer et al., 1992) by trained physicians and psychologists. Furthermore, the included patients scored < 4 on at least one of the following items in the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987): P1 (delusions), P3 (hallucinations), P5 (grandiosity), P6 (suspiciousness or persecution), or G9 (unusual though content).

Measurement

Childhood trauma (CT)

The Childhood Trauma Questionnaire – Short Form (CTQ-SF) is a 28 item self-report questionnaire used to retrospectively assess CT experiences (Bernstein et al., 2003). The original Childhood Trauma Questionnaire (CTQ) consists of 70 items, and there exists versions consisting of 53 items and 34 items (Dovran et al., 2013). The 28-item CTQ-SF is the most widely used and researched to date (Baker & Maiorino, 2010), and was the one used in the present study.

The CTQ-SF consists of five subscales that measure the five subtypes of CT: physical, sexual, and emotional abuse, and emotional and physical neglect (Bernstein et al., 2003). Each of these subscales is comprised of five items (Bernstein et al., 2003). The items consist of a mix between specific behavioral events reflecting each of the subtypes and general exposure to childhood abuse (Dovran et al., 2013), which is in line with recommendations on test generation (Myers & Winters, 2002). An example of a specific behavioral event in the questionnaire is “punished with hard object” (Bernstein et al., 2003). An example of general exposure to CT in the questionnaire is “was molested” (Bernstein et al., 2003). The items are rated on a 5-point Likert scale ranging from one (never), two (rarely), three (sometimes), four (often), to five (very often). The total score ranges from 25 to 125, and the subscale scores ranges from 5 to 25 (Bernstein et al., 2003). The last three items in CTQ-SF is a minimization scale, which is a validation scale (Bernstein & Fink, 1998). Moreover, the established thresholds of none, low, moderate, and severe CT make it possible to evaluate and describe the severity and frequency of CT (Dovran et al., 2013). Research has shown that the CTQ-SF holds good specificity and sensitivity, good internal consistency and test-retest reliability, and good to excellent reliability for the subscales and the total scale (Bernstein et al., 2003; Dovran et al., 2013).

The Norwegian version of the CTQ-SF (Winje et al., 2003) was used in the present study. Dovran et al. (2013) examined the psychometric properties of the Norwegian version of CTQ-SF in groups at high risk of trauma exposure, including psychiatric patients. They found that the psychometric properties were acceptable, with satisfactory accuracy and good reliability to assess different dimensions of CT, across sex and various high-risk groups (Dovran et al., 2013). The reliability estimates of the Norwegian version of the CTQ-SF ranged from .78 to .95 (Dovran et al., 2013). In addition, the internal consistency of the subscales was satisfactory to excellent (Dovran et al., 2013).

The present study was based on the scores from the administration of CTQ-SF six weeks after inclusion, increasing the chance of the patients to be in a stable clinical phase, thus increasing validity. The CTQ-SF scores were categorized into none, low, moderate, and severe abuse and neglect according to the threshold scores in the CTQ-SF manual (Bernstein & Fink, 1998). None and low levels of CT were grouped together as CT absent, and moderate and severe levels were grouped together as CT present. This created a dichotomous variable, and the sample was divided into two groups where one group consisted of those who reported CT (n = 68), and the other group consisted of those who reported no CT (n = 65). This particular grouping was done because statistically there is some level of CT in the general population, thus including a mild level of CT in the no CT group might increase sensitivity (Baker & Maiorino, 2010). The grouping of the sample into the CT and no CT groups was performed to further examine the relation of CT and demographic variables to achieve a fuller description of the sample.

The overall reliability estimates for the CTQ-SF were strong with a Cronbach's alpha = 0.866 in the present study. The subscale Cronbach's alphas were physical abuse = 0.913, emotional abuse = 0.862, sexual abuse = 0.913, physical neglect = 0.662, and emotional neglect = 0.900. The subscale Chronbach's alphas were strong for all subscales except physical neglect, however this is in line with previous research (Bernstein et al., 2003; Dovran et al., 2013).

Parental history of mental disorders

Information on paternal and/or maternal history of mental disorders was collected through a direct patient interview conducted by a trained research nurse at baseline, yielding information on the following various mental disorders: bipolar disorder, schizophrenia, suicide attempts, alcohol use or dependence, substance use or dependence and other specified mental disorders. The category other specified mental disorders yielded eight categories:

anxiety, personality disorder, eating disorder, burn-out, possibly bipolar disorder, describing the family as "crazy" (diagnosis unknown), hospitalization in a psychiatric unit (diagnosis unknown), and violent, lacking empathy (diagnosis unknown). Answers of no diagnosis and missing data were included as parental mental disorders not present. Answers of known or likely parental diagnosis were categorized as parental mental disorder present. Both confirmations of maternal and paternal history of mental disorders were assessed, yielding four groups based on having a 1) mother, 2) father, 3) both or 0) neither with a history of mental disorder. We excluded the categories death by suicide, obesity (Body Mass Index [BMI] > 30) and other not specified. Death by suicide was excluded as it entails the loss of a parent which, though a major trauma, also involves several other serious consequences which makes it qualitatively different from other measures of parental mental disorders. Obesity was excluded due to not being a measure of mental disorders, and other not specified was excluded because we have no information of what was included in that category.

Symptom severity in SSDs

The Structural Clinical Interview for the Positive and Negative Syndrome Scale (SCI-PANSS) was used to assess symptom severity in SSDs through a clinician administered clinical interview (Kay et al., 1987). The PANSS was developed to assess negative and positive symptoms of schizophrenia, as well as symptoms of general psychopathology (Leucht et al., 2005). The PANSS consists of a total of 30 items which distributes three subscales: positive symptoms, negative symptoms, and general psychopathology symptoms. Each item is rated on a 7-point Likert scale ranging from one (absent), two (minimal), three (mild), four (moderate), five (moderate severe), six (severe) to seven (extreme). The PANSS total score ranges from 30 to 120 points, whereas the score range for each subscale is 7 to 49 for positive symptoms, 7 to 49 for negative symptoms, and 16 to 112 for general psychopathology symptoms. The psychometric properties of PANSS are strong, with strong

validity, reliability, and sensitivity (Kay et al., 1987; Leucht et al., 2005). The present study was based on the PANSS total scale score and the three PANSS subscale scores measured at baseline, one week after inclusion.

Statistical analyses

All models were fitted using R version 4.22 (R Core Team, 2022). A *p*-level of <.05 was considered statistically significant for all analyses. Measures are presented as number (*n*) and percentages (*%*), or as mean (*M*) and standard deviations (*SD*). The adjusted R^2 (R^2adj) was used as a measure of the goodness of fit which was assessed as small if <0.09, moderate between 0.1 and 0.3 and large effect if >0.3 (Mehmetoglu & Jakobsen, 2022). Model assumptions underlying linear multiple regression were checked in R, including assumptions of linearity, homoskedasticity, and normality (Osborne & Waters, 2002). The residuals were checked for normality using a QQ-plot. The residuals were also checked for multicollinearity, homoscedasticity, that the data met the linear assumption, and if the confounding variables were incorporated in an appropriate manner. All assumptions were adequately met in the present study, decreasing the risk of a Type 1 or a Type 2 error, or an over- or under-estimation of significance or effect sizes (Osborne & Waters, 2002).

Independent sample *t*-tests or Chi-square tests were used to compare the relation between the demographic variables and between the CT and no CT groups. Chi-square tests were used for the categorical variables, and *t*-tests were used for the continuous variables. It is recommended to use the Mann-Whitney-test if the data set is small and if the data is not normally distributed. However, in the present study, the amount of data made it sufficient to use the *t*-tests to compare the CT (*n*= 68) and no CT groups (*n* = 65), also when the data was not normally distributed. The Fisher's exact test was used to verify the *p*-values from the Chi-square tests for the categorical variables with few observations, as an extra quality measure.

For the linear regression analyses, all models were fitted to the data using the PANSS total scale and PANSS positive, PANSS negative or PANSS general psychopathology subscale scores as dependent variables. Age, sex, parental mental disorders, CTQ-SF sum score, as well as the interaction between parental mental disorder and the CTQ-SF sum score, were included as independent variables. Age and the CTQ-SF sum score were included as continuous variables, whereas sex and parental mental disorder were included as categorical variables.

Firstly, the CTQ-SF sum score was used as a predictor for the PANSS total scale and PANSS subscale scores, whereas age and sex were included as confounders in the regression models. The interaction term was included to examine whether parental mental disorders moderated the overall level of the CTQ-SF sum score.

Secondly, regression models were fitted to the data using the CTQ-SF subscale scores (physical, sexual, and emotional abuse, and physical and emotional neglect) as predictors for the PANSS total and subscale scores, whereas age and sex were included as confounders. The interaction term was also included in these models to examine whether parental mental disorders moderated the overall level of the CTQ-SF subscale scores. By the inclusion of a larger number of independent variables, false positive findings may be a problem. One could either perform a correction for multiple testing like a Bonferroni correction to account for the potential multiple comparison problem, or alternatively interpret the results with caution. We chose the latter approach.

Results

Demographic and clinical data

See Table 1 for details on clinical and demographic characteristics. When examining the CTQ-SF, we found that the mean CTQ-SF sum score was 43.3 (*SD* = 15.9), and the mean subscale scores were 6.9 (*SD* = 3.4) for physical abuse, 10.0 (*SD* = 4.9) for emotional abuse,

6.4 (*SD* = 3.6) for sexual abuse, 8.1 (*SD* = 3.4) for physical neglect, and 11.8 (*SD* = 5.3) for emotional neglect.

Table 1

Mean (SD) or n (%) for Clinical and Demographic Characteristics by CT and No CT Group.

Baseline characteristics	No CT group (*n* = 65) [a]	CT group (*n* = 68) [a]	Statistics (*t* or X^2) [b]	*p*	Total (*N* = 133)
Age, years	30 (12.6)	30.1 (11.9)	- 0.021	.983	30.1 (12.2)
Male	43 (66.2%)	40 (58.8%)	0.481	.488	83 (62.4%)
Caucasian	54 (90%)	55 (88.7%)	0	1	109 (89.3%)
Years of education	12.6 (3.2)	11.8 (2.7)	1.654	.101	12.2 (3)
Living alone (yes)	21 (34.4%)	30 (47.6%)	1.716	.190	51 (41.1%)
Employed (yes)	14 (23%)	14 (22.2%)	0	1	28 (22.6%)
DDD [c]	1.1 (0.5)	1.1 (0.4)	0.145	.885	1.1 (0.5)
DUP, weeks	43.4 (72.5)	68 (118.1)	- 1.168	.247	56 (98.7)
Psychosis onset age, years	23.3 (7.4)	24.8 (9.9)	- 0.845	.400	24.1 (8.8)
Diagnosis					
Schizophrenia	23 (35.4%)	38 (55.9%)	4.828	.028*	61 (45.9%)
Schizotypal disorder	0 (0%)	2 (2.9%)	0.463	.496	2 (1.5%)
Delusional disorder	8 (12.3%)	7 (10.3%)	0.009	.926	15 (11.3%)
Brief psychotic disorder	10 (15.4%)	7 (10.3%)	0.383	.536	17 (12.8%)
Schizoaffective disorder	6 (9.2%)	2 (2.9%)	1.346	.246	8 (6%)
Other psychotic disorder	1 (1.5%)	0 (0%)	0.001	.982	1 (0.8%)
Unspecified psychotic disorder	5 (7.7%)	5 (7.4%)	0	1	10 (7.5%)
Smoking [d] (yes)	33 (54.1%)	45 (73.8%)	4.301	.038*	78 (63.9%)
CAUS (abuse or dependence)	4 (6.6%)	7 (10.8%)	0.272	.602	11 (8.7%)
CDUS (abuse or dependence)	17 (27.9%)	17 (26.2%)	0	.987	34 (27%)
Antipsychotic naive	22 (33.8%)	18 (26.5%)	0.545	.460	40 (30.1%)
PANSS total	70.6 (19)	77.2 (15.2)	- 2.209	.029*	74 (17.4)
PANSS positive	18.5 (5.7)	20.7 (5.5)	- 2.271	.025*	19.6 (5.7)
PANSS negative	15.9 (6.1)	17.9 (5.9)	- 1.987	.049*	16.9 (6.1)
PANSS general psychopathology	36.3 (10.2)	38.6 (7.9)	- 1.453	.149	37.5 (9.1)
CGI	4.7 (1.1)	4.9 (0.9)	- 1.562	.121	4.8 (1)
GAF	39.1 (9.6)	37.9 (11)	0.677	.500	38.5 (10.4)
CDSS	5.8 (4.8)	8.6 (5.3)	- 3.139	.002**	7.2 (5.2)
BMI	24.5 (4.2)	25.4 (5.7)	- 1.012	.314	24.9 (5)
Mental disorder, mother	12 (18.5%)	12 (17.6%)	0	1	24 (18%)
Bipolar	4 (6.2%)	4 (5.9%)	0	1	8 (6%)

Schizophrenia	0 (0%)	3 (4.4%)	1.274	.259	3 (2.3%)
Suicide attempts	1 (1.5%)	4 (5.9%)	0.741	.389	5 (3.8%)
Suicide	0 (0%)	0 (0%)	-	-	0 (0%)
Alcohol use/dependence	1 (1.5%)	6 (8.8%)	2.227	.136	7 (5.3%)
Substance use/dependence	2 (3.1%)	2 (2.9%)	0	1	4 (3%)
Other	5 (7.7%)	2 (2.9%)	0.703	.402	7 (5.3%)
Mental disorder, father	9 (13.8%)	11 (16.2%)	0.018	.894	20 (15%)
Bipolar	4 (6.2%)	3 (4.4%)	0.004	.951	7 (5.3%)
Schizophrenia	2 (3.1%)	2 (2.9%)	0	1	4 (3%)
Suicide attempts	1 (1.5%)	3 (4.4%)	0.213	.644	4 (3%)
Suicide	1 (1.5%)	1 (1.5%)	0	1	2 (1.5%)
Alcohol use/dependence	7 (10.8%)	14 (20.6%)	1.728	.189	21 (15.8%)
Substance use/dependence	2 (3.1%)	3 (4.4%)	0	1	5 (3.8%)
Other	1 (1.5%)	2 (2.9%)	0	1	3 (2.3%)
CTQ-SF sum	31.9 (4.3)	54.2 (15.2)	- 11.634	<.001***	43.3 (15.9)
Emotional abuse	7 (2)	12.9 (5.1)	- 8.969	<.001***	10 (4.9)
Physical abuse	5.3 (0.7)	8.5 (4.1)	- 6.251	<.001***	6.9 (3.4)
Sexual abuse	5 (0.2)	7.8 (4.6)	- 4.879	<.001***	6.4 (3.6)
Emotional neglect	8.3 (2.6)	15.2 (5.1)	- 9.756	<.001***	11.8 (5.3)
Physical neglect	6.3 (1.5)	9.9 (3.8)	- 7.377	<.001***	8.1 (3.4)

Note. *p <.05. **p <.01. ***p <.001. p = p-value; n = Number of individuals in subsample; N = Number of individuals in total sample; SD = Standard deviation; t = t-value; X^2 = Chi-square test statistic; CT = Childhood trauma; DDD = Defined daily dose of antipsychotic medication; DUP = Duration of Untreated Psychosis; CAUS = Clinical Alcohol Use Scale; CDUS = Clinical Drug Use Scale; PANSS = Positive and Negative Syndrome Scale; CGI = Clinical Global Impression Scale; GAF = Global Assessment of Functioning; CDSS = Calgary Depression Scale for Schizophrenia; BMI = Body Mass Index; CTQ-SF = Childhood Trauma Questionnaire Short-Form.

[a] SD for continuous variables and % for categorical variables. [b] Chi-square tests for % and t-tests for SD. [c] Mean DDD-values from the entirety of the BeSt InTro study, not baseline. [d] Nicotine cigarettes.

When examining the PANSS scores, we found that the mean PANSS total scale score in the sample was 74.0 (*SD* = 17.4), and the mean subscale scores were 19.6 (*SD* = 5.7) for PANSS positive, 16.9 (*SD* = 6.1) for PANSS negative, and 37.5 (*SD* = 9.1) for PANSS general psychopathology.

When examining the history of parental mental disorders, we found that the majority, 97 of 133 patients (72.9%), reported no parental history of mental disorders, while 36 of 133 (27%) reported a parental history of mental disorders. Sixteen of 133 (12.0%) reported only maternal mental disorders, 12 of 133 (9.0%*)* reported only paternal mental disorders, and 8 of 133 (6.0%) reported both maternal and paternal mental disorders. When adding those who reported mental disorders in both parents to those reporting only maternal or paternal disorders, 24 of 133 (18%) reported maternal mental disorders, and 20 of 133 (15%) reported paternal mental disorders.

Demographic and clinical data by CT and no CT groups

When comparing the CT and no CT groups, we found some statistically significant differences between the two groups (see Table 1). There were more patients diagnosed with schizophrenia in the CT group (n = 38), compared to the no CT group (n = 23; p = .028). The CT group had a higher score on PANSS total (M = 77.2) compared to the no CT group (M = 70.6; p = .029). The CT group had a higher score on PANSS positive (M = 20.7), compared to the no CT group (M = 18.5; p = .025), and the CT group had higher score on PANSS negative (M = 17.9) compared to the no CT group (M = 15.9; p = .049). Furthermore, there were higher scores on the Calgary Depression Scale for Schizophrenia (CDSS) in the CT group (M = 8.6) compared to the no CT group (M = 5.8; p = .002). There were more patients who reported smoking in the CT group (n = 45) compared to the no CT group (n = 33; p = .038). There were no statistically significant differences in parental mental disorders between the CT and no CT groups, nor for any of the other clinical and demographic variables.

The moderation of parental mental disorders on the relationship between CT and severity of psychosis symptoms

The first multiple regression models examined CTQ-SF sum score and parental mental disorders as an interaction term on the PANSS total scale score, PANSS positive subscale

score, PANSS negative subscale score, and PANSS general psychopathology subscale score, controlling for age and sex. See Table 2 for an overview comparing the results. The model using the PANSS negative subscale score as outcome was statistically significant. The remaining models using the PANSS total scale score, PANSS positive subscale score, and PANSS general psychopathology subscale score as outcomes were not statistically significant. This implies that the results of these models should be interpreted with caution, as they do not possess a strong goodness of fit.

Table 2

Results of the Estimates (β) and p-values from the Multiple Regression Analyses of CTQ-SF Sum Score and Parental Mental Disorders as an Interaction Term on the PANSS Total Scale Score and Subscale Scores, Controlling for Age and Sex.

	PANSS total scale		PANSS positive subscale		PANSS negative subscale		PANSS general psychopathology subscale	
	Estimate [b]	*p*	Estimate	*p*	Estimate	*p*	Estimate	*p*
Intercept [a]	70.616	0	17.898	0	16.836	0	35.963	0
CT [c]	0.222	.049*	0.046	.213	0.087	.024*	0.084	.146
Age	- 0.215	.091	0.013	.765	- 0.134	.002**	- 0.091	.167
Sex	- 1.081	.736	- 0.997	.356	0.308	.779	- 0.312	.851
Maternal mental disorder	- 2.100	.877	- 1.171	.798	0.712	.878	- 1.782	.801
Paternal mental disorder	19.615	.143	0.285	.949	8.661	.059	10.523	.131
Both parental mental disorder [d]	- 44.604	.141	- 10.199	.317	- 2.665	.796	- 31.91	.044*
CT X Maternal mental disorder	0.112	.709	0.001	.995	0.015	.887	0.101	.519
CT X Paternal mental disorder	- 0.252	.356	- 0.02	.829	- 0.121	.198	- 0.107	.455
CT X Both parental mental disorder	0.852	.205	0.186	.412	- 0.023	.919	0.695	.048*

Note. *p <.05. **p <.01. p = p value; β = beta, regression coefficient; PANSS = the Positive and Negative Syndrome Scale; CT = Childhood trauma; CTQ-SF = Childhood Trauma Questionnaire Short-Form.

[a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected change in independent variable with one unit change of dependent variable (β). [c] CTQ-SF sum score. [d] Mental disorders of both parents.

The first model showed that the CTQ-SF sum score was statistically significantly associated with the PANSS total scale score (p = .049), controlling for age and sex (see Table 2). The analysis showed no statistically significant moderation effect of parental mental disorder (maternal, paternal or both; Table 2) on the PANSS total scale score. The association between the CTQ-SF sum score and the PANSS total scale score is indicative of a dose-response relationship, where an increase of 1 on the CTQ-SF sum score would yield an average increase of the PANSS total scale score by 0.22. To illustrate, an increase of 50 in the CTQ-SF total score would yield an average increase of 11 in the PANSS total scale score in this sample. However, model statistics showed < small goodness of fit with an R^2adj = 0.033, $F(9,123) = 1.5$, p = .154, indicating that these results should be interpreted with some caution.

Moreover, the analyses showed no statistically significant association of CTQ-SF sum score and PANSS positive subscale score (p = .213), nor did the analyses show any moderation effect of parental mental disorder. However, this model showed poor model statistics of R^2adj = - 0.03, $F(9,123) = 0.54$, p = .842.

The analyses showed a statistically significant association of the CTQ-SF sum score and the PANSS negative subscale score (p = .024). For instance, an increase of 1 on the CTQ-SF sum score would yield an average increase of the PANSS negative subscale score by 0.087. The analyses did not show any moderation effect of parental mental disorder (Table 2).

This model showed the strongest model statistics, though still < small goodness of fit, with an R^2adj = 0.08, $F(9,123) = 2.28$, $p = .021$.

The analyses showed no statistically significant association of the CTQ-SF sum score and the PANSS general psychopathology subscale score. The analyses showed a statistically significant moderation effect of parental mental disorders on the relation of the CTQ-SF sum score and the PANSS general psychopathology subscale score ($p = .048$). Adding the CTQ-SF sum score ($\beta = 0.084$) and the interaction with mental disorders in both parents ($\beta = 0.695$) resulted in a moderation effect with an increase of $\beta = 0.779$ on PANSS general psychopathology subscale score when the CTQ-SF sum score increased by 1 point. However, this model showed < small goodness of fit, with an R^2adj = 0.04, $F(9,123) = 1.69$, $p = .099$.

Summarized, we found an association of the CTQ-SF sum score on the PANSS total scale score and PANSS negative subscale score. However, the associations were not moderated by a history of parental mental disorders. We found that a history of both parental mental disorders moderated the effect of the CTQ-SF sum score on the PANSS general psychopathology subscale score.

The moderation of parental mental disorders on the relationship between the CT subtypes and severity of psychosis symptoms

The second multiple regression models examined the CTQ-SF subscale scores on the PANSS total scale score, PANSS positive subscale score, PANSS negative subscale score, and PANSS general psychopathology subscale score, with parental mental disorders as an interaction term, controlling for age and sex. None of the models were statistically significant. This implies that the results of these models should be interpreted with caution, as they do not possess a strong goodness of fit.

The analyses showed no statistically significant associations of the CTQ-SF subscale scores on the PANSS total scale score, PANSS positive subscale score, or PANSS general

psychopathology subscale score. The analyses did not show any moderation of parental mental disorders on PANSS total and subscale scores.

The analyses showed a statistically significant negative association of the sexual abuse subscale score and the PANSS negative subscale score (p = .046; see Table 3). An increase of 1 on the sexual abuse subscale score would yield an average decrease of the PANSS negative subscale score by β = - 0.436. Further, the analyses showed a statistically significant moderation effect of maternal mental disorders on the relation of the sexual abuse subscale score and the PANSS negative subscale score (p = .042). However, this relationship disappeared when we performed an additional analysis where the sexual abuse subscale score was isolated as a variable, indicating that the initial relationship could be a result of multicollinearity in the model, type I error, or a statistic coincidence in the sample. We did not perform a Bonferroni correction; thus, one should put less emphasize on the findings and acknowledge the problems of multiple testing when interpreting the results of this model.

Table 3

Results of Multiple Regression Analysis of the CTQ-SF Subscale Scores and the PANSS Negative Subscale Scores with Parental Mental Disorder as an Interaction Term, Controlling for Age and Sex.

	PANSS negative subscale			
	Estimate [b]	SE	*t*-value	*p*
Intercept [a]	16.827	2.187	7.695	0
Emotional abuse	0.106	0.186	0.569	.571
Physical abuse	0.171	0.275	0.620	.537
Sexual abuse	- 0.436	0.217	- 2.015	.046*
Emotional neglect	0.180	0.146	1.229	.222
Physical neglect	0.269	0.222	1.208	.230
Maternal mental disorder	0.840	5.624	0.149	.882
Paternal mental disorder	10.796	5.265	2.050	.043*

Both parental mental disorder [c]	0.832	13.104	0.064	.949
Age	- 0.139	0.047	- 2.972	.004**
Sex	0.593	1.197	0.495	.621
Emotional abuse X Maternal mental disorder	0.231	0.613	0.377	.707
Emotional abuse X Paternal mental disorder	- 0.123	1.002	- 0.122	.903
Emotional abuse X Parental mental disorder	0.650	1.660	0.392	.696
Physical abuse X Maternal mental disorder	- 1.597	1.337	- 1.194	.235
Physical abuse X Paternal mental disorder	- 0.771	1.125	- 0.685	.495
Physical abuse X Parental mental disorder	- 1.624	1.681	- 0.966	.336
Sexual abuse X Maternal mental disorder	1.125	0.546	2.060	.042*
Sexual abuse X Paternal mental disorder	1.019	1.222	0.834	.406
Sexual abuse X Parental mental disorder	0.624	2.550	0.245	.807
Emotional neglect X Maternal mental disorder	0.762	0.545	1.398	.165
Emotional neglect X Paternal mental disorder	- 0.360	0.470	- 0.768	.444
Emotional neglect X Parental mental disorder	- 0.958	1.056	- 0.907	.366
Physical neglect X Maternal mental disorder	- 0.943	0.966	- 0.976	.331
Physical neglect X Paternal mental disorder	- 0.448	0.900	- 0.498	.620
Physical abuse X Parental mental disorder	0.774	1.553	0.499	.619

Note. *p <.05. **p <.01. p = p value; SE = Standard error; β = beta, regression coefficient; PANSS = the Positive and Negative Syndrome Scale.

[a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected

change in independent variable with one unit change of dependent variable (β). [c] Mental disorders of both parents.

Summarized, we did not find an association of the CTQ-SF subscales scores on the PANSS total scale score, PANSS positive subscale score, or PANSS general psychopathology subscale score. We found a negative association of the CTQ-SF sexual abuse subscale score on the PANSS negative symptoms subscale score, moderated by a history of maternal mental disorder, likely due to statistical or methodological error. The analyses of the CT subtypes on psychosis symptom severity moderated by parental mental disorders, therefore yielded no meaningful results in this sample.

Discussion

In the present study, we examined the possible moderation of parental mental disorders on the relationship between CT and psychosis symptom severity in SSDs. The regression analyses showed an association between CT and psychosis symptom severity of SSDs, especially for the PANSS total scale scores and the PANSS negative subscale scores; the latter with the best model fit. Overall, we found that parental mental disorders did not moderate the relation of CT on the psychosis symptom severity in SSDs. We did however find that reporting mental disorders in both parents moderated the association between the CTQ-SF sum score and the PANSS general psychopathology subscale score. Regarding neglect, we did not find any moderation effect of parental mental disorders on the association between the physical and emotional neglect subscale scores and the PANSS total nor the PANSS subscale scores. Lastly, regarding the direct group comparisons, patients in the CT group showed higher overall symptoms of psychosis, more positive and negative symptoms, in addition to more severe disorders of psychosis (diagnosis of F20 Schizophrenia), more symptoms of depression, and more patient reported nicotine smoking, as compared to patients in the no CT group. However, no group differences emerged in relation to parental mental disorders.

Support for an independent effect of CT on SSDs

Overall, we did not find a history of parental mental disorders to moderate the association of CT and psychosis symptom severity in SSDs; suggesting that the effect of CT on psychosis symptom severity in SSDs was not affected by having reported maternal, paternal or both parental mental disorders. This strengthens the findings from previous research emphasizing CT as an important risk factor for psychosis and SSDs (Bonoldi et al., 2013; Chaiyachati & Gur, 2021; Matheson et al., 2013; Varese et al., 2012).

We did however find a possible moderating effect of having both parents with mental disorders on the relationship between CT and the PANSS general psychopathology subscale. A measure of general psychopathology provides information of more global symptoms that could impact the overall symptom load, such as anxiety, depression and poor attention (Kay et al., 1987). Research has suggested that having parental mental disorders increases the risk for psychopathology (Stracke et al., 2019). Possibly, having parents with mental disorders could increase the risk of more global symptoms of psychopathology not necessary directly associated with psychosis. Although we found one moderation effect, the main findings in this study were that parental mental disorders did not moderate the association between CT and symptoms of psychosis in SSDs, suggesting that the relation of CT in SSDs did not depend on parental mental disorders. This single moderation finding should therefore be interpreted with caution.

Contrary to our hypothesis, we did not find that parental mental disorders moderated the association of the subscales physical and emotional neglect and symptoms of SSDs. This is perhaps in contrast to what could be expected based on research finding parental mental health problems, such as depression and drug use, to be associated with childhood neglect (Slack et al., 2011). It is important to note that our findings do not imply that parental mental disorders are of no importance for SSD symptoms, rather our findings suggest that parental

mental disorders did not affect the association of childhood neglect and symptoms of SSDs in this study. However, the second main models had poor model statistics and included many independent variables, making any finding of these models less reliable. This will further be discussed in limitations below.

The direct group comparisons in relation to the clinical and demographic variables further strengthens that parental mental disorders did not explain the relationship between CT and symptoms of SSDs. Contrary to previous research that has suggested that children of mentally ill parents were two to three times more likely to report CT than those who did not report having parents with mental disorders (Walsh et al., 2002), we did not find that a history of parental mental disorders was more frequent in the CT group as compared to the no CT group. This could be due to a small number of patients reporting parental mental disorders. However, even though the minority of our sample reported a parental history of mental disorders, similar studies have found similar numbers of parental mental disorders in patients with psychosis as in the present study (Fisher et al., 2014; Trauelsen et al., 2015). This may indicate that the independent relation of CT on SSDs found in the present study was not due to a possible underreporting of a parental history of mental disorders. Thus, this further strengthens the finding of a relation between CT and SSDs, independent of parental mental disorders. It is important to note that there may still be several other confounding variables involved in the association between CT and SSDs (Baldwin et al., 2023). Studies specifically controlling for a family history of psychosis or other mental disorder as a measure of genetic liability, have however found that the independent effect of CT on SSDs remained unaffected (Arseneault et al., 2011; Fisher et al., 2014; Janssen et al., 2004). Considering our results and that previous research supports that the association between CT and SSDs might be at least partly independent of other risk factors that has been examined (Bendall et al., 2013; Varese et

al., 2012), it is worth discussing the effects of CT as possible underlying mechanisms of the relationship.

The existence of an association between CT and psychosis development is already well-established through extensive research (Misiak et al., 2017; Varese et al., 2012), and several studies have suggested that the link between CT and SSDs is at least partly causal (Baldwin et al., 2023; Lecei et al., 2019; Misiak et al., 2017). The present study provides further support for the first claim, as we found a positive association between level of CT and total symptom severity, as well as the level of CT and negative symptom severity. Although an independent or direct association between CT and SSDs is not consistently reported in research (Cutajar et al., 2010; Murray et al., 2014), such association is still supported in other studies (Carr et al., 2013; Varese et al., 2012).

Previous research has suggested a dose-response relationship between CT and psychosis, where more severe CT is associated with more severe psychotic symptoms (Şahin et al., 2013; Trauelsen et al., 2015; Varese et al., 2012). Our findings provide additional support for such an association, at least for total and negative symptom severity. Though we cannot establish a causal link between CT and psychosis symptom severity, CT might predate psychosis onset and may thus act as a vulnerability risk factor. This is supported by research showing that a reverse association is unlikely (van Winkel et al., 2013). Furthermore, research has found that CT is associated with neurobiological alterations that increase the stress reactivity and harmful effects of stress (Hoy et al., 2012; Lardinois et al., 2011; McLaughlin & Lambert, 2017). These mechanisms do not rule out the possibility of genetic and environmental vulnerability present before CT exposure, however they imply that CT may cause harm in the developing brain that increases the risk of psychopathology, including SSDs (Read et al., 2001). The stress-vulnerability model (Zubin & Spring, 1977) could explain some of the dose-response relationship, as CT may cumulatively elevate the risk of SSDs

through gene-environment interactions. Research using neuroimaging has found that CT may exert harmful effects on the brain, and these effects are also seen in SSD patients (Read et al., 2014). The severity of CT might therefore entail more severe biological impairments, which in turn could have implications of more severe psychosis symptoms in a dose-response relationship.

Research surrounding CT and psychosis have previously found a link between CT and specifically positive symptoms (Scott et al., 2007; Shevlin et al., 2007). Therefore, it was perhaps surprising that our regression analyses indicated no significant association between CT and the PANSS positive scale nor the PANSS general psychopathology scale. However, when viewing the demographic and clinical data in our sample, we found a group difference between the CT and no CT groups which was statistically significant for all PANSS scales, except the PANSS general psychopathology scale. In other words, a statistically significant effect of CT on positive symptom severity was observed on a group level, but not in the multiple regression analyses. This might be due to how the CT variable is handled; either categorical or continuous. In the demographic and clinical data CT was included as a categorical variable to compare the mean PANSS positive subscale score between the CT and no CT groups. However, in our regression models CT was included as a continuous variable, and we also adjusted for other variables within the models. Summarized, the statistical methods behind each model differ, and subsequently the findings do as well. Therefore, contradictory findings between them do not necessarily signify an issue.

Regarding CT and negative symptom severity, the association is not yet well established (Degnan et al., 2022). In our findings, higher levels of CT predicted more severe negative symptoms, which is interesting as both CT and negative symptoms are associated with poorer treatment outcomes with less response to medical treatment (Hassan & De Luca, 2014; Leucht et al., 2011; Mørkved et al., 2022; Thomas et al., 2019). The PANSS negative

subscale involves the reported level of negative symptoms commonly found in SSDs such as deficits in affective, cognitive, and social functioning (e.g. blunted affect, social withdrawal etc.; Kay et al., 1987). Clinically, the severity of negative symptoms has shown to be the most disabling for those affected (Velligan & Alphs, 2013), with only marginal response to medical treatment (Leucht et al., 2011). Consequently, negative symptoms are commonly found to be more difficult to treat and have a tendency to persist longer (Velligan & Alphs, 2013). A better understanding of aspects of negative symptoms therefore has both scientific and clinical value.

As mentioned previously, attachment style has been proposed as a mediating, psychological factor and an environmental vulnerability factor in the relationship between CT and psychosis (Berry et al., 2017). Some specific negative symptoms such as social anhedonia, and social and emotional withdrawal has been linked to an insecure-avoidant attachment style (Berry et al., 2006; Korver-Nieberg et al., 2015), which has been found to be overrepresented in those with psychosis (Gumley et al., 2014). In a recent empirical study, Degnan et al. (2022) found support for the role of disorganized attachment and dissociative experiences as potential important mediators in the pathways between CT and negative psychosis symptoms. In other words, the positive association between CT and negative symptom severity might be partly due to CT interacting with insecure attachment style, which in turn influences negative symptom severity.

Another understanding of the relation between CT and negative symptom severity is that CT may have an impact through neurobiological impairment. As earlier mentioned, CT might influence neurobiological development and has been associated with alterations in multiple brain regions (Teicher & Samson, 2016), as well as being implicated in brain alterations commonly associated with SSDs (Read et al., 2014; Sheffield et al., 2013). Although negative and cognitive symptoms in SSDs are regarded as separate

psychopathological domains (Foussias et al., 2014), similarities between them suggest that symptoms from one domain might influence the other or that they might share similar neurobiological structures (Correll & Schooler, 2020), with research suggesting a possible symptom domain overlap of up to approximately 20% (Foussias et al., 2014). In a recently published 12-year follow up study, Suen et al. (2023) found that early negative symptoms might influence long-term functioning through cognitive functions, particularly executive functioning. Overall these findings relate to our previous point, that environmental stress factors such as CT might interact with genetic and environmental vulnerability (Zubin & Spring, 1977), and cumulatively increases the risk of SSDs.

Summarized, our results suggest that CT might be linked to more severe overall symptom load, which is reflected when comparing the CT and no CT groups in the clinical and demographic data. For instance, there were more depressive symptoms as well as more F20 Schizophrenia diagnosis in the CT group, compared to the no CT group. Schizophrenia is considered the most severe diagnosis in the psychosis spectrum (Johannessen & Joa, 2021), and together with the co-occurrence of depressive symptoms, it further implicates the severity associated with CT. Additionally, the CT group was associated with more nicotine cigarette smoking as compared to the no CT group, and smoking behavior has previously been connected to trauma, as the prevalence was found to be 2-6 times higher among those with PTSD than in the general population (Chou et al., 2018). This has been implicated as a way of regulating emotions in those with PTSD (Chou et al., 2018), and such might also be the case for patients with SSDs and CT experiences. However, we cannot draw any such conclusion based on the present study.

Limitations and strengths

The present study is based on a sample from a naturalistic, cross-sectional, pragmatic study, which entails both strengths and weaknesses. Strengths of a naturalistic study are

improved external validity and flexibility. We would argue that the data from the present sample appears to have satisfactory external validity, as the level of CT and reported parental mental disorders both are in line with that of other psychiatric samples (Fisher et al., 2014; Trauelsen et al., 2015). Our findings therefore appear to be representative of the experience of those with SSDs regarding CT and parental mental health. However, naturalistic research methods also provide less opportunity for scientific control of other external variables which could affect our results. Moreover, a common limitation with cross-sectional studies is the inability to make causal inferences as data is collected at a single point in time (Wang & Cheng, 2020). Though CT might occur before psychosis onset, one cannot make certain temporal assumptions as the CTQ-SF measures include experiences up to sixteen years of age, which also allows for an opposite temporal relationship between CT and psychosis onset. Hence, we cannot ascertain neither causal direction nor the possibility of other confounding variables in the present study.

Statistically, there are several limitations. In the present study we only included age and sex as confounding variables, and the model with the best model statistics could still only predict approximately 8% of the variance in psychosis symptoms. Overall, the model statistics of each model were poor, with the model examining CT and the PANSS negative subscale being the only one which was statistically significant. However, we would argue that the results are still worth being interpreted, as small effect sizes could still hold clinical and scientific value. An argument for this is the significant associations we found on group level in the same demographical and clinical data, which were in line with our multiple regression results and the majority of previous research reporting on an association between CT and psychosis (Chaiyachati & Gur, 2021; Gil et al., 2009; Misiak et al., 2017; Varese et al., 2012). The moderation effect of parental mental disorders on the PANSS general psychopathology symptoms should perhaps be viewed with the most caution, due to the poor model statistics

and less basis in other research to the best of our knowledge. Hence, we have put less emphasis on this result in our discussion. Overall, our findings should be viewed with caution, but they might still contribute to a better and more nuanced understanding regarding the association between CT and SSDs.

The risk for multicollinearity and type 1 error is a possible limitation when performing multiple regression analyses. This occurs when one or more independent variables in a model are correlated with each other, which has a higher likelihood of occurring when adding more variables to the model (Cohen et al., 2002). This is potentially problematic as a possible correlation between the independent variables could lead to a difficulty for the model to estimate the relationship between each of the independent variables and the outcome, making the estimate more unreliable (Cohen et al., 2002). One solution to the potential problem of multiple testing is to perform a Bonferroni correction, however another solution is to put less emphasize on the findings and acknowledge the problem when interpreting the results of the second main regression models. We opted for the latter approach. When examining the actual scores in these models, we found that the number of patients reporting sexual abuse were small, and that there were some who scored higher on sexual abuse and lower on the PANSS negative subscale. These outliers could increase the risk of Type 1 error, which means finding a statistically significant association between the independent variable (sexual abuse) and the dependent variable (the PANSS negative subscale) when no such association existed. Therefore, we put less emphasis on this finding, as the results could have been due to a coincidence in the sample.

Regarding the measurements, what qualified as parental mental disorders in the present study was based on self-report through an interview with a trained research nurse. Our measure of parental mental disorders is therefore not objective and could be influenced by bias and other subjective factors. A more objective approach could be to ascertain parental

mental disorders through reviewing medical records, however this is considered ethically questionable, and permission would have to be granted by both the participants and the ethics research board. Another approach could be to interview or administer self-report questionnaires to the patients' parents, in addition to the patients' self-report. This would have provided a source of inter-rater reliability; however, it would require extensive resources. Moreover, this would still qualify as a measure of self-report in which, given the nature of the research question, parents could be incentivized to underreport their own mental health problems. However, it could still provide increased reliability as the information is given from the subject it concerns. Both attempts at a more objective measure of parental mental disorders could therefore increase reliability, however it would be more costly in terms of both time and monetary funding and could potentially limit the sample size due to for instance increased attrition.

On the other hand, we would argue that a subjective measure of parental mental disorders could have its advantages. A self-report from patients regarding their parents' mental disorders could provide a relevant form of cut-off value. In our research question we were interested in whether parental mental disorders exerted consequences for the patients, meaning that the severity of mental disorders may have caused the patient to experience CT or notice that their parent(s) were mentally ill. Therefore, it is more interesting to examine if the patients themselves have experienced their parent(s) as being mentally ill, rather than if the parent(s) had an objective diagnosis which had gone unnoticed by the patient.

Furthermore, we chose to include missing data as parental mental disorders not present, which could potentially lead to an underreporting of parental mental disorders in our sample. However, we chose to balance this out by including not only reports on formal diagnoses but also diagnoses probable and the category other: specified. In addition, since information on the parental history was collected through patients' self-report, it could be

affected by openness in the family and the related insight and understanding of mental disorders and their parents' mental health. These were reasons to be more liberal in what was included as parental mental disorders present in the study, considering the inclusion of missing data as parental mental disorders not present. Even though not fully accurate reports, the number of reported histories of parental mental disorder found in our sample seem plausible in line with findings in other studies (Fisher et al., 2014; Trauelsen et al., 2015).

Another consideration in the present study is the implication of the psychosis itself in the present sample. The data was collected when the patients were admitted to psychiatric wards, which entails that the patients likely had a level of active psychosis at baseline. As previously discussed, SSDs and active psychosis will commonly affect the patients understanding of themselves and the world around them (Johannessen & Joa, 2021). Additionally, a level of paranoia and delusions is also common, as they are core symptoms of SSDs (WHO, 2016). Thus, the patients in the present sample may give biased or inaccurate information, for example regarding parental mental disorders and CT, due to the core features of their disorder. Early childhood experiences such as CT, as well as familial mental health, can be regarded as both highly personal and sensitive information. This could lead to underreporting, as the patients could be cautious to share such information for research or acknowledge it at all. In line with this, Misiak et al. (2017) suggested that patients experiencing acute psychotic symptoms should be considered a possible limitation when using self-reports of CT as a measure. However, the self-reported CT in the present study was conducted six weeks after inclusion, increasing the validity due to the patients being in a more stable clinical phase.

It is further important to note that the CTQ-SF measures CT experience retrospectively through a self-reporting questionnaire, which implies that the results of the CTQ-SF is dependent on the recollection of the patients and cannot be differentiated with actual CT

history (Dovran et al., 2013). There has been somewhat of a controversy regarding the accuracy when assessing CT experiences retrospectively (Bernstein et al., 2003). Retrospective assessment of CT has been criticized and some authors have therefore been skeptical to the strength of the association of CT and SSDs found in research (Bendall et al., 2013). Susser and Widom (2012) suggested that retrospective self-reports of CT experiences in psychosis could be biased towards overreporting due to the need of finding an explanation for the psychosis symptoms. However, research suggests that an overreporting of CT in patients with SSDs is unlikely (Bendall et al., 2013).

Contrary to studies suggesting a risk of overreporting of CT experiences in SSD patients, Hardt and Rutter (2004) found that retrospective assessment of CT could rather lead to an underreporting of CT experiences. However, retrospective reports of CT in patients with psychosis have demonstrated to be stable over time, unaffected by ongoing psychosis symptoms, correspond with other sources of information on CT, and showing reasonable reliability and validity (Fisher et al., 2011). It could be an option to verify the CT experiences by asking third parties, such as the parents, however this could also be controversial and potentially unethical as the CT experiences, such as abuse and neglect, have a high chance of being conducted by the parents themselves (Misiak et al., 2017). In addition, as previously mentioned the reported CTQ-SF scores in the present sample are comparable to other studies examining CT in clinical samples (Dovran et al., 2013), which suggests that the level of CT found in the present study was representative. The CTQ-SF has advantages where it comprises fewer items compared to the original CTQ version, which may lessen the burden on the respondent by not being too lengthy (Bernstein et al., 2003). In sum, we would argue that the CTQ-SF provides a good measure of CT experiences for the present study.

The PANSS comprising the positive, negative and the global psychopathology subscales was used to assess the symptom severity of the SSDs in the BeSt InTro study, on

which the present study was based. However, which PANSS subscale structure are best suited for capturing the diversity of SSD symptoms has been debated in research (Nicotra et al., 2015). Factor-analysis studies have suggested that a five-factor model could be better suited (Wallwork et al., 2012), and some studies have adopted to a five-factor model (Nicotra et al., 2015; von Knorring & Lindström, 1995). Even though there has previously been a lack of consensus of a five-factor model (Wallwork et al., 2012), more recent research supported a five-factor model as the best fit for the PANSS data (Lim et al., 2021). In the present study, we did not perform a factor analysis on the PANSS scores, as the sample was too small. However, the PANSS used in the present study is still supported by research as the instrument has shown good psychometric properties when assessing symptom severity of SSDs and are the most widely used in research (Leucht et al., 2005; Nicotra et al., 2015).

Scientific and clinical implications

In the present study, we found an independent relation between CT (i.e., emotional, physical, and sexual abuse, and emotional and physical neglect) and SSDs, which was not moderated by parental mental disorders. In sum, our results indicate that the overall CT and not necessarily the specific CT subtypes increased the psychosis symptom severity of SSDs, in line with research emphasizing a dose-response relationship where the total severity of CTs are the significant factor in SSDs (Trauelsen et al., 2015). Clinically, the strengthened association between CT and SSDs has several implications. As our findings further support a dose-response relationship between CT and SSDs, effort might be advised to be put in both the prevention and intervention of CT in relation to psychosis development. Varese et al. (2012) proposed prevention of CT could reduce the prevalence of SSDs by approximately 33%, alongside the human suffering associated with it. In line with the dose-response relationship, intervention once CT has occurred could reduce the severity of psychotic symptoms. Furthermore, as CT has shown to be associated with worse prognosis and

treatment outcome in SSDs (Thomas et al., 2019), it could be plausible that treatment of CT in patients with SSDs could have a positive impact. It has been suggested that psychosis with CT could be understood as a distinct psychiatric phenotype (Misiak et al., 2017), which might call for specific, targeted treatment. Relatedly, Eye Movement Desensitization and Reprocessing (EMDR) therapy and trauma-focused CBT (TF-CBT) have been proposed for people with SSDs and trauma experiences, and although further research is needed, both appear to be feasible and safe methods of treatment for this psychiatric group (Adams et al., 2020; Peters et al., 2022; van den Berg et al., 2016). Our findings could therefore have clinical implications, in that they provide additional support for the acknowledgement of CT in psychosis treatment.

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References

Adams, R., Ohlsen, S., & Wood, E. (2020). Eye Movement Desensitization and Reprocessing (EMDR) for the treatment of psychosis: A systematic review. *European Journal of Psychotraumatology*, *11*(1), 1711349. https://doi.org/10.1080/20008198.2019.1711349

Aminoff, S. R., Onyeka, I. N., Ødegaard, M., Simonsen, C. E., Lagerberg, T. V., Andreassen, O., Romm, K. L., & Melle, I. (2022). Lifetime and point prevalence of psychotic symptoms in adults with bipolar disorders: A systematic review and meta-analysis. *Psychological Medicine*, *52*(13), 2413-2425. https://doi.org/10.1017/S003329172200201X

Anda, L., Bronnick, K. K., Johannessen, J. O., Joa, I., Kroken, R. A., Johnsen, E., & Rettenbacher, M. (2019). Cognitive profile in ultra high risk for psychosis and schizophrenia: A comparison using coordinated norms. *Frontiers in Psychiatry*, *10*, 695. https://doi.org/10.3389/fpsyt.2019.00695

Arseneault, L., Cannon, M., Fisher, H. L., Polanczyk, G., Moffitt, T. E., & Caspi, A. (2011). Childhood trauma and children's emerging psychotic symptoms: A genetically sensitive longitudinal cohort study. *The American Journal of Psychiatry*, *168*(1), 65-72. https://doi.org/10.1176/appi.ajp.2010.10040567

Babenko, O., Kovalchuk, I., & Metz, G. A. S. (2015). Stress-induced perinatal and transgenerational epigenetic programming of brain development and mental health. *Neuroscience & Biobehavioral Reviews*, *48*, 70-91. https://doi.org/10.1016/j.neubiorev.2014.11.013

Baker, A. J. L., & Maiorino, E. (2010). Assessments of emotional abuse and neglect with the CTQ: Issues and estimates. *Children and Youth Services Review*, *32*(5), 740-748. https://doi.org/10.1016/j.childyouth.2010.01.011

Baldwin, J. R., Wang, B., Karwatowska, L., Schoeler, T., Tsaligopoulou, A., Munafò, M. R., & Pingault, J.-B. (2023). Childhood maltreatment and mental health problems: A systematic review and meta-analysis of quasi-experimental studies. *The American Journal of Psychiatry*, *180*(2), 117-126. https://doi.org/10.1176/appi.ajp.20220174

Bendall, S., Alvarez-Jimenez, M., Nelson, B., & McGorry, P. (2013). Childhood trauma and psychosis: New perspectives on aetiology and treatment. *Early Intervention in Psychiatry*, *7*(1), 1-4. https://doi.org/10.1111/eip.12008

Bentall, R. P., Wickham, S., Shevlin, M., & Varese, F. (2012). Do specific early-life adversities lead to specific symptoms of psychosis? A study from the 2007 the adult psychiatric morbidity survey. *Schizophrenia Bulletin*, *38*(4), 734-740. https://doi.org/10.1093/schbul/sbs049

Bernstein, D. P., & Fink, L. (1998). *Childhood trauma questionnaire : A retrospective self-report : Manual*. The Psychological Corporation, Harcourt Brace & Company 1998.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse & Neglect*, *27*(2), 169-190. https://doi.org/10.1016/S0145-2134(02)00541-0

Berry, K., Varese, F., & Bucci, S. (2017). Cognitive attachment model of voices: Evidence base and future implications. *Frontiers in Psychiatry*, *8*, 111. https://doi.org/10.3389/fpsyt.2017.00111

Berry, K., Wearden, A., Barrowclough, C., & Liversidge, T. (2006). Attachment styles, interpersonal relationships and psychotic phenomena in a non-clinical student sample. *Personality and Individual Differences*, *41*(4), 707-718. https://doi.org/10.1016/j.paid.2006.03.009

Bonoldi, I., Simeone, E., Rocchetti, M., Codjoe, L., Rossi, G., Gambi, F., Balottin, U., Caverzasi, E., Politi, P., & Fusar-Poli, P. (2013). Prevalence of self-reported childhood abuse in psychosis: A meta-analysis of retrospective studies. *Psychiatry Research*, *210*(1), 8-15. https://doi.org/10.1016/j.psychres.2013.05.003

Brietzke, E., Sant'anna, M. K., Jackowski, A., Grassi-Oliveira, R., Bucker, J., Zugman, A., Mansur, R. B., & Bressan, R. A. (2012). Impact of childhood stress on psychopathology. *Revista Brasileira de Psiquiatria*, *34*(4), 480-488. https://doi.org/10.1016/j.rbp.2012.04.009

Carr, A., Duff, H., & Craddock, F. (2020). A systematic review of reviews of the outcome of noninstitutional child maltreatment. *Trauma, Violence, & Abuse*, *21*(4), 828-843. https://doi.org/10.1177/1524838018801334

Carr, C. P., Martins, C. M. S., Stingel, A. M., Lemgruber, V. B., & Juruena, M. F. (2013). The role of early life stress in adult psychiatric disorders: A systematic review according to childhood trauma subtypes. *The Journal of Nervous and Mental Disease*, *201*(12), 1007-1020. https://doi.org/10.1097/NMD.0000000000000049

Chaiyachati, B. H., & Gur, R. E. (2021). Effect of child abuse and neglect on schizophrenia and other psychotic disorders. *Pharmacology, Biochemistry, and Behavior*, *206*, 173-195. https://doi.org/10.1016/j.pbb.2021.173195

Chou, C.-Y., Herbst, E., Cloitre, M., & Tsoh, J. Y. (2018). An emotion regulation-focused theoretical framework for co-occurring nicotine addiction and PTSD: Comments on existing treatments and future directions. *Cogent Medicine*, *5*(1), 1558731. https://doi.org/10.1080/2331205X.2018.1558731

Cohen, J., Cohen, P., West, S. G., Aiken, L. S., West, S. G., & Aiken, L. S. (2002). *Applied multiple regression/correlation analysis for the behavioral sciences*. Taylor & Francis

Group. http://ebookcentral.proquest.com/lib/bergen-ebooks/detail.action?docID=1222653

Collip, D., Habets, P., Marcelis, M., Gronenschild, E., Lataster, T., Lardinois, M., Nicolson, N. A., & Myin-Germeys, I. (2013). Hippocampal volume as marker of daily life stress sensitivity in psychosis. *Psychological Medicine*, *43*(7), 1377-1387. https://doi.org/10.1017/S003329171200219X

Correll, C. U., & Schooler, N. R. (2020). Negative symptoms in schizophrenia: A review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatric Disease and Treatment*, *16*, 519-534. https://doi.org/10.2147/NDT.S225643

Cougnard, A., Marcelis, M., Myin-Germeys, I., De Graaf, R. O. N., Vollebergh, W., Krabbendam, L., Lieb, R., Wittchen, H.-U., Henquet, C., Spauwen, J., & Van Os, J. I. M. (2007). Does normal developmental expression of psychosis combine with environmental risk to cause persistence of psychosis? A psychosis proneness–persistence model. *Psychological Medicine*, *37*(4), 513-527. https://doi.org/10.1017/S0033291706009731

Cutajar, M. C., Mullen, P. E., Ogloff, J. R. P., Thomas, S. D., Wells, D. L., & Spataro, J. (2010). Schizophrenia and other psychotic disorders in a cohort of sexually abused children. *Archives of General Psychiatry*, *67*(11), 1114-1119. https://doi.org/10.1001/archgenpsychiatry.2010.147

De Bellis, M. D. (2001). Developmental traumatology: The psychobiological development of maltreated children and its implications for research, treatment, and policy. *Development and Psychopathology*, *13*(3), 539-564. https://doi.org/10.1017/S0954579401003078

De Bellis, M. D., Hooper, S. R., Spratt, E. G., & Woolley, D. P. (2009). Neuropsychological findings in childhood neglect and their relationships to pediatric PTSD. *Journal of the*

International Neuropsychological Society, *15*(6), 868-878. https://doi.org/10.1017/S1355617709990464

De Bellis, M. D., Keshavan, M. S., Shifflett, H., Iyengar, S., Beers, S. R., Hall, J., & Moritz, G. (2002). Brain structures in pediatric maltreatment-related posttraumatic stress disorder: A sociodemographically matched study. *Biological Psychiatry*, *52*(11), 1066-1078. https://doi.org/10.1016/S0006-3223(02)01459-2

De Matteis, T., D'Andrea, G., Lal, J., Berardi, D., & Tarricone, I. (2020). The impact of peri-natal stress on psychosis risk: Results from the Bo-FEP incidence study. *BMC Research Notes*, *13*(1), 153. https://doi.org/10.1186/s13104-020-04992-9

Degnan, A., Berry, K., Humphrey, C., & Bucci, S. (2022). The role of attachment and dissociation in the relationship between childhood interpersonal trauma and negative symptoms in psychosis. *Clinical Psychology & Psychotherapy*, *29*(5), 1692-1706. https://doi.org/10.1002/cpp.2731

DeRosse, P., Nitzburg, G. C., Kompancaril, B., & Malhotra, A. K. (2014). The relation between childhood maltreatment and psychosis in patients with schizophrenia and non-psychiatric controls. *Schizophrenia Research*, *155*(1), 66-71. https://doi.org/10.1016/j.schres.2014.03.009

Dovran, A., Winje, D., Øverland, S. N., Breivik, K., Arefjord, K., Dalsbø, A. S., Jentoft, M. B., Hansen, A. L., & Waage, L. (2013). Psychometric properties of the Norwegian version of the Childhood Trauma Questionnaire in high-risk groups. *Scandinavian Journal of Psychology*, *54*(4), 286-291. https://doi.org/10.1111/sjop.12052

Fawzi, M. H., Kira, I. A., Fawzi, M. M., Mohamed, H. E., & Fawzi, M. M. (2013). Trauma profile in Egyptian adolescents with first-episode schizophrenia: Relation to psychopathology and plasma brain-derived neurotrophic factor. *The Journal of*

Nervous and Mental Disease, *201*(1), 23-29. https://doi.org/10.1097/NMD.0b013e31827ab268

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) study. *American Journal of Preventive Medicine*, *14*(4), 245-258. https://doi.org/10.1016/S0749-3797(98)00017-8

Fisher, H. L., Craig, T. K., Fearon, P., Morgan, K., Dazzan, P., Lappin, J., Hutchinson, G., Doody, G. A., Jones, P. B., McGuffin, P., Murray, R. M., Leff, J., & Morgan, C. (2011). Reliability and comparability of psychosis patients' retrospective reports of childhood abuse. *Schizophrenia Bulletin*, *37*(3), 546-553. https://doi.org/10.1093/schbul/sbp103

Fisher, H. L., Jones, P. B., Fearon, P., Craig, T. K., Dazzan, P., Morgan, K., Hutchinson, G., Doody, G. A., McGuffin, P., Leff, J., Murray, R. M., & Morgan, C. (2010). The varying impact of type, timing and frequency of exposure to childhood adversity on its association with adult psychotic disorder. *Psychological Medicine*, *40*(12), 1967-1978. https://doi.org/10.1017/S0033291710000231

Fisher, H. L., McGuffin, P., Boydell, J., Fearon, P., Craig, T. K., Dazzan, P., Morgan, K., Doody, G. A., Jones, P. B., Leff, J., Murray, R. M., & Morgan, C. (2014). Interplay between childhood physical abuse and familial risk in the onset of psychotic disorders. *Schizophrenia Bulletin*, *40*(6), 1443-1451. https://doi.org/10.1093/schbul/sbt201

Flaherty, E. G., Perez-Rossello, J. M., Levine, M. A., & Hennrikus, W. L. (2014). Evaluating children with fractures for child physical abuse. *Pediatrics*, *133*(2), E477-E489. https://doi.org/10.1542/peds.2013-3793

Foussias, G., Agid, O., Fervaha, G., & Remington, G. (2014). Negative symptoms of schizophrenia: Clinical features, relevance to real world functioning and specificity versus other CNS disorders. *European Neuropsychopharmacology : the Journal of the European College of Neuropsychopharmacology*, *24*(5), 693-709. https://doi.org/10.1016/j.euroneuro.2013.10.017

Fuchshuber, J., Hiebler-Ragger, M., Kresse, A., Kapfhammer, H.-P., & Unterrainer, H. F. (2019). The influence of attachment styles and personality organization on emotional functioning after childhood trauma. *Frontiers in Psychiatry*, *10*, 643. https://doi.org/10.3389/fpsyt.2019.00643

Gardner, M. J., Thomas, H. J., & Erskine, H. E. (2019). The association between five forms of child maltreatment and depressive and anxiety disorders: A systematic review and meta-analysis. *Child Abuse & Neglect*, *96*, 104082. https://doi.org/10.1016/j.chiabu.2019.104082

Gehred, M. Z., Knodt, A. R., Ambler, A., Bourassa, K. J., Danese, A., Elliott, M. L., Hogan, S., Ireland, D., Poulton, R., Ramrakha, S., Reuben, A., Sison, M. L., Moffitt, T. E., Hariri, A. R., & Caspi, A. (2021). Long-term neural embedding of childhood adversity in a population-representative birth cohort followed for 5 decades. *Biological Psychiatry*, *90*(3), 182-193. https://doi.org/10.1016/j.biopsych.2021.02.971

Gil, A., Gama, C. S., de Jesus, D. R., Lobato, M. I., Zimmer, M., & Belmonte-de-Abreu, P. (2009). The association of child abuse and neglect with adult disability in schizophrenia and the prominent role of physical neglect. *Child Abuse & Neglect*, *33*(9), 618-624. https://doi.org/10.1016/j.chiabu.2009.02.006

Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., & Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. *The Lancet (British edition)*, *373*(9657), 68-81. https://doi.org/10.1016/S0140-6736(08)61706-7

Gracie, A., Freeman, D., Green, S., Garety, P. A., Kuipers, E., Hardy, A., Ray, K., Dunn, G., Bebbington, P., & Fowler, D. (2007). The association between traumatic experience, paranoia and hallucinations: A test of the predictions of psychological models. *Acta Psychiatrica Scandinavica*, *116*(4), 280-289. https://doi.org/10.1111/j.1600-0447.2007.01011.x

Green, J. G., McLaughlin, K. A., Berglund, P. A., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I: Associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry*, *67*(2), 113-123. https://doi.org/10.1001/archgenpsychiatry.2009.186

Gumley, A. I., Taylor, H. E. F., Schwannauer, M., & MacBeth, A. (2014). A systematic review of attachment and psychosis: Measurement, construct validity and outcomes. *Acta Psychiatrica Scandinavica*, *129*(4), 257-274. https://doi.org/10.1111/acps.12172

Gürel, C., Kuşçu, G. C., Yavaşoğlu, A., & Biray Avci, Ç. (2020). The clues in solving the mystery of major psychosis: The epigenetic basis of schizophrenia and bipolar disorder. *Neuroscience and Biobehavioral Reviews*, *113*, 51-61. https://doi.org/10.1016/j.neubiorev.2020.03.005

Haijma, S. V., Van Haren, N., Cahn, W., Koolschijn, P. C. M. P., Hulshoff Pol, H. E., & Kahn, R. S. (2013). Brain volumes in schizophrenia: A meta-analysis in over 18 000 subjects. *Schizophrenia Bulletin*, *39*(5), 1129-1138. https://doi.org/10.1093/schbul/sbs118

Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. *Journal of Child Psychology and Psychiatry*, *45*(2), 260-273. https://doi.org/10.1111/j.1469-7610.2004.00218.x

Hasan, A., von Keller, R., Friemel, C. M., Hall, W., Schneider, M., Koethe, D., Leweke, F. M., Strube, W., & Hoch, E. (2020). Cannabis use and psychosis: A review of reviews.

European Archives of Psychiatry and Clinical Neuroscience, *270*(4), 403-412. https://doi.org/10.1007/s00406-019-01068-z

Hassan, A. N., & De Luca, V. (2014). The effect of lifetime adversities on resistance to antipsychotic treatment in schizophrenia patients. *Schizophrenia Research*, *161*(2), 496-500. https://doi.org/10.1016/j.schres.2014.10.048

Heins, M., Simons, C., Lataster, T., Pfeifer, S., Versmissen, D., Lardinois, M., Marcelis, M., Delespaul, P., Krabbendam, L., van Os, J., & Myin-Germeys, I. (2011). Childhood trauma and psychosis: A case-control and case-sibling comparison across different levels of genetic liability, psychopathology, and type of trauma. *American Journal of Psychiatry*, *168*(12), 1286-1294. https://doi.org/10.1176/appi.ajp.2011.10101531

Helsedirektoratet (HDIR). (2013). *Nasjonal faglig retningslinje for utredning, behandling og oppfølging av personer med psykoselidelser*. Helsedirektoratet. https://www.helsedirektoratet.no/retningslinjer/psykoselidelser

Hornor, G. (2014). Child Neglect: Assessment and intervention. *Journal of Pediatric Health Care*, *28*(2), 186-192. https://doi.org/10.1016/j.pedhc.2013.10.002

Howes, O. D., & Kapur, S. (2009). The dopamine hypothesis of schizophrenia: Version III - the final common pathway. *Schizophrenia Bulletin*, *35*(3), 549-562. https://doi.org/10.1093/schbul/sbp006

Hoy, K., Barrett, S., Shannon, C., Campbell, C., Watson, D., Rushe, T., Shevlin, M., Bai, F., Cooper, S., & Mulholland, C. (2012). Childhood trauma and hippocampal and amygdalar volumes in first-episode psychosis. *Schizophrenia Bulletin*, *38*(6), 1162-1169. https://doi.org/10.1093/schbul/sbr085

Husted, J. A., Ahmed, R., Chow, E. W. C., Brzustowicz, L. M., & Bassett, A. S. (2010). Childhood trauma and genetic factors in familial schizophrenia associated with the

NOS1AP gene. *Schizophrenia Research*, *121*(1), 187-192. https://doi.org/10.1016/j.schres.2010.05.021

Häfner, H., Maurer, K., Löffler, W., Heiden, W. a. d., Hambrecht, M., & Schultze-Lutter, F. (2003). Modeling the early course of schizophrenia. *Schizophrenia Bulletin*, *29*(2), 325-340. https://doi.org/10.1093/oxfordjournals.schbul.a007008

Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., de Graaf, R., & van Os, J. (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavia*, *109*(1), 38-45. https://doi.org/10.1046/j.0001-690X.2003.00217.x

Johannessen, J. O., & Joa, I. (2021). Modern understanding of psychosis: From brain disease to stress disorder. And some other important aspects of psychosis. *Psychosis*, *13*(4), 289-301. https://doi.org/10.1080/17522439.2021.1985162

Johnsen, E., Kroken, R. A., Løberg, E.-M., Rettenbacher, M., Joa, I., Larsen, T. K., Reitan, S. K., Walla, B., Alisauskiene, R., Anda, L. G., Bartz-Johannessen, C., Berle, J. Ø., Bjarke, J., Fathian, F., Hugdahl, K., Kjelby, E., Sinkeviciute, I., Skrede, S., Stabell, L., . . . Fleischhacker, W. W. (2020). Amisulpride, aripiprazole, and olanzapine in patients with schizophrenia-spectrum disorders (BeSt InTro): A pragmatic, rater-blind, semi-randomised trial. *Lancet Psychiatry*, *7*(11), 945-954. https://doi.org/10.1016/S2215-0366(20)30341-2

Jongsma, H. E., Turner, C., Kirkbride, J. B., & Jones, P. B. (2019). International incidence of psychotic disorders, 2002–17: A systematic review and meta-analysis. *Lancet Public Health*, *4*(5), 229-244. https://doi.org/10.1016/S2468-2667(19)30056-8

Kahn, R. S., & Keefe, R. S. E. (2013). Schizophrenia is a cognitive illness: Time for a change in focus. *JAMA Psychiatry*, *70*(10), 1107-1112. https://doi.org/10.1001/jamapsychiatry.2013.155

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261-276. https://doi.org/10.1093/schbul/13.2.261

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A. O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., de Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., . . . Williams, D. R. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry*, *197*(5), 378-385. https://doi.org/10.1192/bjp.bp.110.080499

Kilian, S., Asmal, L., Chiliza, B., Olivier, M. R., Phahladira, L., Scheffler, F., Seedat, S., Marder, S. R., Green, M. F., & Emsley, R. (2018). Childhood adversity and cognitive function in schizophrenia spectrum disorders and healthy controls: Evidence for an association between neglect and social cognition. *Psychological Medicine*, *48*(13), 2186-2193. https://doi.org/10.1017/S0033291717003671

Kisely, S., Abajobir, A. A., Mills, R., Strathearn, L., Clavarino, A., & Najman, J. M. (2018). Child maltreatment and mental health problems in adulthood: Birth cohort study. *The British Journal of Psychiatry*, *213*(6), 698-703. https://doi.org/10.1192/bjp.2018.207

Korver-Nieberg, N., Berry, K., Meijer, C., de Haan, L., & Ponizovsky, A. M. (2015). Associations between attachment and psychopathology dimensions in a large sample of patients with psychosis. *Psychiatry Research*, *228*(1), 83-88. https://doi.org/10.1016/j.psychres.2015.04.018

Kramer, I., Simons, C. J. P., Wigman, J. T. W., Collip, D., Jacobs, N., Derom, C., Thiery, E., van Os, J., Myin-Germeys, I., & Wichers, M. (2014). Time-lagged moment-to-moment interplay between negative affect and paranoia: New insights in the affective pathway

to psychosis. *Schizophrenia Bulletin*, *40*(2), 278-286. https://doi.org/10.1093/schbul/sbs194

Lardinois, M., Lataster, T., Mengelers, R., Van Os, J., & Myin-Germeys, I. (2011). Childhood trauma and increased stress sensitivity in psychosis: Childhood trauma and stress sensitivity in psychosis. *Acta Psychiatrica Scandinavica*, *123*(1), 28-35. https://doi.org/10.1111/j.1600-0447.2010.01594.x

Lecei, A., Decoster, J., De Hert, M., Derom, C., Jacobs, N., Menne-Lothmann, C., van Os, J., Thiery, E., Rutten, B. P. F., Wichers, M., & van Winkel, R. (2019). Evidence that the association of childhood trauma with psychosis and related psychopathology is not explained by gene-environment correlation: A monozygotic twin differences approach. *Schizophrenia Research*, *205*, 58-62. https://doi.org/10.1016/j.schres.2018.05.025

Leeb, R. T., Lewis, T., & Zolotor, A. J. (2011). A review of physical and mental health consequences of child abuse and neglect and implications for practice. *American Journal of Lifestyle Medicine*, *5*(5), 454-468. https://doi.org/10.1177/1559827611410266

Leucht, S., Heres, S., Kissling, W., & Davis, J. M. (2011). Evidence-based pharmacotherapy of schizophrenia. *The International Journal of Neuropsychopharmacology*, *14*(2), 269-284. https://doi.org/10.1017/S1461145710001380

Leucht, S., Kane, J. M., Kissling, W., Hamann, J., Etschel, E., & Engel, R. R. (2005). What does the PANSS mean? *Schizophrenia Research*, *79*(2), 231-238. https://doi.org/10.1016/j.schres.2005.04.008

Li, X.-B., Bo, Q.-J., Zhang, G.-P., Zheng, W., Wang, Z.-M., Li, A.-N., Tian, Q., Liu, J.-T., Tang, Y.-L., & Wang, C.-Y. (2017). Effect of childhood trauma on cognitive functions in a sample of Chinese patients with schizophrenia. *Comprehensive Psychiatry*, *76*, 147-152. https://doi.org/10.1016/j.comppsych.2017.04.010

Lim, K., Peh, O.-H., Yang, Z., Rekhi, G., Rapisarda, A., See, Y.-M., Rashid, N. A. A., Ang, M.-S., Lee, S.-A., Sim, K., Huang, H., Lencz, T., Lee, J., & Lam, M. (2021). Large-scale evaluation of the Positive and Negative Syndrome Scale (PANSS) symptom architecture in schizophrenia. *Asian Journal of Psychiatry*, *62*, 102732. https://doi.org/10.1016/j.ajp.2021.102732

Linscott, R. J., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, *43*(6), 1133-1149. https://doi.org/10.1017/S0033291712001626

Marconi, A., Di Forti, M., Lewis, C. M., Murray, R. M., & Vassos, E. (2016). Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophrenia Bulletin*, *42*(5), 1262-1269. https://doi.org/10.1093/schbul/sbw003

Matheson, S. L., Shepherd, A. M., Pinchbeck, R. M., Laurens, K. R., & Carr, V. J. (2013). Childhood adversity in schizophrenia: A systematic meta-analysis. *Psychological Medicine*, *43*(2), 225-238. https://doi.org/10.1017/S0033291712000785

McGuffin, P., Asherson, P., Owen, M., & Farmer, A. (1994). The strength of the genetic effect. Is there room for an environmental influence in the aetiology of schizophrenia? *The British Journal of Psychiatry: the Journal of Mental Science*, *164*(5), 593-599. https://doi.org/10.1192/bjp.164.5.593

McLaughlin, K. A., & Lambert, H. K. (2017). Child trauma exposure and psychopathology: Mechanisms of risk and resilience. *Current Opinion in Psychology*, *14*, 29-34. https://doi.org/10.1016/j.copsyc.2016.10.004

Mehmetoglu, M., & Jakobsen, T. G. (2022). *Applied statistics using Stata: A guide for the social sciences* (2nd ed.). Sage.

Miller, C. L. (2022). The epigenetics of psychosis: A structured review with representative loci. *Biomedicines*, *10*(3), 561. https://doi.org/10.3390/biomedicines10030561

Misiak, B., Frydecka, D., Zawadzki, M., Krefft, M., & Kiejna, A. (2014). Refining and integrating schizophrenia pathophysiology - Relevance of the allostatic load concept. *Neuroscience & Biobehavioral Reviews*, *45*, 183-201. https://doi.org/10.1016/j.neubiorev.2014.06.004

Misiak, B., Krefft, M., Bielawski, T., Moustafa, A. A., Sąsiadek, M. M., & Frydecka, D. (2017). Toward a unified theory of childhood trauma and psychosis: A comprehensive review of epidemiological, clinical, neuropsychological and biological findings. *Neuroscience and Biobehavioral Reviews*, *75*, 393-406. https://doi.org/10.1016/j.neubiorev.2017.02.015

Moe, A. M., & Docherty, N. M. (2014). Schizophrenia and the sense of self. *Schizophrenia Bulletin*, *40*(1), 161-168. https://doi.org/10.1093/schbul/sbt121

Morgan, C., & Fisher, H. (2007). Environment and schizophrenia: Environmental factors in schizophrenia: Childhood trauma-a critical review. *Schizophrenia Bulletin*, *33*(1), 3-10. https://doi.org/10.1093/schbul/sbl053

Murray, R. M., Sideli, L., Mulè, A., & La Barbera, D. (2014). Searching for the truth about schizophrenia requires the application of similarly high standards of proof to biological and social risk factors. *Psychosis*, *6*(1), 85-87. https://doi.org/10.1080/17522439.2013.801033

Myers, K., & Winters, N. C. (2002). Ten-year review of rating scales. I: Overview of scale functioning, psychometric properties, and selection. *Journal of the American Academy of Child and Adolescent Psychiatry*, *41*(2), 114-122. https://doi.org/10.1097/00004583-200202000-00004

Myin-Germeys, I., & van Os, J. (2007). Stress-reactivity in psychosis: Evidence for an affective pathway to psychosis. *Clinical Psychology Review*, *27*(4), 409-424. https://doi.org/10.1016/j.cpr.2006.09.005

Mørkved, N., Endsjø, M., Winje, D., Johnsen, E., Dovran, A., Arefjord, K., Kroken, R. A., Helle, S., Anda-Ågotnes, L. G., Rettenbacher, M. A., Huber, N., & Løberg, E. M. (2017). Childhood trauma in schizophrenia spectrum disorder as compared to other mental health disorders. *Psychosis*, *9*(1), 48-56. https://doi.org/10.1080/17522439.2016.1201135

Mørkved, N., Johnsen, E., Kroken, R. A., Gjestad, R., Winje, D., Thimm, J., Fathian, F., Rettenbacher, M., Anda, L. G., & Løberg, E. M. (2020). Does childhood trauma influence cognitive functioning in schizophrenia? The association of childhood trauma and cognition in schizophrenia spectrum disorders. *Schizophrenia Research: Cognition*, *21*, 100179. https://doi.org/10.1016/j.scog.2020.100179

Mørkved, N., Johnsen, E., Kroken, R. A., Winje, D., Larsen, T. K., Thimm, J. C., Rettenbacher, M. A., Johannesen, C. A. B., & Løberg, E. M. (2022). Impact of childhood trauma on antipsychotic effectiveness in schizophrenia spectrum disorders: A prospective, pragmatic, semi-randomized trial. *Schizophrenia Research*, *246*, 49-59. https://doi.org/10.1016/j.schres.2022.05.022

National Collaborating Centre for Mental Health (UK). (2014). *Psychosis and schizophrenia in adults: Treatment and management*. National Institute for Health and Care Excellence (UK). https://doi.org/https://pubmed.ncbi.nlm.nih.gov/25340235/

Nicotra, E., Casu, G., Piras, S., & Marchese, G. (2015). On the use of the Positive and Negative Syndrome Scale in randomized clinical trials. *Schizophrenia Research*, *165*(2), 181-187. https://doi.org/10.1016/j.schres.2015.04.006

Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The long-term health consequences of child physical abuse, emotional abuse, and neglect: A systematic review and meta-analysis. *Plos Medicine*, *9*(11), e1001349. https://doi.org/10.1371/journal.pmed.1001349

Osborne, J. W., & Waters, E. (2002). Four assumptions of multiple regression that researchers should always test. *Practical Assessment, Research & Evaluation*, *8*, 2.

Paquola, C., Bennett, M. R., & Lagopoulos, J. (2016). Understanding heterogeneity in grey matter research of adults with childhood maltreatment—A meta-analysis and review. *Neuroscience & Biobehavioral Reviews*, *69*, 299-312. https://doi.org/10.1016/j.neubiorev.2016.08.011

Pechtel, P., & Pizzagalli, D. A. (2011). Effects of early life stress on cognitive and affective function: An integrated review of human literature. *Psychopharmacology*, *214*(1), 55-70. https://doi.org/10.1007/s00213-010-2009-2

Pedraz-Petrozzi, B., Elyamany, O., Rummel, C., & Mulert, C. (2020). Effects of inflammation on the kynurenine pathway in schizophrenia - a systematic review. *Journal of Neuroinflammation*, *17*(1), 56. https://doi.org/10.1186/s12974-020-1721-z

Peters, E., Hardy, A., Dudley, R., Varese, F., Greenwood, K., Steel, C., Emsley, R., Keen, N., Bowe, S., Swan, S., Underwood, R., Longden, E., Byford, S., Potts, L., Heslin, M., Grey, N., Turkington, D., Fowler, D., Kuipers, E., & Morrison, A. (2022). Multisite randomised controlled trial of trauma-focused cognitive behaviour therapy for psychosis to reduce post-traumatic stress symptoms in people with co-morbid post-traumatic stress disorder and psychosis, compared to treatment as usual: Study protocol for the STAR (Study of Trauma And Recovery) trial. *Trials*, *23*(1), 429. https://doi.org/10.1186/s13063-022-06215-x

Pinckaers, F. M. E., Rotee, I. L. M., Nwosu, C. V., Krolinski, P., Smeets, A. P. W., Guloksuz, S., de Jong, L., Vaessen, T. S. J., Damen, T., Uittenboogaard, A., Schafer, A. T., Menne-Lothmann, C., Decoster, J., van Winkel, R., Collip, D., Delespaul, P., De Hert, M., Derom, C., Thiery, E., . . . kker, M. (2019). Evidence for interaction between genetic liability and childhood trauma in the development of psychotic symptoms. *Social Psychiatry and Psychiatric Epidemiology*, *54*(9), 1045-1054. https://doi.org/10.1007/s00127-019-01711-z

R Core Team. (2022). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/

Radhakrishnan, R., Guloksuz, S., ten Have, M., de Graaf, R., van Dorsselaer, S., Gunther, N., Rauschenberg, C., Reininghaus, U., Pries, L.-K., Bak, M., & van Os, J. (2019). Interaction between environmental and familial affective risk impacts psychosis admixture in states of affective dysregulation. *Psychological Medicine*, *49*(11), 1879-1889. https://doi.org/10.1017/S0033291718002635

Read, J., Bentall, R. P., & Fosse, R. (2009). Time to abandon the bio-bio-bio model of psychosis: Exploring the epigenetic and psychological mechanisms by which adverse life events lead to psychotic symptoms. *Epidemiology and Psychiatric Sciences*, *18*(4), 299-310. https://doi.org/10.1017/S1121189X00000257

Read, J., Fosse, R., Moskowitz, A., & Perry, B. (2014). The traumagenic neurodevelopmental model of psychosis revisited. *Neuropsychiatry*, *4*(1), 65-79. https://doi.org/10.2217/npy.13.89

Read, J., Perry, B. D., Moskowitz, A., & Connolly, J. (2001). The contribution of early traumatic events to schizophrenia in some patients: A traumagenic neurodevelopmental model. *Psychiatry*, *64*(4), 319-345. https://doi.org/10.1521/psyc.64.4.319.18602

Şahin, S., Yüksel, Ç., Güler, J., Karadayı, G., Akturan, E., Göde, E., Özhan, A. A., & Üçok, A. (2013). The history of childhood trauma among individuals with ultra high risk for psychosis is as common as among patients with first-episode schizophrenia. *Early Intervention in Psychiatry*, *7*(4), 414-420. https://doi.org/10.1111/eip.12022

Sallis, H. M., Croft, J., Havdahl, A., Jones, H. J., Dunn, E. C., Davey Smith, G., Zammit, S., & Munafò, M. R. (2021). Genetic liability to schizophrenia is associated with exposure to traumatic events in childhood. *Psychological Medicine*, *51*(11), 1814-1821. https://doi.org/10.1017/S0033291720000537

Santesteban-Echarri, O., Sandel, D., Liu, L., Bearden, C. E., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Keshavan, M., Mathalon, D. H., McGlashan, T. H., Perkins, D. O., Seidman, L. J., Stone, W. S., Tsuang, M. T., Walker, E. F., Woods, S. W., & Addington, J. (2022). Family history of psychosis in youth at clinical high risk: A replication study. *Psychiatry Research*, *311*, 114480. https://doi.org/10.1016/j.psychres.2022.114480

Santvoort, F. v., Hosman, C. M. H., Janssens, J. M. A. M., Doesum, K. T. M. v., Reupert, A. E., & Loon, L. M. A. v. (2015). The impact of various parental mental disorders on children's diagnoses: A systematic review. *Clinical Child and Family Psychology Review*, *18*(4), 281-299. https://doi.org/10.1007/s10567-015-0191-9

Schalinski, I., Breinlinger, S., Hirt, V., Teicher, M. H., Odenwald, M., & Rockstroh, B. (2019). Environmental adversities and psychotic symptoms: The impact of timing of trauma, abuse, and neglect. *Schizophrenia Research*, *205*, 4-9. https://doi.org/10.1016/j.schres.2017.10.034

Scher, C. D., Forde, D. R., McQuaid, J. R., & Stein, M. B. (2004). Prevalence and demographic correlates of childhood maltreatment in an adult community sample. *Child Abuse & Neglect*, *28*(2), 167-180. https://doi.org/10.1016/j.chiabu.2003.09.012

Scott, J., Chant, D., Andrews, G., Martin, G., & McGrath, J. (2007). Association between trauma exposure and delusional experiences in a large community-based sample. *The British Journal of Psychiatry*, *190*(4), 339-343. https://doi.org/10.1192/bjp.bp.106.026708

Seow, L. S. E., Ong, C., Mahesh, M. V., Sagayadevan, V., Shafie, S., Chong, S. A., & Subramaniam, M. (2016). A systematic review on comorbid post-traumatic stress disorder in schizophrenia. *Schizophrenia Research*, *176*(2-3), 441-451. https://doi.org/10.1016/j.schres.2016.05.004

Sheffield, J. M., Williams, L. E., Woodward, N. D., & Heckers, S. (2013). Reduced gray matter volume in psychotic disorder patients with a history of childhood sexual abuse. *Schizophrenia Research*, *143*(1), 185-191. https://doi.org/10.1016/j.schres.2012.10.032

Shevlin, M., Dorahy, M., & Adamson, G. (2007). Childhood traumas and hallucinations: An analysis of the national comorbidity survey. *Journal of Psychiatric Research*, *41*(3), 222-228. https://doi.org/10.1016/j.jpsychires.2006.03.004

Sidebotham, P., & Golding, J. (2001). Child maltreatment in the "Children of the nineties": A longitudinal study of parental risk factors. *Child Abuse & Neglect*, *25*(9), 1177-1200. https://doi.org/10.1016/S0145-2134(01)00261-7

Sideli, L., Mule, A., La Barbera, D., & Murray, R. M. (2012). Do child abuse and maltreatment increase risk of schizophrenia? *Psychiatry Investigation*, *9*(2), 87-99. https://doi.org/10.4306/pi.2012.9.2.87

Simeone, J. C., Ward, A. J., Rotella, P., Collins, J., & Windisch, R. (2015). An evaluation of variation in published estimates of schizophrenia prevalence from 1990-2013: A systematic literature review. *BMC Psychiatry*, *15*(1), 193. https://doi.org/10.1186/s12888-015-0578-7

Slack, K. S., Berger, L. M., DuMont, K., Yang, M.-Y., Kim, B., Ehrhard-Dietzel, S., & Holl, J. L. (2011). Risk and protective factors for child neglect during early childhood: A cross-study comparison. *Children and Youth Services Review*, *33*(8), 1354-1363. https://doi.org/10.1016/j.childyouth.2011.04.024

Sommer, I. E., & Kahn, R. S. (2015). The contribution of neuroimaging to understanding schizophrenia; past, present, and future. *Schizophrenia Bulletin*, *41*(1), 1-3. https://doi.org/10.1093/schbul/sbu141

Sommer, I. E. C., Daalman, K., Rietkerk, T., Diederen, K. M., Bakker, S., Wijkstra, J., & Boks, M. P. M. (2010). healthy individuals with auditory verbal hallucinations; who are they? Psychiatric assessments of a selected sample of 103 subjects. *Schizophrenia Bulletin*, *36*(3), 633-641. https://doi.org/10.1093/schbul/sbn130

Spitzer, R. L., Williams, J. B., Gibbon, M., & First, M. B. (1992). The Structured Clinical Interview for DSM-III-R (SCID). I: History, rationale, and description. *Archives of General Psychiatry*, *49*(8), 624-629. https://doi.org/10.1001/archpsyc.1992.01820080032005

Sprooten, E., Papmeyer, M., Smyth, A. M., Vincenz, D., Honold, S., Conlon, G. A., Moorhead, T. W. J., Job, D., Whalley, H. C., Hall, J., McIntosh, A. M., Owens, D. C. G., Johnstone, E. C., & Lawrie, S. M. (2013). Cortical thickness in first-episode schizophrenia patients and individuals at high familial risk: A cross-sectional comparison. *Schizophrenia Research*, *151*(1), 259-264. https://doi.org/10.1016/j.schres.2013.09.024

Stith, S. M., Liu, T., Davies, L. C., Boykin, E. L., Alder, M. C., Harris, J. M., Som, A., McPherson, M., & Dees, J. E. M. E. G. (2008). Risk factors in child maltreatment: A meta-analytic review of the literature. *Aggression and Violent Behavior*, *14*(1), 13-29. https://doi.org/10.1016/j.avb.2006.03.006

Stoltenborgh, M., Bakermans-Kranenburg, M. J., & van Ijzendoorn, M. H. (2013). The neglect of child neglect: A meta-analytic review of the prevalence of neglect. *Social Psychiatry and Psychiatric Epidemiology*, *48*(3), 345-355. https://doi.org/10.1007/s00127-012-0549-y

Stracke, M., Gilbert, K., Kieser, M., Klose, C., Krisam, J., Ebert, D. D., Buntrock, C., & Christiansen, H. (2019). CoMPARE family (Children of mentally ill parents at risk evaluation): A study protocol for a preventive intervention for children of mentally ill parents (Triple P, evidence-based program that enhances parentings skills, in addition to gold-standard CBT with the mentally ill parent) in a multicenter RCT—Part II. *Frontiers in Psychiatry*, *10*, 54. https://doi.org/10.3389/fpsyt.2019.00054

Suen, Y. N., Pang, S. W. T., Cheung, C., Wong, T. Y., Hui, L. M. C., Lee, H. M. E., Chang, W. C., Chen, Y. H. E., & Chan, S. K. W. (2023). Impact of early negative symptom patterns on the long-term outcomes of patients with first-episode schizophrenia-spectrum disorders: A 12-year follow up study. *Psychiatry Research*, *323*, 115180. https://doi.org/10.1016/j.psychres.2023.115180

Susser, E., & Widom, C. S. (2012). Still searching for lost truths about the bitter sorrows of childhood. *Schizophrenia Bulletin*, *38*(4), 672-675. https://doi.org/10.1093/schbul/sbs074

Szilagyi, M. A., Rosen, D. S., Rubin, D., Zlotnik, S., Szilagyi, M. A., Harmon, D., Harmon, D., Jaudes, P., Jones, V. F., Lee, P., Nalven, L., Prock, L., Sagor, L., Schulte, E., Springer, S., Tonniges, T., Fouras, G., Harvey, J., Hill, M., . . . Zia, C. (2015). Health care issues for children and adolescents in foster care and kinship care. *Pediatrics*, *136*(4), E1142-E1166. https://doi.org/10.1542/peds.2015-2656

Teicher, M. H., & Samson, J. A. (2016). Annual research review: Enduring neurobiological effects of childhood abuse and neglect. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *57*(3), 241-266. https://doi.org/10.1111/jcpp.12507

Thomas, S., Höfler, M., Schäfer, I., & Trautmann, S. (2019). Childhood maltreatment and treatment outcome in psychotic disorders: A systematic review and meta-analysis. *Acta Psychiatrica Scandinavica*, *140*(4), 295-312. https://doi.org/10.1111/acps.13077

Thompson, A. D., Nelson, B., Yuen, H. P., Lin, A., Amminger, G. P., McGorry, P. D., Wood, S. J., & Yung, A. R. (2014). Sexual trauma increases the risk of developing psychosis in an Ultra High-Risk «prodromal" population. *Schizophrenia Bulletin*, *40*(3), 697-706. https://doi.org/10.1093/schbul/sbt032

Trauelsen, A. M., Bendall, S., Jansen, J. E., Nielsen, H.-G. L., Pedersen, M. B., Trier, C. H., Haahr, U. H., & Simonsen, E. (2015). Childhood adversity specificity and dose-response effect in non-affective first-episode psychosis. *Schizophrenia Research*, *165*(1), 52-59. https://doi.org/10.1016/j.schres.2015.03.014

Uldall, S. W., Nielsen, M. Ø., Carlsson, J., Glenthøj, B., Siebner, H. R., Madsen, K. H., Madsen, C. G., Leffers, A.-M., Nejad, A. B., & Rostrup, E. (2020). Associations of neural processing of reward with posttraumatic stress disorder and secondary psychotic symptoms in trauma-affected refugees. *European Journal of Psychotraumatology*, *11*(1), 1730091. https://doi.org/10.1080/20008198.2020.1730091

Valle, R. (2020). Schizophrenia in ICD-11: Comparison of ICD-10 and DSM-5. *Revista De Psiquiatria Y Salud Mental*, *13*(2), 95-104. https://doi.org/10.1016/j.rpsm.2020.01.001

van den Berg, D. P. G., de Bont, P. A. J. M., van der Vleugel, B. M., de Roos, C., de Jongh, A., van Minnen, A., & van der Gaag, M. (2016). Trauma-Focused Treatment in PTSD patients with psychosis: Symptom exacerbation, adverse Events, and revictimization. *Schizophrenia Bulletin*, *42*(3), 693-702. https://doi.org/10.1093/schbul/sbv172

van Lutterveld, R., van den Heuvel, M. P., Diederen, K. M. J., de Weijer, A. D., Begemann, M. J. H., Brouwer, R. M., Daalman, K., Blom, J. D., Kahn, R. S., & Sommer, I. E. (2014). Cortical thickness in individuals with non-clinical and clinical psychotic symptoms. *Brain: A Journal of Neurology*, *137*(10), 2664-2669. https://doi.org/10.1093/brain/awu167

van Nierop, M., Lataster, T., Smeets, F., Gunther, N., van Zelst, C., de Graaf, R., Ten Have, M., van Dorsselaer, S., Bak, M., Myin-Germeys, I., Viechtbauer, W., van Os, J., & van Winkel, R. (2014a). Psychopathological mechanisms linking childhood traumatic experiences to risk of psychotic symptoms: Analysis of a large, representative population-based sample. *Schizophrenia Bulletin*, *40*(S2), S123-S130. https://doi.org/10.1093/schbul/sbt150

van Os, J., Hanssen, M., Bak, M., Bijl, R. V., & Vollebergh, W. (2003). Do urbanicity and familial liability coparticipate in causing psychosis? *The American Journal of Psychiatry*, *160*(3), 477-482. https://doi.org/10.1176/appi.ajp.160.3.477

van Os, J., & Kapur, S. (2009). Schizophrenia. *The Lancet (British edition)*, *374*(9690), 635-645. https://doi.org/10.1016/S0140-6736(09)60995-8

van Os, J., Kenis, G., & Rutten, B. P. F. (2010). The environment and schizophrenia. *Nature*, *468*(7321), 203-212. https://doi.org/10.1038/nature09563

van Rossum, I., Dominguez, M.-d.-G., Lieb, R., Wittchen, H.-U., & van Os, J. (2011). Affective dysregulation and reality distortion: A 10-year prospective study of their association and clinical relevance. *Schizophrenia Bulletin*, *37*(3), 561-571. https://doi.org/10.1093/schbul/sbp101

van Schalkwyk, G. I. (2017). 6.1 Psychotic symptoms in autism spectrum disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*(10), S9. https://doi.org/10.1016/j.jaac.2017.07.033

van Schalkwyk, G. I., Volkmar, F. R., & Corlett, P. R. (2017). A predictive coding account of psychotic symptoms in autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *47*(5), 1323-1340. https://doi.org/10.1007/s10803-017-3065-9

van Winkel, R., van Nierop, M., Myin-Germeys, I., & van Os, J. (2013). Childhood trauma as a cause of psychosis: Linking genes, psychology, and biology. *The Canadian Journal of Psychiatry*, *58*(1), 44-51. https://doi.org/10.1177/070674371305800109

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., Read, J., van Os, J., & Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin*, *38*(4), 661-671. https://doi.org/10.1093/schbul/sbs050

Velligan, D. I., & Alphs, L. D. (2013). Negative symptoms in schizophrenia: The importance of identification and treatment. *The Psychiatric times*, *30*(5), 24. https://doi.org/https://www.proquest.com/trade-journals/negative-symptoms-schizophrenia-importance/docview/1350369690/se-2

Vita, A., De Peri, L., Deste, G., Barlati, S., & Sacchetti, E. (2015). The Effect of antipsychotic treatment on cortical gray matter changes in schizophrenia: Does the class matter? A meta-analysis and meta-regression of longitudinal magnetic resonance imaging studies. *Biological Psychiatry*, *78*(6), 403-412. https://doi.org/10.1016/j.biopsych.2015.02.008

von Knorring, L., & Lindström, E. (1995). Principal components and further possibilities with the PANSS. *Acta Psychiatrica Scandinavica*, *92*(s388), 5-10. https://doi.org/10.1111/j.1600-0447.1995.tb05937.x

Wallwork, R. S., Fortgang, R., Hashimoto, R., Weinberger, D. R., & Dickinson, D. (2012). Searching for a consensus five-factor model of the Positive and Negative Syndrome

Scale for schizophrenia. *Schizophrenia Research*, *137*(1), 246-250. https://doi.org/10.1016/j.schres.2012.01.031

Walsh, C., MacMillan, H., & Jamieson, E. (2002). The relationship between parental psychiatric disorder and child physical and sexual abuse: Findings from the Ontario health supplement. *Child Abuse & Neglect*, *26*(1), 11-22. https://doi.org/10.1016/S0145-2134(01)00308-8

Wang, X., & Cheng, Z. (2020). Cross-sectional studies: Strengths, weaknesses, and recommendations. *Chest*, *158*(1S), S65-S71. https://doi.org/10.1016/j.chest.2020.03.012

Winje, D., Dovran, A., & Murison, R. (2003). Spørreskjema om traumer i barndom og ungdom (Instrumentoversettelse fra engelsk: David P. Bernstein; Childhood Trauma Questionnaire (CTQ). Translated and reproduced by permission from The Psychological Corporation, Harcourt Assessment Company. Norwegian translation copyright © 2003 by The Psychological Corporation. In.

World Health Organization (WHO). (2016). *International statistical classification of diseases and related health problems* (10th ed.). World Health Organization. https://doi.org/https://icd.who.int/browse10/2016/en

World Health Organization (WHO). (2019). *International statistical classification of diseases and related health problems* (11th ed.). World Health Organization. https://doi.org/https://icd.who.int/

World Health Organization (WHO). (2022a, 19.09.2022). *Child maltreatment*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/child-maltreatment

World Health Organization (WHO). (2022b). *Schizophrenia [Fact sheet]*. https://www.who.int/news-room/fact-sheets/detail/schizophrenia

Zubin, J., & Spring, B. (1977). Vulnerability: A new view of schizophrenia. *Journal of Abnormal Psychology*, *86*(2), 103-126. https://doi.org/10.1037/0021-843X.86.2.103

Aas, M., Alameda, L., di Forti, M., Quattrone, D., Dazzan, P., Trotta, A., Ferraro, L., Roiguez, V., Vassos, E., Sham, P., Tripoli, G., Cascia, C. L., Barbera, D. L., Tarricone, I., Muratori, R., Berardi, D., Lasalvia, A., Tosato, S., Szöke, A., . . . Morgan, C. (2021). Synergistic effects of childhood adversity and polygenic risk in first-episode psychosis: The EU-GEI study. *Psychological Medicine*, 1-9. https://doi.org/10.1017/S0033291721003664

Appendix A. Family history form

FAMILIEHISTORIE:

19. Har noen av pasientens førstegrads slektninger hatt noen av de følgende tilstander?
Basert på all tilgjengelig informasjon.

	1. Depresjon	2. Bipolar lidelse	3. Schizofreni	4. Selvmordsforsøk	4b. Død ved selvmord	5. Alkoholisme	6. Stoffmisbruk	7. Fedme (BMI ≥ 30)	8a.Andre psykiske lidelser	8b. vennligst spesifiser
A. Mor										
B. Far										
C. Søsken *(kryss av)* ☐ Bror ☐ Søster										
D. Søsken *(kryss av)* ☐ Bror ☐ Søster										
E. Søsken *(kryss av)* ☐ Bror ☐ Søster										
F. Søsken *(kryss av)* ☐ Bror ☐ Søster										
G. Barn *(kryss av)* ☐ Sønn ☐ Datter										
H. Barn *(kryss av)* ☐ Sønn ☐ Datter										
I. Barn *(kryss av)* ☐ Sønn ☐ Datter										
J. Barn *(kryss av)* ☐ Sønn ☐ Datter										

1=Ja
(Diagnostisert/sikker)

2 = sannsynlig

Tomt = ikke

20. Har noen av pasientens andregrads slektninger (besteforeldre, søskenbarn) hatt noen av de følgende tilstander?
Depresjon, bipolar lidelse, schizofreni, andre psykiske lidelser?
(Bruk all tilgjengelig informasjon)

Slektning: _____ sykdom_____

Slektning: _____ sykdom_____

Slektning: _____ sykdom_____

Slektning: _____ sykdom_____

Slektning: _____ sykdom_____

Slektning: _____ sykdom_____

Appendix B. Practical process of statistical analyses

As a quality measure, all analyses were done with the help and guidance of statistician Christoffer A. Bartz-Johannessen, Sandviken Psychiatric Hospital, Bergen. The guidance and involvement of the statistician was pre-approved per email by the subject manager of the PROPSY317: Hovudoppgåve psykologprogrammet, professor Per Einar Binder.

Choice of the statistical method best suited for our research aim was discussed amongst ourselves, our supervisors, and the statistician, and we independently decided on a multiple regression model with an interaction term. All analyses were performed in multiple sessions with guidance of the statistician, where we independently decided statistical choices such as exclusion/inclusion criteria for the sample, confounding variables, the choice of models and quality measures. Our interpretation of the data was thoroughly discussed with the statistician during the process. This process facilitated and ensured that we understood every step of the rather complicated statistical analysis, and the important statistical factors and considerations surrounding multiple regression models in general.

HELSE BERGEN
Haukeland University Hospital

Appendix C. Elaboration of students' roles

Bergen, 12.05.23

Til rette vedkommende

UTDYPING AV STUDENTENES ROLLE KNYTTET TIL HOVEDOPPGAVE

Pia Sophie Bryntesen og Ida Marie Eggen ble utfordret på å skrive en empirisk hovedoppgave med plan om publisering. For å belyse problemstillingen vurderte vi sammen at mer avanserte statistiske metoder enn vanlig for dette nivået av vitenskapelig utvikling (master) var hensiktsmessig.

I denne prosessen har studentene hele veien vist en særdeles stor evne til selvstendig tenkning. Dette innebærer stor grad av innsikt i statistisk metode, men også andre komplekse aspekter ved temaområdet. De har fått veiledning på statistikk og skriving, men har selv stått for veivalg og tolkninger formidlet gjennom deres skriftlige arbeide og drøftinger i veiledning. Mao – selv om en egen statistiker har veiledet studentene er dette absolutt deres eget selvstendige arbeide.

Med vennlig hilsen

Else-Marie Løberg, hovedveileder
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Appendix D. Supplementary tables

Tables (4 – 7) showing the full results from the first multiple regression analyses of CTQ-SF sum score and parental mental disorders as an interaction term on PANSS total and subscale scores, controlling for age and sex, including *t*-value and standard error (SE).

Table 4

Results of Multiple Regression Analyses of CTQ-SF Sum Score and Parental Mental Disorders as an Interaction Term on PANSS Total Scale Score, Controlling for Age and Sex.

	PANSS total scale			
	Estimate [b]	SE	*t*	*p*
Intercept [a]	70.616	6.147	11.488	0
CT [c]	0.222	0.112	1.990	.049*
Age	- 0.215	0.126	- 1.701	.091*
Sex	- 1.081	3.206	- 0.337	.736
Maternal mental disorder	- 2.100	13.569	- 0.155	.877
Paternal mental disorder	19.615	13.309	1.474	.143
Both parental mental disorder	- 44.604	30.098	- 1.482	.141
CT X maternal mental disorder	0.112	0.300	0.373	.710
CT X paternal mental disorder	- 0.252	0.274	- 0.920	.360
CT X parental mental disorder	0.852	0.668	1.275	.205

Note. *p <.05. p = p-value; t = t-value; SE = Standard error; PANSS = the Positive and Negative Syndrome Scale; CT = Childhood trauma. CTQ-SF = Childhood Trauma Questionnaire Short-Form. [a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected change in independent variable with one unit change of dependent variable (β). [c] CTQ-SF sum score.

Table 5

Results of Multiple Regression Analyses of CTQ-SF Sum Score and Parental Mental Disorders as an Interaction Term on PANSS Positive Subscale Score, Controlling for Age and Sex.

	PANSS positive subscale			
	Estimate [b]	SE	*t*	*p*
Intercept [a]	17.898	2.071	8.642	0
CT [c]	0.046	0.037	1.252	.213
Age	0.013	0.042	0.300	.765
Sex	- 0.997	1.076	- 0.926	.356
Maternal mental disorder	- 1.171	4.574	- 0.256	.798
Paternal mental disorder	0.285	4.486	0.064	.949
Both parental mental disorder	- 10.199	10.152	- 1.005	.317
CT X maternal mental disorder	0.001	0.101	0.006	.995
CT X paternal mental disorder	- 0.020	0.092	- 0.216	.829
CT X parental mental disorder	0.186	0.225	0.824	.412

Note. *p <.05. **p <.01. p = p-value; t = t-value; SE = Standard error; PANSS = the Positive and Negative Syndrome Scale; CT = Childhood trauma. CTQ-SF = Childhood Trauma Questionnaire Short-Form.

[a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected change in independent variable with one unit change of dependent variable (β). [c] CTQ-SF sum score.

Table 6

Results of Multiple Regression Analyses of CTQ-SF Sum Score and Parental Mental Disorders as an Interaction Term on PANSS Negative Subscale Score, Controlling for Age and Sex.

	PANSS negative subscale			
	Estimate [b]	SE	*t*	*p*
Intercept [a]	16.836	2.100	8.019	0
CT [c]	0.087	0.038	2.280	.024*
Age	- 0.134	0.043	- 3.106	.002**
Sex	0.308	1.095	0.281	.779
Maternal mental disorder	0.712	4.635	0.154	.878
Paternal mental disorder	8.661	4.546	1.905	.059
Both parental mental disorder	- 2.665	10.281	- 0.259	.796
CT X maternal mental disorder	0.015	0.103	0.143	.887
CT X paternal mental disorder	- 0.121	0.094	- 1.294	.198
CT X parental mental disorder	- 0.023	0.228	- 0.101	.920

Note. *p <.05. **p <.01. p = p-value; t = t-value; SE = Standard error; PANSS = the Positive and Negative Syndrome Scale; CT = Childhood trauma. CTQ-SF = Childhood Trauma Questionnaire Short-Form.

[a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected change in independent variable with one unit change of dependent variable (β). [c] CTQ-SF sum score.

Table 7

Results of Multiple Regression Analyses of CTQ-SF Sum Score and Parental Mental Disorders as an Interaction Term on PANSS General Psychopathology Subscale Score. Controlling for Age and Sex.

	PANSS general psychopathology subscale			
	Estimate [b]	SE	*t*	*p*
Intercept [a]	35.963	3.197	11.250	0
CT [c]	0.084	0.057	1.462	.146
Age	- 0.091	0.066	- 1.391	.167
Sex	- 0.312	1.661	- 0.188	.851
Maternal mental disorder	- 1.782	7.061	- 0.252	.801
Paternal mental disorder	10.523	6.925	1.520	.131
Both parental mental disorder	- 31.910	15.671	- 2.036	.044*
CT X maternal mental disorder	0.101	0.156	0.647	.519
CT X paternal mental disorder	- 0.107	0.142	- 0.750	.455
CT X parental mental disorder	0.695	0.348	1.999	.048*

Note. *p <.05. **p <.01. p = p-value; t = t-value; SE = Standard error; PANSS = the Positive and Negative Syndrome Scale; CT = Childhood trauma. CTQ-SF = Childhood Trauma Questionnaire Short-Form.

[a] Mean value of dependent variables when all independent variables equal 0. [b] Estimate of the expected change in independent variable with one unit change of dependent variable (β). [c] CTQ-SF sum score.