



## A better understanding of the impact of childhood trauma on depression in early psychosis: A differential item functioning approach

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### ABSTRACT

**Background:** Childhood trauma (CT) has been shown to impact depressive symptoms measured broadly in early psychosis patients. Beyond the broad intensity of such impact, less is known about which depressive features are more impacted.

**Methods:** Patients of a specialized early intervention programme were evaluated after the first two and six months of treatment with the Montgomery-Asberg Depression Rating Scale (MADRS). We used the first assessment available. We estimated an Item-response model to reveal potential differential item functioning (DIF) in order to highlight depressive features that could be impacted differently than others by experiences of abuse (sexual physical and emotional) and neglect (physical and emotional).

**Results:** Two hundred and sixty-two recent onset patients with psychosis were assessed. Results at the beginning of the Treatment and Early Intervention in Psychosis Program (TIPP) showed that abuse but not neglect was associated with more severe depression levels, measured at a global MADRS score. Concerning specific depressive symptoms, concentration difficulties were left largely unaffected by abuse in contrast with other aspects of depression.

**Conclusions:** The cognitive item of the depressive dimension assessed by the MADRS was not impacted by experiences of abuse, while the remaining subdomains involving anxiety, suicidality, somatic symptoms, and anhedonia were. Trials focusing on improving the impact of depression in traumatised individuals should account for the possible diluting effect of concentration when measuring the depression broadly. DIF is a promising method to better understand the impact many variables may have on various psychological dimensions at the item level.

### 1. Introduction

The topic of trauma in the context of early psychosis has received substantial attention specially in the last 10 years following meta-analytical evidence showing an association between childhood trauma (CT; sexual, physical, emotional abuse, physical and emotional neglect) and psychosis with an odds ratio of 2.8 (Varese et al., 2012b). This has led to further research investigating more specific aspects of this

association, such as that patients with psychosis and CT, regardless of the type, present more severe cognitive deficits (Vargas et al., 2019), poor functional outcomes (Christy et al., 2023), and more severe depressive symptoms (correlation ranging from  $r = 0.16$  to  $r = 0.32$ ; Alameda et al., 2021). Moreover, the depressive dimension appears as an important mediator (Alameda et al., 2022; Alameda et al., 2020; Bebbington, 2015; van Os et al., 2022) between the link between traumatic events and psychosis, meaning that it may “explain”, at least in

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part, such link. In this line, the hypothesis of an “affective pathway to psychosis” postulates that CT may lead to psychosis through a pathway of heightened emotional distress, characterised by hypersensitivity to daily-life stressors and leading to anxiety and depression (Bebbington, 2015; Myin-Germeys and van Os, 2007). These findings are relevant as they suggest that treating depressive symptoms, even at subthreshold levels, may improve psychotic symptoms of those exposed to CT (Alameda et al., 2022; Alameda et al., 2020; Bebbington, 2015; van Os et al., 2022). However, a better understanding of which aspects of the depressive syndrome are more affected by the various forms of CT is a necessary step, prior to the definition of specific treatment targets.

Research conducted to date has focused on a composite global measure of a depression score, usually measured with various validated instruments such as the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979), Calgary (Addington et al., 1993) or Hamilton (Hamilton, 1960) depression scales. There is not yet a clear understanding on which specific items (e.g. concentration, anxiety, sleep problem) are more sensitive to the various forms of adversity subtypes, or broadly measured; and whether there are general effects across individual items and adversities or whether these effects are more specific in nature.

When evaluating a psychological dimension using a scale or a questionnaire, the probability of responding to an item in a certain manner should be the same for all persons in the population with the same level on the dimension we are trying to evaluate. When this condition is not met, this phenomenon is called differential item functioning (DIF). “Differential item functioning exists when examinees of equal ability differ, on average, according to their group membership in their responses to a particular item” (American Educational Research Association et al., 1999, p.81). Differential item functioning (DIF) analysis is a tool that can highlight items that have a different behaviour or response pattern than other items in relation with a certain group membership (like having a trauma or not for instance) (Westers and Kelderman, 1992). This approach can be applied within an item response model which has the advantage of estimating the intensity of the psychological trait at the latent level (i.e. with no measurement error; only the common variance of interest of each item is used to estimate the overall dimension). It also allows to distinguish for each item which part of the variance is attributable to depression (the common variance) and which part is unique to a single item. DIF has been extensively used in the field of psychometrics and personality assessment. Although the interest in DIF is probably growing in the field of psychiatry (Hagquist, 2019; Jones, 2019; Taple et al., 2022), it has received less attention so far.

Focusing on the topic of interest of our study, if all depression items

are functioning the same way, there should be no direct effect from abuse or neglect to any of the MADRS items (Fig. 1). In other words, the whole impact of CT or neglect on depression would be captured by the covariate effect of CT or neglect on depression.

The goal of this study was to (i) better understand the nature of the association between abuse and neglect and the depressive dimension as well as its subdomains, and (ii) apply for the first time a DIF approach to a relevant clinical question with an applicability for the treatment of patients with early psychosis (EP).

## 2. Material and methods

### 2.1. Participants

The Treatment and early Intervention in Psychosis Programme (TIPP) is a specialized EP programme run by Lausanne University Hospital’s Department of Psychiatry, in Switzerland (Baumann et al., 2013). Participants’ inclusion criteria are: being aged from 18 to 35, living in the hospital’s catchment area (population about 350,000) and meeting the criteria for psychosis as defined by the ‘psychosis threshold’ subscale in the Comprehensive Assessment of At-Risk Mental States (CAARMS) instrument (Yung et al., 2005). Here psychotic disorder threshold is defined as having frank psychotic symptoms such as delusions, hallucinations and thought disorder persisting for longer than one week, with a frequency of at least 3–6 times a week for longer than 1 h each time or daily for <1 h each time. This is a standard and widely used criterion for first episode psychosis threshold (Nelson et al., 2014).

Patients with drug-induced brief psychotic states, organic brain disease, an IQ < 70, or those on antipsychotic medication for more than six months are referred to other programmes. The TIPP paradigm of care is based on the principles of both case management interventions and assertive community treatment. Over a three-year period, case managers are available to each patient up to twice a week. Patients are seen at least 100 times over the three-year programme, primarily by their case manager but also by a resident physician or an intern in psychiatry. A consultant psychiatrist supervises each case.

All patients treated within the TIPP are assessed at baseline. A specially designed questionnaire (the TIPP Initial Assessment Tool: TIAT; available online (2021)) is completed for all patients enrolled in the programme by case managers. It allows assessment of demographic characteristics and past medical history. Follow-up assessments exploring various aspects of treatment and co-morbidities as well as evolution of psychopathology and functional level are conducted by a psychologist and by case managers after 2, 6, 12, 18, 24, 30 and 36

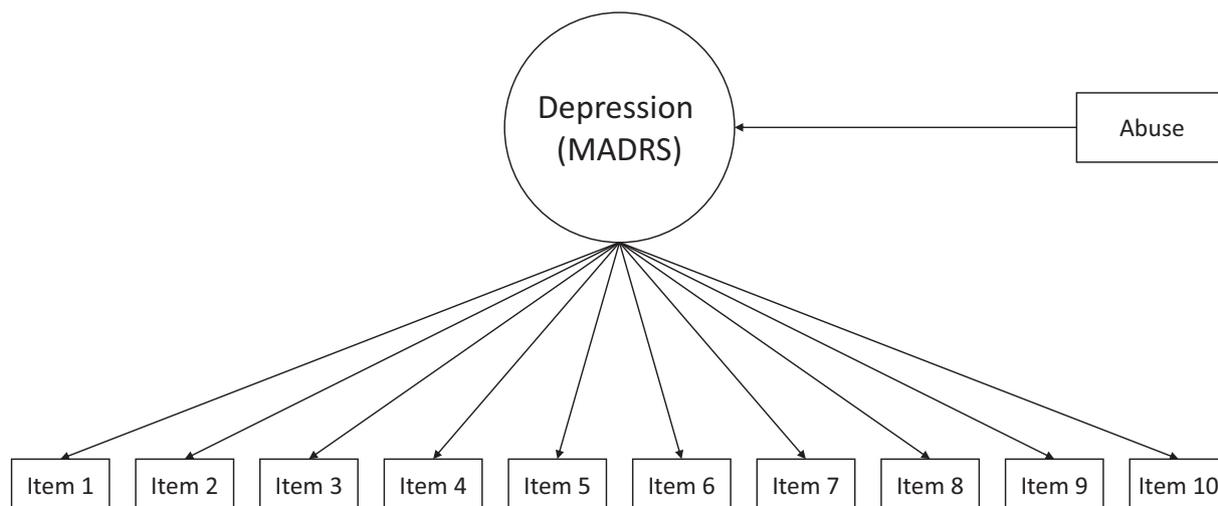


Fig. 1. Differential item functioning (DIF) analysis of the impact of abuse on depression.

months of treatment.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by the Human Research Ethics Committee of the Canton of Vaud (CER-VD; protocol #2020–00272). The data generated by the follow-up of all patients were used in the study if the latter did not explicitly object to the use of their data for research purposes. Only four patients refused the use of their clinical data for research.

## 2.2. Clinical assessments

Detailed evaluation of past medical history, demographic characteristics, exposure to adverse life events as well as symptoms and functioning were performed by case managers (CM) and a psychologist, through semi-structured interviews and a questionnaire. Depression levels were scored at each assessment with the MADRS (Montgomery and Asberg, 1979). The depression assessment was performed by a psychologist who was not involved in patients' treatment and had received standardized training prior to the study to conduct the symptom assessment. The MADRS is a 10-item scale commonly used to measure the severity of depressive symptoms and includes the following items that are graded from 0 to 6: 1. Apparent sadness 2. Reported sadness 3. Inner tension 4. Reduced sleep 5. Reduced appetite 6. Concentration difficulties 7. Lassitude 8. Inability to feel 9. Pessimistic thoughts 10. Suicidal thoughts. Since we were interested in depression at the beginning of the programme, we used the first MADRS assessment available in the first 6 months of the programme (assessment after 2 months for 179 patients and, because the 2-months assessment was missing, assessment after 6 months for 83 patients).

Diagnosis is the result of an expert consensus and is based on the following elements: (1) Diagnosis based on DSM-IV criteria reported by a treating psychiatrist in all medical documents and at the end of any hospitalization; (2) longitudinal assessment by psychiatrist, psychologist and clinical case manager over the 3 years of treatment. The consensus diagnosis procedure is realized by a senior psychiatrist and the senior psychologist in charge of scale-based assessment over the treatment period. They both review the entire file once after 18 months and again after 36 months (or at the end of treatment) and conduct a diagnostic process discussing any unclear issue with the case manager. In this study, we considered the latest diagnostic consensus available.

### 2.2.1. Assessment of history of abuse and neglect

Clinicians at TIPP are trained to conduct a comprehensive assessment of patients, including evaluation of exposure to traumatic life events. Case managers meet patients frequently over the treatment period, which provides the framework to establish a trusting relationship, where extensive knowledge of patients' history can be gathered. If patients agree, information can also be completed with family. In case of inconsistency between information obtained from the family and the patient's information, or in case of doubt about the exposure (or the age of the exposure), CM could gather information from other source for verification. Case managers complete a table during the patients' 3 years of treatment, where exposure to traumatic life events can be recorded as follows: (1) type of traumatic life event, rated as present or absent (sexual abuse, physical abuse, emotional and physical neglect, emotional abuse, among others...); (2) time of occurrence in relation to psychosis stage (during the premorbid phase, during the prodrome or after onset of psychosis); (3) age at the time of first exposure to each one of the traumas that occurred; and (4) single or repeated exposure to each one of the traumas that occurred. Considering that the clinicians who assessed exposure to life events did not rate the subjective perception of severity of the different forms of stressful events, patients were considered traumatised if they had been exposed to at least one type of abuse (physical, sexual, or emotional) before the age of 16. The consideration

was that such events would undoubtedly be considered as highly traumatizing by anyone, and have been shown to be associated with risk for psychosis and functional deficits in psychotic samples (Varese et al., 2012a). Sexual abuse refers to sexual molestation and/or rape. Physical abuse refers to physical attack or assault, or being repetitively beaten by parents, relatives or caregivers. Emotional abuse was defined as verbal assaults on a child's sense of worth or well-being or any humiliating or demeaning behaviour directed toward a child by an adult or older person. Neglect was defined on the basis of experiences of emotional or physical needs that were consistently ignored or disregarded before age 16.

## 2.3. Statistical analysis

MADRS item data were treated as categorical ordinals and the Item response models were estimated using a robust-weighted least squares estimator with adjustments for the mean and variance (WLSMV). A depression factor was defined on the basis of all ten items (Fig. 1). The regression of depression on trauma was included in the model.

The presence of DIF was evaluated through modification indices derived from the statistical estimation of the model. A modification index gives the expected drop in chi-square should the parameter in question be freely estimated instead of being constrained to zero. We focused on the regression between trauma and the ten items (that are fixed to zero in the initial model). Modification indices over 3.84 were considered because they correspond to the critical value for significant chi square test with one degree of freedom. If a direct relationship between trauma and one or several items was highlighted, the parameters were freely estimated in a second model. Model parameters of the effect of trauma were standardized using only the standard deviation of the dependent variable because the standard deviation of the binary trauma variable is not meaningful (Muthén and Muthén, 2017). Those standard coefficients are to be interpreted as the change in depression in fractions of standard deviation of the depression when trauma changes from no to yes. Several indicators of model fit were used: the Root Mean Square Error of Approximation (RMSEA), the Comparison Fit Index (CFI), the Tucker–Lewis fit Index (TLI) and the Standardized root mean square residual (SRMR). RMSEA values  $\leq 0.06$ , CFI and TLI values  $\geq 0.95$  and SRMRS below 0.08 were interpreted as good fits, (Hu and Bentler, 1998). All statistical analyses were performed using the Mplus statistical package, version 8.3 and IBM SPSS, version 25.

## 3. Results

The final sample (Table 1) consisted of 262 EP patients (Mean age = 24.81; SD = 4.97), and included a majority of male (63.4 %). Among these patients, 53.4 % met diagnostic criteria for schizophrenia, 15.6 % for schizophreniform or brief psychotic disorder, 9.5 % for schizoaffective disorder, 8.4 % for bipolar disorder with psychotic features, 3.1 % for depression with psychotic features, and 9.9 % for other psychotic disorders.

The first model with abuse was estimated and showed adequate fit overall (RMSEA = 0.111, CFI = 0.954, TLI = 0.942, SRMR = 0.052). Although the value of the RMSEA was over the acceptable threshold, all other indicators of model fit indicated excellent fit. All items' loadings were significant. Abuse was associated with significant 0.319 standard deviation increase in depression measured with the MADRS (Fig. 2).

Examination of the modification indices revealed a coefficient of 5.140 (and a standardized expected parameter change of  $-0.278$ ) for the regression between abuse and the sixth item (Concentration difficulties) of the MADRS scale. This parameter was freed and the model was estimated again (Fig. 3). The model fit was adequate overall (RMSEA = 0.111, CFI = 0.954, TLI = 0.942, SRMR = 0.051).

As expected, the direct relationship between abuse and the sixth MADRS item was significant ( $\beta = -0.278, p = .041$ ). This indicated that while depression level was higher in presence of abuse, item 6 was

**Table 1**  
Demographic and baseline patients' characteristics.

	N = 262
Age in y, M (SD)	24.81 (4.97)
Sex, male, % (N)	63.4 (166)
SES, % (N)	
Low	20.2 (53)
Intermediate	43.5 (114)
High	36.3 (95)
DUP in days, median (IQR)	67.50 (416.50)
Age of onset in y, M (SD)	23.42 (5.21)
Diagnosis, % (N)	
Schizophrenia	53.4 (140)
Schizophreniform/BPE	15.6 (41)
Schizoaffectif disorder	9.5 (25)
Major depression <sup>a</sup>	3.1 (8)
Bipolar disorder <sup>a</sup>	8.4 (22)
Others	9.9 (26)
Abuse <sup>b</sup> , % (N)	34.4 (90)
Neglect <sup>c</sup> , % (N)	15.6 (41)
Diagnostic of major depression <sup>a</sup> in the abuse category, % (N)	3.3 (3)
Diagnostic of major depression <sup>a</sup> in the neglect category, % (N)	7.3 (3)
MADRS, M (SD)	15.24 (9.85)
GAF, M (SD)	27.98 (11.47)

Note. IQR: interquartile range, BPE: brief psychotic episode.

<sup>a</sup> With psychotic features.

<sup>b</sup> Abuse is defined as being exposed to at least one experience of abuse (sexual, physical and emotional) prior to age 17 years old.

<sup>c</sup> Neglect is defined as being exposed to at least one experience of neglect (physical and emotional) prior to age 17 years old.

simultaneously rated lower, compensating the expected increase due to the impact of abuse on depression (total effect of abuse via depression + the direct effect of trauma on the sixth MADRS item =  $-0.128$ ,  $p = .383$ ).

A model involving neglect instead of abuse was also estimated (RMSEA = 0.108, CFI = 0.957, TLI = 0.946, SRMR = 0.049). Neglect was not associated with a significant increase in depression ( $\beta = -0.028$ ,  $p = .881$ ). Examination of the modification indices also revealed no significant potential modification for the model.

#### 4. Discussion

To our knowledge, this is the first study investigating the impact of abuse and neglect on depression in EP using a DIF approach. Although results showed that abuse was associated with increased levels of the depressive dimension at the beginning of the programme, this was not the case for neglect. Concerning specific symptoms within the depressive

dimension, concentration difficulties were left largely unaffected by abuse while all other aspect of depression were impacted.

Depression, even at a sub diagnostic (subthreshold) level, is a key component of psychosis; is crucial to the evolution of a psychotic episode (Krabbendam and van Os, 2005), and is associated with poorer outcomes (Ramain et al., 2022). Particularly, patients with psychosis and exposure to experiences of abuse tend to have more severe depression levels (Alameda et al., 2021) and these depression levels appear to mediate around a third of the association between abuse and positive symptoms of psychosis (Alameda et al., 2022; van Os et al., 2022). Patients exposed to abuse and with sub-diagnostic depressive levels also tend to have poorer functional outcomes (Alameda et al., 2017). This supports the hypothesis that depression improvement via psychological or pharmacological means may improve not only the depressive dimension itself, but also the related positive symptoms of psychosis, and even the functioning levels of patients. This hypothesis should be tested and a refined understanding of the nature of the association between abuse and the depressive domain is needed. Our study shows that only abuse, and not neglect should be considered in terms of CT experience, and the lack of link between abuse and concentration difficulties should be taken into consideration in further studies.

Our results on the lack on effect of abuse on the concentration levels could be due to the “floor effect” hypothesis (van Os et al., 2017), which is based on findings showing that the effect of CT on cognition is greater in healthy controls (with not compromised cognitive capacity), than in patients with psychosis, possible due to the influence of other factors such as genetic risk, or the co-occurrence of additional adversities during the illness on cognitive abilities of patients. This may make the independent effect of premorbid CT on cognition less visible during the disease (Christy et al., 2023; Vargas et al., 2019). On the other hand, emerging evidence is showing that the specific impact of CT is greater on social cognition rather than in neurocognition, with a review on the topic showing emerging evidence pointing at a key role of neglect on various social cognitions domains (Rodriguez et al., 2021). This is in line with a recent meta-analysis showing that is the social/interpersonal, and not the academic/vocational domain of functioning that is associated to CT (Christy et al., 2023), which had already been observed at a pre-morbid level (Alameda et al., 2015) in people with early psychosis.

From a methodological standpoint, DIF is a promising method to better understand the impact many variables may have on various psychological dimensions at the item level. This is of key relevance in psychiatry research where there is a need to refine specific targets for treatments (psychological or biological), or that can be sensitive to specific risk factors, therefore helping to understand putative mediating

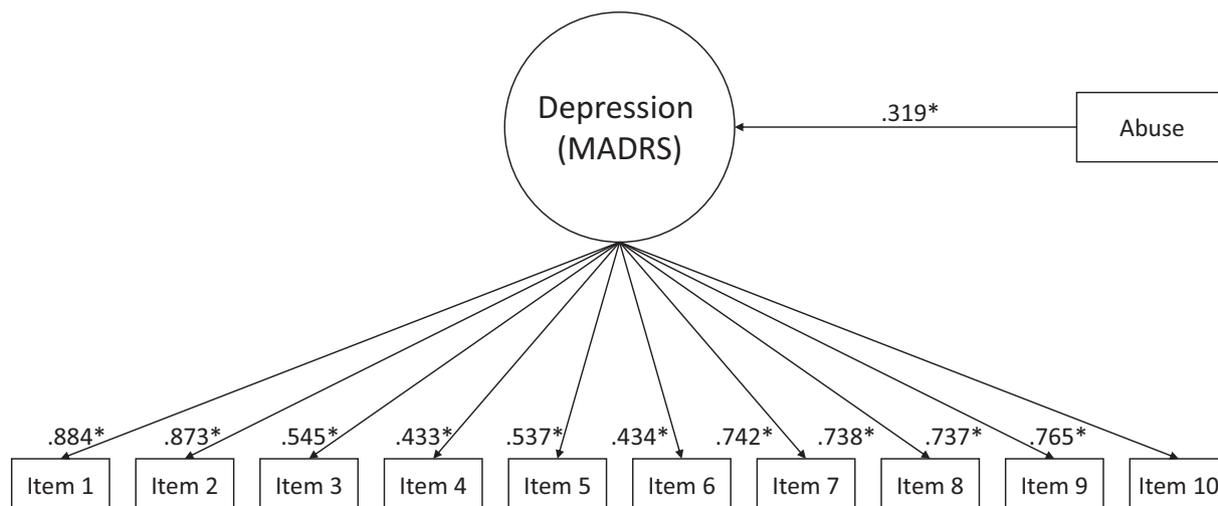


Fig. 2. Relationship between abuse and depression.

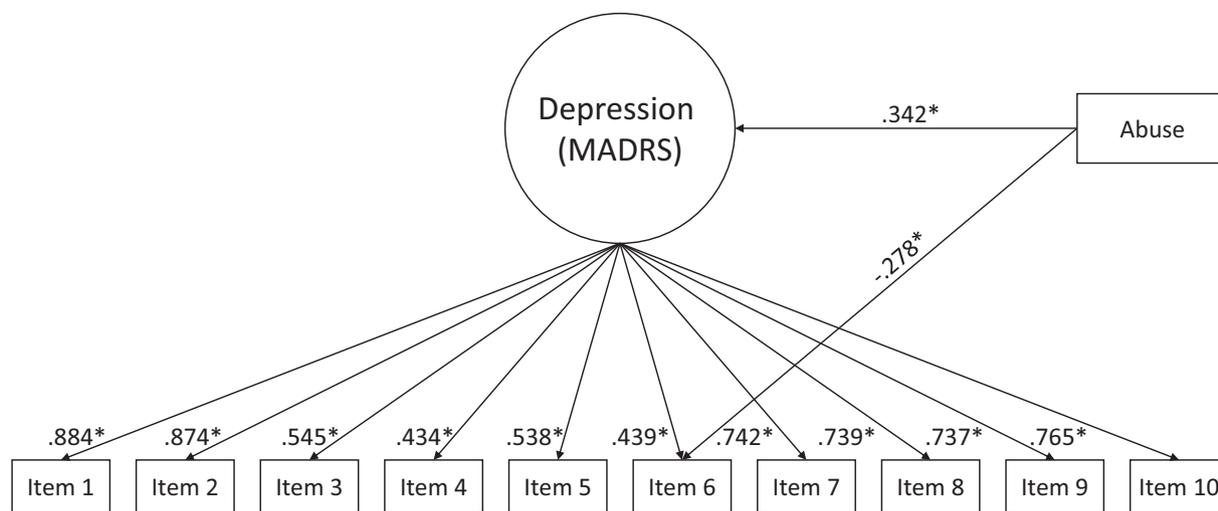


Fig. 3. Direct effect of abuse on concentration difficulties.

pathways. Usually, RCT, and research on etiological mechanisms tend to focus on the improvement or effect of a specific intervention or risk factor on a given clinical dimension, broadly measured. However, clinical dimensions are usually heterogeneous and contain various subdomains, therefore solely focusing on the overall effect on a dimension may lead to a dilution of the specific effects of some individual subdomains relevant for an intervention. As highlighted in our study, we believe that DIF can help investigating more in depth such sub-items within a dimension and reveal specific predictors or targets for treatments. DIF is better suited than approaches using simple regression of items on CT: in the latter case, the estimation of the influence of CT on items does not adequately take depression into account and largely ignores which part of variance is unique to a single item.

Regarding potential limitations, because of the naturalistic nature of the cohort, some patients of our representative clinical sample of patients could not be included because data on depression in the first six months of the programme was not available. Depression was assessed with the MADRS scale only. Similar analysis using other measures of depression should be conducted to strengthen the generalisability of our results. Likewise, the cognitive domain was assessed using a one-item rating of the MADRS rather than standardized neuropsychological tests.

In conclusion, results showed that EP patients exposed to abuse experienced greater level of depression after a recent onset of psychosis compared to those who were not exposed to such events. All aspects of depression with the notable exception of concentration difficulties were likely impacted by abuse, but not neglect. This should be accounted for when conducting clinical studies of depression treatment in traumatised individuals with psychosis. Thus, DIF is a useful tool that should be used in RCT and in psychiatry research investigating the etiological risk factor in psychosis when for a more fine grained understanding of links between clinical subdomains and specific predictors or interventions in psychiatry. We hope that the current study facilitates its use in future.

**CRedit authorship contribution statement**

PG and LA designed this study. PG analyzed and interpreted the data. PG and LA drafted the first version of the manuscript. LAE, NM, and PC critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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**Declaration of competing interest**

The authors declare no conflict of interest in relation to the subject of the study.

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