The synergetic effect of childhood trauma and recent stressful events in psychosis: associated neurocognitive dysfunction

Ayesa-Arriola R, Setién-Suero E, Marques-Feixa L, Neergaard K, Butjosa A, Vázquez-Bourgon J, Fañanás L, Crespo-Facorro B. The synergetic effect of childhood trauma and recent stressful events in psychosis: associated neurocognitive dysfunction.

**Background:** A higher incidence of childhood trauma (CT) has been reported in first episode of psychosis (FEP). There is, however, a lack of knowledge about the synergetic effect between CT and recent stressful events (RSE).

**Methods:** Information on specific types of CT (under 17 years) and RSE (within the past 3 years) was available for 290 FEP patients and 52 healthy controls (HC). Cognitive function at baseline was assessed through a comprehensive neuropsychological test battery.

**Results:** While 45.2% of FEP patients and 25% of HC reported at least one CT event, 62.7% of FEP and 21.2% of HC reported an RSE. Meanwhile, 36.2% of FEP patients and 9.6% of HC encountered both childhood and recent stressful events. The patients that just reported CT showed normality in all but the verbal memory cognitive domain; those with additive CT and RSE presented worse general cognitive function, specifically on working memory, processing speed, and executive function. RSE and general cognitive dysfunction were significant determinants of psychosis onset.

**Conclusions:** These results support a synergetic influence of trauma and stressful events on brain function and allow a better understanding of mediators for psychotic disorders useful in the design of specific strategies based on stress-targeted therapies.

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**Significant outcomes**

- The subgroup of FEP patients that reported only childhood trauma showed a cognitive performance almost within the normal limits.
- Recent stressful events and general cognitive dysfunction were significant mediators of experiencing an FEP.
- The FEP patients who reported cumulatively (both childhood and recent) trauma showed worse general cognitive function, specifically in working memory, processing speed, and executive function domains.

**Limitations**

- The present results may be affected by sample selection, considering recruitment was confined to FEP patients who had agreed to complete trauma assessment.
- The subjective and retrospective assessment of childhood and recent trauma may pose significant conflict in accurately evaluating trauma.
- It cannot be disregarded that a substantial proportion (27.9%) of FEP patients do not report a history of trauma or stressful events.
Introduction

Childhood trauma (CT) has been consistently linked to psychosis in adulthood (1, 2). The relationship between trauma and the development of psychotic symptoms extends to children and adolescents as young as 7 years of age (3). Individuals reporting a history of multiple adversities were more likely to be psychotic patients regardless of their genetic risk (4).

While evidence has been accumulated for the association between CT and psychosis, the role of recent stressful events (RSE), defined as occurrences that were likely to bring about readjustment-requiring changes in people’s usual activities (5), remains inconclusive (6). Up to 44% of first episode of psychosis (FEP), patients experienced an RSE prior to symptoms onset (7). However, under the so-called ‘dose-response’ relationship, which suggest that with increased CT experiences, the risk for psychosis becomes greater (8), it is not clear whether the impact of adult events depends on cumulative effects of adversities. Existing literature confirms that cumulative life adversity is especially important for long-term health risks (9). Nevertheless, as stated by Mayo et al. (10), no study has formally tested the possibility of an interaction between CT and RSE in psychosis onset. The majority of studies have tended to consider each exposure separately. Among the limited attempts to explore mediation between CT and adult adversity, Morgan et al. (11) found that exposure to childhood and adult disadvantage may combine in the pathway to psychosis, suggesting that these two types of adversities act synergistically.

Neuropsychology offers a reasonable proxy measure to examine the potential relationship between trauma and brain dysfunction. Etkin et al. (12) suggested that the pathway from stressful events to psychosis may be mediated through poor cognitive function and interactions between key brain networks. Yet, studies integrating effects of CT on cognitive functioning comparing FEP patients and healthy population are scarce (13). To the best of our knowledge, no study has examined the possibility of an interaction between CT and RSE, under the hypothesis of cumulative effects, associated with the severity of cognitive dysfunction.

The objective of this study was to clarify the influence of cumulative trauma on experiencing a FEP. Two hypotheses on the nature of this influence were tested: (i) CT and RSE experiences are more prevalent in FEP patients than in healthy controls; and (ii) CT and RSE interacts synergistically, mediated through cognitive dysfunction.

Methods

This investigation was designed as an observational retrospective study. Data were obtained from February 2001 to February 2017 in a cohort of patients representative of individuals suffering from a FEP, defined as first contact for schizophrenia or related syndromes (according to the ICD-10) with any public mental health service of a catchment area, which is the autonomous community of Cantabria, located in the Northern coast of Spain (14). FEP patients were treated in an intervention program (Programa de Atención a Fases Iniciales de Psicosis, PAFIP) conducted at the University Hospital Marqués de Valdecilla (15–17). In accordance with international standards for research ethics, this program, which is fully funded through public funds by the regional Mental Health Services, was approved by the local institutional review board (Ethics Committee of Cantabria, CEIC-C; Internal Code: 2014.245).

Subjects

The inclusion process of FEP patients was based on the following criteria: between 15 and 60 years of age; living in the catchment area; experiencing their first episode of psychosis; no prior treatment with antipsychotic medication for more than 6 weeks; and meeting criteria for schizophrenia spectrum disorders. Exclusion criteria were as follows: drug or alcohol dependence; intellectual disability; and/or having a history of neurological disease or head injury. Diagnoses were made by an experienced psychiatrist (BC-F) using the Structured Clinical Interview for DSM-IV (SCID-I) 6 months after the baseline visit.

A group of healthy controls (HC) was recruited that were of similar sociodemographic characteristics, with no current or past history of psychiatric, neurological, or general medical illnesses as determined by using an abbreviated version of the Comprehensive Assessment of Symptoms and History (CASH).

Subjects meeting inclusion criteria provided written informed consent.

Measures

Trauma assessment. The traumatic events were assessed using the Childhood Traumatic Events Scale (CTES) and the Recent Traumatic Events Scale (RTES) from Pennebaker, J.W. & Susman, J.R. (18). CTES is a brief survey of six types of trauma experienced before the age of 17 (death of close friend or family member; parents’ divorce;
psychological assessments, which occurred for psychologists (RA-A and ES-S) carried out the neuropsychological assessments, which occurred for the last 3 years traumatic events. Both forms assess the degree of trauma using a seven-point scale (where 1 = not at all traumatic; 4 = somewhat traumatic; and 7 = extremely traumatic). To operationalize the degree of severity of trauma, childhood traumatic (CT) and recent stressful events (RSE) were defined as scores >4 on any CTES and RTES domain. In order to derive total scores, CTES and RTES items were summed, with values ranging from 0 to 42 and from 0 to 49 respectively. The terms ‘poly-trauma’ and ‘poly-stressful events’ were used in those cases when more than one of the experiences included in CTES, and the RTES were respectively reported.

Premorbid, sociodemographic, and clinical information. Patients and their relatives were screened for the following sociodemographic characteristics: sex, age, age at illness onset, years of education, first degree family history of psychosis (‘yes’ vs. ‘no’, based on the subject and family reports), living area (‘urban’ vs. ‘rural’, defined as more or less than 10 000 inhabitants respectively), previous work (‘yes’ vs. ‘no’), hospitalization at intake (‘yes’ vs. ‘no’), and cannabis use (‘yes’ vs. ‘no’). Duration of untreated illness (DUI, defined as the time in months from the first unspecific symptom related to psychosis to initiation of adequate antipsychotic drug treatment) and duration of untreated psychosis (DUP, defined as the time in months from the first continuous psychotic symptom to initiation of adequate antipsychotic drug treatment) were estimated. Premorbid social adjustment and global functioning were measured by the Premorbid Adjustment Scale (PAS) (19) and Disability Assessment Scale (DAS) (20) respectively.

Scale for the Assessment of Negative Symptoms (SANS)(21) and the Scale for the Assessment of Positive Symptoms (SAPS) (22) were used to assess clinical symptoms of psychosis. SANS-SAPS dimensions of positive (hallucinations and delusions), negative (scores for alogia, affective fattening, apathy, and anhedonia), and disorganized (formal thought disorder, bizarre behavior, and inappropriate affect) symptoms were calculated (23). Depressive symptoms were assessed with the Calgary Depression Scale for Schizophrenia (CDSS) (24). Diagnosis (‘schizophrenia’ vs. ‘others’) and antipsychotic treatment (as mean chlorpromazine equivalent dosage (25)) were also considered in the present study.

Neuropsychological assessment. Trained neuropsychologists (RA-A and ES-S) carried out the neuropsychological assessments, which occurred for both out-patients and in-patients at clinical stabilization, and in the later cases at discharge from the acute treatment unit, which resulted in an average of 10.5 weeks after treatment initiation. A detailed description has been reported elsewhere (26). Premorbid IQ was estimated using the WAIS-III vocabulary subtest (27). The following cognitive domains, which have consistently been shown to be impaired in schizophrenia (28), were tested: 1- Verbal memory: the Rey Auditory Verbal Learning Test (RAVLT) (29) (list recall score); 2- Visual memory: Rey Complex Figure (RCF) (30) (delayed recall); 3- Working memory: WAIS-III digits forward and backward subtests (31) (standard total score); 4- Executive function: Trail Making Test (TMT) (32) (trail B-A score); 5- Processing speed: WAIS-III digit symbol subtest (27) (standard total score); 6- Motor dexterity: Grooved Pegboard Test (33) (time to complete with dominant hand); and 7- Attention: Continuous Performance Test (CPT) (34) (correct responses). Based on z scores (derived from the healthy comparison sample) of these seven domains, an index of General Cognitive Functioning (GCF) was calculated. A detailed description has been reported elsewhere (35).

Statistical analysis

The Statistical Package for Social Science, version 19.0 (SPSS Inc., Chicago, IL, USA), was used for the analyses. First, t-test and chi-square test analyses (for continuous and categorical variables respectively) were used to compare the frequency of CT and RSE and the general characteristics between FEP patients and HC. Descriptive data were presented according to mean ± standard deviation, or to percentages, as appropriate. Second, ANOVAs were used for detailed analyses on the combinations of CT and RSE (i.e., CT no RSE, CT+RSE, RSE no CT, and neither CT nor RSE) on premorbid, clinical, and neurocognitive variables. Post hoc comparisons were Bonferroni corrected. Third, significant variables (P < 0.05) in the primary analyses were entered into a logistic regression analysis that examined (via Nagelkerke’s R²) the proportion of explained variation of a model to explain the onset of psychosis, based on the trauma exposure hypothesis. All the analyses were two-tailed with a significance level set at 5%.

Results

Descriptive analyses

Of the 380 FEP patients eligible for inclusion, 290 patients (those available and agreed to provide...
trauma information) were included in the present study. Exclusively, differences on education \( (P = 0.036) \) were observed between those who completed trauma scales and those who not, showing lower level of education this latter group. In addition, 52 HC completed trauma scales information.

Per group, 131 FEP (45.2%) and 13 HC (25%) reported experiencing a significant traumatic event prior to the age of 17. Concerning recent traumatic events, 182 FEP (63%) and 11 HC (21.2%) reported experiencing a significant stressful event within the last 3 years. In general, 182 FEP (62.7%) and 11 HC (21.2%) reported experiencing at least one recent stressful event; 85 FEP (29.3%) and 4 HC (7.7) recently experienced poly-stressful events. Estimated premorbid IQ and general cognitive function were significantly lower in the FEP patients. As expected, FEP patients presented a more frequent family history of psychosis (26.4%) (see Table 1).

Table 1. Comparison of FEP patients and HC on childhood trauma and recent traumatic events

|                      | FEP Mean (SD) | HC Mean (SD) | Statistic  | P     |
|----------------------|---------------|--------------|------------|-------|
| Age (years)          | 30.46 (9.65)  | 28.25 (7.83) | t = 1.8    | 0.07  |
| Sex (female)         | 45.90%        | 44.20%       |            |       |
| Education (years)    | 10.69 (3.33)  | 10.69 (2.32) | t = 0.01   | 0.99  |
| Family history (yes) | 26.40%        | 0%           |            |       |
| Urbanicity (yes)     | 68.40%        | 69.20%       |            |       |
| Cannabis (yes)       | 37.90%        | 30.80%       |            |       |
| Estimated IQ         | 96.47 (12.61) | 100.96 (11.8)|            |       |
| General cognitive function | 1.29 (0.89) | 0.45 (0.49) | t = 16.34 | <0.001|

| Childhood trauma     |                |              |            |       |
|----------------------|----------------|--------------|------------|-------|
| Dead trauma          | 18.60%         | 6%           |            |       |
| Divorce trauma       | 14.50%         | 3.80%        |            |       |
| Sick/accident trauma | 6.90%          | 0%           |            |       |
| Sexual trauma        | 4.50%          | 1.90%        |            |       |
| Physical trauma      | 5.20%          | 0%           |            |       |
| Other trauma         | 22.10%         | 17.30%       |            |       |
| Any trauma           | 45.20%         | 25%          |            |       |
| Poly-trauma          | 19%            | 9.60%        |            |       |
| Total childhood trauma | 6.36 (6.74) | 3.08 (4.33) | t = 7.94   | <0.001|
| Recent stressful events |            |              |            |       |
| Dead                 | 19.70%         | 5.80%        |            |       |
| Divorce              | 20.40%         | 7.70%        |            |       |
| Sick/accident        | 7.60%          | 0%           |            |       |
| Sexual abuse         | 1.40%          | 0%           |            |       |
| Physical abuse       | 2.80%          | 0%           |            |       |
| Work                 | 23.90%         | 3.80%        |            |       |
| Other                | 37.40%         | 13.50%       |            |       |
| Any stressful event  | 63%            | 21.20%       |            |       |
| Poly-stressful events| 29.40%         | 7.70%        |            |       |
| Total recent stressful events | 9.16 (7.69) | 3.35 (4.88) | t = 7.17   | 0.001 |

In the attempt to explore the effect of cumulative trauma, FEP patients and HC were classified as: (i) those who presented at least one CT and no RSE (CT no RSE: 9% FEP vs. 15.4% HC); (ii) those who presented at least one CT and one RSE (CT + RSE: 36.2% FEP vs. 9.6% HC); (iii) those who did not present a CT but presented at least one RSE (RSE no CT: 26.9% FEP vs. 11.5% HC); and (iv) those who reported no traumatic events (neither RSE nor CT: 27.9% FEP vs. 63.5% HC). Slight differences were found among the four subgroups of patients: (i) in the CT no RSE group, there was a higher prevalence of women when compared with the neither CT nor RSE group; (ii) the CT+RSE group showed a higher prevalence of family history of psychosis, a higher rate of hospitalization, and more severe depressive symptoms when they were compared to the neither CT nor RSE group (see Table 2).

As observed in Table 3, z scores on working memory, processing speed, executive function, and the global measure cognitive function, controlled by age, sex, and years of education, emerged as the cognitive measures revealing significant differences among groups. Specifically, those in the CT no RSE group showed normality in all but the verbal memory domain (−1.9 SD); those in the neither CT nor RSE group showed mild deficits in attention (−1.5 SD) and moderate deficits in verbal memory (−2 SD); those who reported RSE showed moderate deficits on verbal memory and attention (−2.2 SD), similar to those with a history of CT + RSE, while also showing these mild deficits on processing speed (−1.4 SD) and executive function (−1.3 SD) (see Fig. 1).

Exploratory model of trauma on the onset of psychosis

Taking into consideration the significant variables, which emerged from our primary analyses, CT, RSE, family history of psychosis, and global cognitive function were entered into a regression model. The best fitted model \((\chi^2(4) = 91.74; P < 0.001; R^2 = 0.47)\) explained psychosis onset with 87.94% of accuracy and correctly classified 95.76% of FEP patients and 47.83% of HC. Total RSE (OR = 1.13; 95% CI 1.05–1.23; \(P = 0.002\)) and general cognitive function (OR = 8.25; 95% CI 3.67–18.54; \(P < 0.001\)) emerged as significant contributors to psychosis onset (see Table 4).

**Discussion**

The present study aimed to clarify the impact of cumulative trauma on experiencing an FEP. The observation that 45% of FEP patients report a CT (under 17 years) and recent traumatic events (within the past 3 years) in contrast to 25% of a
The synergetic effect of trauma in psychosis

Table 2. Comparison of trauma groups on clinical, neuropsychological, premorbid, and sociodemographic variables

|                                           | CT (n = 26) | CT+RSE (n = 106) | RSE (n = 78) | None (n = 81) | Statistic  | P     |
|-------------------------------------------|-------------|------------------|-------------|--------------|------------|-------|
| Sex (female)                              | 50.00%      | 49.50%           | 46.20%      | 39.50%       | $\chi^2 = 2.07$ | 0.559† | CT > None; P = 0.037 |
| Age (years)                               | 29.19 (7.91) | 30.11 (9.42)     | 31.76 (9.53) | 29.2 (9.71)  | $F = 1.33$ | 0.266 |
| Age at illness onset (years)              | 28.66 (8.5)  | 29.06 (9.33)     | 30.89 (8.88) | 28.61 (10.07) | $F = 0.91$ | 0.438 |
| Years of education                       | 9.00 (2.9)   | 10.45 (3.22)     | 10.89 (3.51) | 11.06 (3.43) | $F = 1.1$  | 0.349 |
| Premorbid adjustment                      | 1.59 (1.75)  | 1.93 (2.35)      | 1.79 (2.17)  | 1.86 (1.97)  | $F = 0.17$ | 0.915 |
| Global functioning                        | 1.56 (1.32)  | 1.51 (1.57)      | 1.52 (1.63)  | 1.26 (1.45)  | $F = 0.51$ | 0.674 |
| Duration of untreated illness (months)    | 20.16 (22.84)| 17.89 (23.79)    | 18.48 (23.02)| 19.96 (23.58)| $F = 0.12$ | 0.945 |
| Duration of untreated psychosis (months)  | 8.3 (15.29)  | 8.54 (14.28)     | 9.37 (16.39) | 9.87 (14.86) | $F = 0.14$ | 0.995 |

Symptoms

- Positive dimension
- Disorganized dimension
- Negative dimension
- Depression
- Diagnosis (schizophrenia)
- Antipsychotic (equivalemt)
- Family history of psychosis (yes)
- Urbanicity (yes)
- Previous work (yes)
- Hospitalization at intake (yes)
- Cannabis (yes)

Table 3. Comparison of trauma groups on neuropsychological function ($z$ Scores)

|                          | CT (n = 27) | CT + RE (n = 103) | RE (n = 77) | None (n = 81) | Statistic  | P     |
|--------------------------|-------------|------------------|-------------|--------------|------------|-------|
| Verbal memory            | −1.89       | −2.19            | −2.18       | −2.03        | $F = 0.351$ | 0.788 |
| Visual memory            | −0.52       | −0.54            | −0.49       | −0.37        | $F = 0.149$ | 0.93  |
| Working memory           | −0.17       | −0.66            | −0.39       | −0.24        | $F = 4.34$  | 0.005† |
| Processing speed         | −0.72       | −1.39            | −1.16       | −1.05        | $F = 3.53$  | 0.015‡ |
| Executive function       | −0.48       | −1.26            | −0.77       | −0.6         | $F = 2.71$  | 0.045§ |
| Attention                | −0.54       | −2.18            | −2.21       | −1.47        | $F = 2.24$  | 0.084 |
| Motor dexterity          | −0.25       | −1.09            | −1          | −0.79        | $F = 0.903$ | 0.44  |
| General cognitive function| 0.81        | 1.39             | 1.15        | 1.01         | $F = 3.96$  | 0.009* |

ANOVA with age, sex, and years of education as covariates, and Bonferroni adjusted.

- CT > CT + RE; P = 0.039; CT + RE < None; P = 0.013.
- CT + RE > None; P = 0.024.
- CT > CT + RE; P = 0.09.
- CT < CT + RE; P = 0.018; CT + RE > None; P = 0.076.

healthy group supports the hypothesis of a synergetic effect of trauma on the onset of psychotic symptoms. Several studies found that transitions to psychosis were associated with at least some exposure to environmental risks. For instance, those who had experienced psychosis were 2.72 times more likely to have experienced childhood adversities than HC (36). It has been suggested that those individuals with more childhood adversities may represent a vulnerable subgroup who need more assistance to increase and maintain supportive networks (37). Interestingly, in our study, the frequency of exposure to only CT was lower in FEP patients than in HC, with no differences for multiple CT events. Furthermore, the subgroup of FEP patients that reported only CT showed a cognitive performance almost within the normal limits. These results do not support the possibility that CT in itself would be related to brain abnormalities.

It has been previously suggested that having experienced one adverse childhood experience puts a person at increased risk for more adverse events and that the number of adverse experiences appears to have a ‘dose-response’ relationship later in life (38). Mayo et al. (10) found that the experience of trauma can be pervasive and persistent, under the so-called trauma–psychosis cycle. Arsenault et al. (39) found that 12-year-old children with psychotic symptoms were more likely to have
experienced maltreatment by an adult (OR 3.16), bullying (OR 2.47), or to have had an accident (OR 1.47). A possible explanation is that early adversity may impact on later expression of psychosis either by increasing exposure to later adversity and/or by rendering individuals more sensitive to later adversity if it is severe (40). The cumulative effects of several adversities on the risk of psychosis were specifically explored by Trauelsen et al. (41). They found that the risk of psychosis increased two and a half times for each additional adversity.

The onset of an FEP appears to incorporate several risk factors, both genetic and environmental, with recent stressful events working synergistically with former traumas to result in the onset of psychosis (42). This is consistent with the well-known stress-vulnerability model of schizophrenia (43) that assumes that depending on the stress and the threshold for tolerating it (i.e., one’s vulnerability), some events would lead to an episode of disorder. The reason behind sensitization to stress following CT may be one route whereby genetic vulnerability plays out in a susceptibility to psychosis following recent adverse events, via changes in the hypothalamic-pituitary-adrenal (HPA) axis (44).

Experimental studies indeed suggest that basal as well as stress-induced changes in HPA axis responding lead to brain alterations. Roelofs and Pasman (45) proposed a neurobiological stress model integrating cognitive models with neuroendocrine stress research, in which stress and stress-induced changes in HPA axis function may result in cognitive alterations that in turn contribute to experiencing conversion symptoms.

Stressful life events could be a cause, but also a consequence, of psychosis. The March-Llanes (46) meta-analysis remarked that special attention should be given to the usage of stressful life events and gene–environment interactions. We suggest that CT experiences increase vulnerability to future traumatic experiences and that RSEs increase the risk for developing psychosis. Taken together, this would support the cumulative influence of trauma and stressful events on brain function. Furthermore, our results support what Morgan et al. (11) referred to as the synergetic effects of both trauma exposures in that the combined impact of childhood and adulthood traumatic events are above what would be expected from each one alone. The main findings that support this synergetic effect between CT

![Fig. 1. Comparison of trauma groups on cognitive domains.](wileyonlinelibrary.com)
and RSE were neurocognitive deficits observed in this subgroup of FEP patients.

In the present study, the subgroup of FEP patients who reported both CT and RSE showed worse general cognitive function, specifically in working memory, processing speed, and executive function domains. These results support the contention of a synergetic influence of trauma on brain function. A majority of studies reported that patients who experienced CT displayed deficits in general cognitive ability, memory function, and executive function compared to patients without such a history (13, 47). In a previous study, history of CT was associated with worse cognitive performances, predominantly in affective psychoses and in male patients (48). However, we found that the FEP subgroup of only CT showed a cognitive performance almost within the normal limits. Therefore, we propose that more than CT, it is cumulative trauma (CT+RSE) that appears to explain the relationship between trauma and poor cognitive function in psychosis. Indeed, it could be said that a certain level of CT enhances cognitive function. It has been shown that certain levels of stress facilitate attention and conflict processing associated with improved perception of environmental changes irrespective of valence; yet, this may come a cost to certain functions such as working memory, revealing the differences between adaptive and maladaptive anxiety (49).

The specific impact of stress and emotional trauma on the brain is a complex process dependent on many variables, but particularly age at trauma exposure (50). Schalinski et al. (51) reported that there is not only a dose–response relationship between adversity and symptomatology, but that the age at which an adverse event occurs is crucial. A possible consequence of trauma may be neurotoxic effects on brain development, resulting in cognitive dysfunction and psychotic symptoms risk (52). The subgroup that showed the synergetic effect of trauma (CT + RSE), presented a higher instance of a family history of psychosis, more severe depressive symptoms, and required hospitalization at intake. Everything seems to indicate that individuals that conform to the subgroup representing combined trauma (CT + RSE) were particularly disadvantaged a long time before illness onset. Concerning depression, Aguilera et al. (53) reported that childhood adversity per se predicted higher levels of adult depressive symptoms, and in cases of trauma and psychosis, patients with more depressive symptoms showed higher levels of perceived stress (54), which, based on our results, would explain their worst performance on the neuropsychological assessment. Alameda et al. (55) confirmed the mediating role of depression on the link between early adversity and outcomes in patients suffering from psychosis, suggesting that even mild depressive symptoms might be treated in patients exposed to trauma, particularly in those exposed prior the age of 12. However, although cognitive deficits are stronger in traumatized patients, similar patterns have been observed in patients who do not report a history of traumatic events. In sum, whereas CT and RSE may play an important role in many cases, it cannot be disregarded that a substantial proportion of FEP patients do not report a history of trauma or stressful events.

Strengths and limitations

Research on the effects of RSE on psychosis is scarce (56), and to the best of our knowledge, this is the first to integrate CT, RSE, and cognitive function in a large sample of FEP patients. There are, however, several limitations to this study. First, the disproportion between FEP patients (N = 290) and HC (N = 52) samples should be noted and explained. Despite the PAFIP study having started in 2001, the inclusion of trauma assessment dated from 2011, and only the patients included from that date onwards, and those patients and HC who were contacted for longitudinal studies completed trauma scales. While awaiting for further assessment, we considered the current sample small but very valuable for the purpose of the study. Second, the present results may be affected by sample selection, considering recruitment was confined to FEP patients who had agreed to complete trauma assessment. Thus, our sample might have been biased by either being very collaborative or complaintive. As mentioned by Gianfrancesco et al. (57), among the most frequently reported traumatic experiences were involuntary hospitalization (reported by 62%), being placed in physical restraints (40%), and being forcibly medicated (37%), which are circumstances mentioned by our patients. Similarly, we noted that the subjective and retrospective assessment of CT and RSE may pose significant conflict in accurately evaluating trauma, particularly in the patient group. Despite different measures being used to assess trauma across studies, there is a clear signal that early trauma is prevalent among FEP patients (1). However, it may be useful to find a measure of overall trauma burden (41). This study allows to stress the importance of screening for trauma exposure among individuals seeking treatment for psychotic symptoms and the use of a standard protocol for CT and RSE assessment.
during all initial FEP patient evaluations. Future work should focus on replicating this model in independent samples (i.e., patients’ siblings) and incorporating biological measures that are predictive of conversion to psychosis.

Conclusions

This paper provides a model that explains the relationship between synergetic trauma exposure and psychosis onset. Global cognitive dysfunction together with recent stressful events exposure was found to be the strongest mediators to an FEP. These results need replication, but underline the necessity of investigating biological and psychosocial mechanisms underlying subjects’ sensitivity to the negative effects of cumulative stressful and traumatic events. Preventive interventions aimed at promoting resiliency, and dealing with the accumulation of psychosocial stress may prove valuable in preventing the occurrence of psychosis.

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Disclosure statement

The authors have no conflict of interest to declare.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, RAA.

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The synergetic effect of trauma in psychosis

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