

## Psychotic-like experiences associated with ICD-11 PTSD and cPTSD in a cohort of Italian late adolescents

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**Summary. Introduction.** Post-traumatic stress disorder (PTSD) and complex PTSD (cPTSD) are two sibling stress-related disorders. Evidence suggests a worse clinical picture associated with cPTSD in terms of comorbidities and outcomes. However, little is known about the association between cPTSD and psychotic-like experiences (PLEs). In this study, we aim to explore differences in PLEs in a sample of 1010 late adolescents with PTSD and cPTSD symptoms. **Methods.** A sample of 1010 late-adolescents and young adults attending the last year of high school was selected. PLEs were assessed using the 16-items Prodromal Questionnaire (PQ-16), PTSD and cPTSD were assessed using the International Trauma Questionnaire (ITQ). **Results.** 999 (501 males, 50.15% and 498 females, 49.85%) subjects had complete data on the selected variables. Of these, 91 (9.11%) and 40 (4.00%) screened positive for PTSD and cPTSD, respectively. Mean number of PLEs endorsed in subjects with PTSD, cPTSD and control groups were 7.02 (sd=2.99), 8.17 (sd=3.70) and 4.49 (sd=2.93), respectively. Mean PQ-16 distress score was 5.08 (sd=4.6) in subjects not endorsing PTSD/cPTSD, 10.11 (sd=6.17) in PTSD and 14.51 (sd=9.1) in cPTSD subjects. A linear regression analysis revealed a significant association between PTSD/cPTSD and PLEs scores (respectively,  $b=4.91$  [3.73, 6.10] and  $b=10.05$  [8.40, 11.70]). Such associations were reduced after adjustment for depression, anxiety and dissociation. **Discussion and conclusions.** Our results find higher rates of PLEs in late adolescents screening positive for cPTSD and PTSD compared to negative subjects. Furthermore, cPTSD could be more specifically associated with distressing PLEs. These findings add to the vast literature of a worse psychopathological picture associated with cPTSD compared to PTSD, emphasizing the need for a separation between PTSD and cPTSD in terms of diagnosis and possibly treatment.

**Key words.** cPTSD, ICD-11, late adolescents, psychotic-like experiences, PTSD.

*Esperienze simil-psicotiche associate alla diagnosi ICD-11 di PTSD e PTSD complesso in un campione di giovani adulti.*

**Riassunto. Scopo.** Il disturbo post-traumatico da stress complesso (cPTSD) è un disturbo correlato allo stress, recentemente incluso nell'undicesima edizione della Classificazione Internazionale delle Malattie (ICD-11). Numerose evidenze cliniche e di ricerca suggeriscono un quadro clinico più grave associato al cPTSD in termini di comorbidità e di esiti rispetto al disturbo da stress post-traumatico (PTSD). Tuttavia, la possibile associazione tra cPTSD ed esperienze simil-psicotiche (PLE) è stata scarsamente indagata. In questo studio, ci proponiamo di esplorare le differenze nelle PLE in un campione di giovani adulti con sintomi di PTSD e cPTSD. **Metodi.** Lo studio ha previsto il reclutamento di un campione di 1010 studenti maggiori di Istituti Superiori. La presenza di PLE è stata valutata con il Prodromal Questionnaire a 16 item (PQ-16), mentre la sintomatologia PTSD e cPTSD è stata valutata utilizzando l'International Trauma Questionnaire (ITQ). **Risultati.** 999 (501 maschi, 50,15% e 498 femmine, 49,85%) soggetti hanno riportato dati completi per le variabili selezionate. Di questi, 91 (9,11%) e 40 (4,00%) sono risultati positivi al PTSD e al cPTSD, rispettivamente. Il numero medio di PLE riportate nei soggetti con PTSD, cPTSD e nel gruppo di controllo era, rispettivamente, 7,02 (sd=2,99), 8,17 (sd=3,70) e 4,49 (sd=2,93). Per quanto riguarda il distress associato, il punteggio medio PQ-16 era di 5,08 (sd=4,6) nei soggetti di controllo, di 10,11 (sd=6,17) nei soggetti con PTSD e di 14,51 (sd=9,1) nei soggetti con cPTSD. L'analisi di regressione lineare ha rivelato un'associazione significativa tra i punteggi PTSD/cPTSD e PLE (rispettivamente,  $b=4,91$  [3,73, 6,10] e  $b=10,05$  [8,40, 11,70]). **Discussione e conclusioni.** I risultati evidenziano tassi più elevati di PLEs negli individui con sintomi di cPTSD e PTSD rispetto ai soggetti di controllo. Inoltre, il cPTSD sembra essere associato in modo più specifico a PLE con elevato distress. Questi risultati suggeriscono la necessità di una separazione tra PTSD e cPTSD in termini di diagnosi e di trattamento.

**Parole chiave.** cPTSD, esperienze simil-psicotiche, ICD-11, PTSD.

### Introduction

Complex Post-traumatic stress disorder (cPTSD) is a stress-related disorder recently included in the

11th edition of the International Classification of Diseases in 2019<sup>1,2</sup>, aimed at capturing the pervasive psychological dysfunctions deriving from exposure to prolonged interpersonal traumatic experiences (TEs), mostly occurring during childhood and deve-

lopment, including repeated physical, psychological or sexual abuse, and neglect.

Clinical features of cPTSD include core PTSD symptom triad, i.e. re-experiencing (RE), avoidance (AV) and sense-of-threat (TH), in addition to three clusters of symptoms termed “Disturbance of Self-Organization” (DSO), which include affective dysregulation (AD), disturbances in relationships (DR) and negative self-concept (NSC)<sup>3,4</sup>.

cPTSD could be associated with the psychotic continuum for at least two reasons: firstly, prolonged interpersonal TEs associated with cPTSD are also associated with psychosis<sup>5-7</sup>. Secondly, the clinical dimensions composing DSO have been suggested as potential mediators of the effect of TEs on psychotic symptoms, including psychotic-like experiences (PLEs)<sup>8-10</sup>.

Evidence regarding a potential association between cPTSD and psychosis is still scarce. A recent work found that 40% of people already suffering from a psychotic disorder endorse cPTSD symptoms, compared to 10% of PTSD<sup>11</sup>. In a community sample, PLEs and cPTSD were found to be moderately correlated<sup>6</sup>. In a latent class analysis on 1051 subjects from the general population, cPTSD and PLEs were co-occurring in 3.6% of the sample<sup>12</sup>.

Given the evidence suggesting a link between psychosis and cPTSD, we sought to explore the link between PLEs, PTSD and cPTSD in a community sample of late adolescents. PLEs are an established risk factor for subsequent transition to full-blown psychotic disorder<sup>13</sup>. Exploring the association between cPTSD and PLEs could help inform better preventive strategies aimed to reduce the rate of transition to full-blown psychotic disorders.

Our hypothesis is that subjects endorsing cPTSD would display a higher number of PLEs and more psychological distress associated with PLEs. Because PLEs could also be associated with general psychopathology, we will explore the role of such variables, including anxiety, depression and dissociation, as potential confounders.

## Methods

### PARTICIPANTS

Participants were enrolled in the context of a cross-sectional cohort study at the University of L'Aquila that focused on a sample of 1010 late-adolescents and young adults attending the last year of high school in the province of L'Aquila, during the academic year 2019-2020. Inclusion criteria were attending the last year of high school and being >18 years old. Exclusion criteria included being on supported teaching as a proxy of mild to severe cognitive impairment. Details on clustered sampling have already been provided elsewhere<sup>14</sup>.

The local ethics committee at the University of L'Aquila approved the study. This study adheres to the declaration of Helsinki. Written informed consent was obtained from all participants before the study.

Recruitment and data collection took place between November 2019 and January 2020. A total of 1010 subjects participated in the study, 485 (48.02%) attending Lycei, 318 (31.46%) technical schools and 207 (20.05%) vocational schools. 11 subjects provided all incomplete data and were thus excluded from subsequent analysis. Of the 999 participants remaining, 501 (50.15%) were male, 498 (49.85%) were female, 66 (6.53%) were not Italian. Mean age was 18.7 (sd=0.65).

### MEASURES

#### *Independent variables: PTSD and cPTSD*

Presence of PTSD and cPTSD was assessed using the International Trauma Questionnaire (ITQ)<sup>14-16</sup>. The ITQ is composed of two subscales assessing PTSD and DSO of 9 items each. The PTSD subscale consists of 6 items assessing core PTSD symptoms, re-experiencing (2 items), avoidance (2 items) and sense of threat (2 items) and 3 items assessing the functional impact. The DSO subscale consists of 9 items assessing affective dysregulation (2 items), negative self-concept (2 items) and disturbances in interpersonal relationships (2 items), and 3 items for functional impact. All items are scored on a 5-point Likert scale ranging from “Not at all (0)” to “Extremely (4)”. Each item is considered endorsed for a score of  $\geq 2$  (“Moderately”). PTSD is considered endorsed if at least one item for each PTSD symptom and at least one impact item is  $\geq 2$ . cPTSD is considered endorsed if PTSD is endorsed plus at least one item for each DSO symptom and at least one impact item is  $\geq 2$ . One subject may endorse only cPTSD or PTSD, not both. In our sample, reliability was  $\alpha=0.88$  for the PTSD subscale and  $\alpha=0.88$  for the DSO subscale. The English and Italian versions of the ITQ are freely downloadable at <https://www.traumameasuresglobal.com/itq>.

#### *Dependent variable: Psychotic-Like Experiences*

PLEs including perceptual aberrations/hallucinations, unusual thought content/delusions, and two negative symptoms, were assessed using the Italian version of the Prodromal Questionnaire-16 (PQ-16)<sup>17</sup>. PQ-16 measures the presence/absence of 16 PLEs on the endorsement score (range 0-16), and their associated psychological distress on the distress score on a 0-3 Likert scale (range 0-48). Although different cut-off points have been proposed for different populations<sup>18</sup>, we chose to use the iPQ-16 endorsement and distress scores as a continuous rather than binary variables in order to avoid sensibility/specificity issues.

Potential confounders

The following variables were selected as potential confounders: gender, age, mothers' age at birth, immigrant status, family affluence. Because PLEs are associated with general psychological distress, depression, anxiety, and dissociation were selected as potential confounders:

- *Patient Health Questionnaire* (PHQ-9)<sup>19</sup>: was used to assess depressive symptoms. PHQ-9 comprises nine depressive symptoms, rated on a 4-point Likert scale (range 0-27). The total score has been taken into consideration as a continuous variable. In our sample, internal consistency was  $\alpha=0.87$ .
- *Generalized Anxiety Disorder questionnaire* (GAD-7)<sup>20</sup>: was used to assess anxiety symptoms. GAD-7 includes 7 symptoms, rated on a 4-point Likert scale, range 0-21. The total score has been taken into consideration as continuous variable. In our sample, internal consistency was  $\alpha=0.91$ .
- *Dissociative Experience Scale Taxon* (DES-T)<sup>21</sup>: is an eight items subscale of the full-scale DES. The format is the same as the full-scale DES, with each item scored on a scale from 1 to 100 and the overall score being the mean of the eight items. For the purpose of this study, the total score has been taken into consideration as a continuous variable. In our sample, internal consistency was  $\alpha=0.8$ .

STATISTICAL ANALYSIS

The endorsement rate for each PLE was estimated for subjects endorsing cPTSD and PTSD. Differences in PQ-16 endorsement and symptom scores were tested using one-way analysis of variance (ANOVA) with Tukey post-hoc test for pairwise comparison. The association between a diagnosis of PTSD or cPTSD and PLEs was assessed using a 3-blocks hierarchical linear regression analysis, with PLEs symptom score modeled as dependent variable. In block 1, PTSD/cPTSD endorsement was the only independent variable. In block 2, gender, age, mothers' age at birth, immigrant status and family affluence were added. In block 3, depression, anxiety and dissociation were introduced.

Results

According to ITQ scoring system, 91 (9.11%) and 40 (4.00%) subjects endorsed PTSD and cPTSD criteria, respectively.

Details of PLEs endorsement rates and PQ-16 symptom scores are reported in table 1. Mean number of PLEs endorsed in subjects not endorsing PTSD/ Cptsd (i.e., control group, CG), PTSD and cPTSD groups were 4.49 (sd=2.93), 7.02 (sd=2.99) and 8.17 (sd=3.70) respectively (table 2). ANOVA test revealed a significant difference in the number of PLEs endorsed

**Table 1.** Endorsement rate for each PLE among three ITQ groups.

|       | Brief item description                    | CG  |        | PTSD |        | CPTSD |        | TOTAL |        |
|-------|---|-----|--------|------|--------|-------|--------|-------|--------|
|       |   | n   | %      | n    | %      | n     | %      | n     | %      |
| PQ-01 | Loss of interest                          | 449 | 53.07% | 63   | 70.79% | 32    | 80.00% | 544   | 55.79% |
| PQ-02 | Déjà-vu                                   | 673 | 79.36% | 80   | 89.89% | 37    | 92.50% | 790   | 80.86% |
| PQ-03 | Olfactory/tast hallucinations             | 244 | 28.88% | 42   | 47.73% | 17    | 42.50% | 303   | 31.14% |
| PQ-04 | Elementary auditory hallucinations        | 159 | 18.86% | 32   | 35.96% | 15    | 37.50% | 206   | 21.19% |
| PQ-05 | Confused about things being real          | 181 | 21.45% | 32   | 36.36% | 25    | 62.50% | 238   | 24.49% |
| PQ-06 | Visual illusions about faces              | 57  | 6.75%  | 12   | 13.64% | 5     | 12.50% | 74    | 7.61%  |
| PQ-07 | Social anxiety                            | 336 | 39.62% | 46   | 52.27% | 30    | 75.00% | 412   | 42.21% |
| PQ-08 | Visual hallucinations                     | 78  | 9.23%  | 13   | 14.61% | 11    | 27.50% | 102   | 10.47% |
| PQ-09 | Audible thoughts                          | 180 | 21.28% | 35   | 39.33% | 22    | 55.00% | 237   | 24.31% |
| PQ-10 | Special meanings around me                | 225 | 26.63% | 32   | 35.96% | 15    | 38.46% | 272   | 27.95% |
| PQ-11 | Passivity (thoughts)                      | 210 | 24.76% | 48   | 53.93% | 29    | 74.36% | 287   | 29.41% |
| PQ-12 | Distractability                           | 280 | 33.06% | 43   | 48.31% | 24    | 60.00% | 347   | 35.55% |
| PQ-13 | Complex auditory hallucinations           | 112 | 13.22% | 24   | 26.97% | 7     | 17.50% | 143   | 14.65% |
| PQ-14 | Paranoid ideation                         | 299 | 35.43% | 52   | 58.43% | 33    | 82.50% | 384   | 39.47% |
| PQ-15 | Sense that some person or force is around | 168 | 19.86% | 39   | 43.82% | 11    | 27.50% | 218   | 22.36% |
| PQ-16 | Body changes                              | 170 | 20.09% | 32   | 35.96% | 14    | 35.00% | 216   | 22.15% |

**Table 2.** Total PLEs endorsement and Total PQ-16 symptom score among ITQ groups (Mean  $\pm$  SD) and ANOVA results.

|                           | CG   |      | PTSD  |      | cPTSD |      | TOTAL |      | Statistics |
|---------------------------|------|------|-------|------|-------|------|-------|------|------------|
|                           | Mean | SD   | Mean  | SD   | Mean  | SD   | Mean  | SD   |            |
| Total PLEs endorsed       | 4.49 | 2.93 | 7.02  | 2.99 | 8.17  | 3.70 | 4.87  | 3.70 | ***        |
| Total PQ-16 symptom score | 5.08 | 4.6  | 10.11 | 6.17 | 14.51 | 9.1  | 5.92  | 5.53 | ***        |

\*\*\*  $p < 0.001$ **Table 3.** Hierarchical Linear regression analysis.

|       | PQ-16 symptom score    |                       |                      |
|-------|------------------------|-----------------------|----------------------|
|       | Block-1                | Block-2 <sup>a</sup>  | Block-3 <sup>b</sup> |
| PTSD  | 4.91<br>[3.73, 6.10]   | 4.63<br>[3.44, 5.82]  | 1.45<br>[0.44, 2.46] |
| cPTSD | 10.05<br>[8.40, 11.70] | 9.63<br>[7.98, 11.28] | 3.50<br>[2.01, 4.99] |

<sup>a</sup>Adjusted for gender, age, mothers' age at birth, immigrant status, family affluence; <sup>b</sup>Adjusted for gender, age, mothers' age at birth, immigrant status, family affluence, PHQ-9, GAD-7, and DES.

sed in the three groups ( $F_{(2,979)}=54.89$ ,  $p < 0.001$ ). Tukey post-hoc tests revealed a higher endorsement rate of PLEs for PTSD and cPTSD vs CG groups (respectively  $p < 0.001$  and  $p < 0.001$ ), but not for cPTSD vs PTSD group ( $p = 0.105$ ).

Mean PQ-16 distress score was 5.08 ( $sd = 4.6$ ) in subjects not endorsing PTSD/cPTSD, 10.11 ( $sd = 6.17$ ) in PTSD and 14.51 ( $sd = 9.1$ ) in cPTSD subjects. ANOVA results indicated a significant difference in PQ-16 symptom scores among the three groups ( $F_{(2,993)}=102.33$ ,  $p < 0.001$ ). Tukey post-hoc test revealed a significant difference between CG vs PTSD group ( $p < 0.001$ ), CG vs cPTSD group ( $p < 0.001$ ) and PTSD vs cPTSD group ( $p < 0.001$ ).

Regression analysis results are reported in table 3. Regression analyses were conducted on a final sample of 900 subjects with complete data. In block 1 - unadjusted regression, PTSD and cPTSD were associated with PQ-16 symptom score, respectively  $b = 4.91$  [3.73, 6.10] and  $b = 10.05$  [8.40, 11.70]. This association was reduced in block 2 and 3, but still statistically significant (block 2 PTSD  $b = 4.63$  [3.44, 5.82] and cPTSD  $b = 9.63$  [7.98, 11.28]; block 3 PTSD  $b = 1.45$  [0.44, 2.46] and cPTSD  $b = 3.50$  [2.01, 4.99]).

## Discussion

To the authors' knowledge, this is the first study to investigate the association of PLEs and ICD-11 PTSD and cPTSD in a community sample of late adolescents in Italy.

Subjects with PTSD or cPTSD endorsed more PLEs compared to subjects without PTSD/cPTSD, but not compared to each other. The PQ-16 symptom score was 40% higher in subjects with cPTSD vs PTSD. Contrary to our initial hypothesis, subjects with PTSD did not endorse fewer PLEs than subjects endorsing cPTSD, even though a substantial difference in PLEs distress was evident.

Both PTSD and cPTSD were strongly associated with PLEs. However, while the association between PTSD and PLEs was strongly reduced after adjustment for anxiety, depression and dissociation, this was much less evident for cPTSD. These results could be summarized together with cPTSD being more specifically associated with distressing PLEs, when controlling for unspecific psychopathological factors, i.e., depression, anxiety and dissociation. These findings are of critical importance for clinical models of psychosis risk.

Well established models of psychosis risk conceptualize distressing PLEs, rather than the presence of PLEs *per sé*, as the core feature of a high-risk or prodromal state for psychosis<sup>22,23</sup>. Because cPTSD was associated with highest levels of PLEs distress, our results suggest that cPTSD could represent a more relevant risk factor for transition to psychosis compared to PTSD. Indeed, in a recent study, cPTSD was nearly four-times more prevalent than PTSD in a clinical sample of subjects with a psychotic disorder<sup>11</sup>.

Introducing cPTSD in the psychotic risk literature could also help elucidate the interplay between psychotic and post-traumatic symptoms. The association between PTSD and psychosis is well established and replicated in the literature<sup>24</sup>. This evidence has led to the proposal of a psychotic subtype of PTSD (PTSD-SP)<sup>25</sup>, which however lacks sufficient validity due to loss of significant association between PTSD and psychotic symptoms after adjusting for depressive symptoms<sup>26</sup>. The mixed evidence regarding an association between PTSD and psychotic symptoms could be partially due to the lack of separation between PTSD and cPTSD. For example, in one study, 40% of those who endorsed PTSD and psychotic symptoms, also fulfilled criteria for Enduring Personality Change After Catastrophic Experience, which is a condition closely resembling cPTSD<sup>27</sup>. In our study,

consistently with previous evidence<sup>26</sup>, adjustment for other psychopathological variables strongly reduced the association between PTSD and PLEs, while this was not the case for cPTSD. This would suggest that PLEs, rather than being generically associated with post-traumatic symptoms, could be specifically associated with cPTSD, or even represent a complication of the latter. Indeed, in a recent latent class analysis, a cPTSD+PLEs phenotype emerged, but not a PTSD+PLEs one<sup>12</sup>.

### LIMITATIONS

Firstly, this study is based on self-report measures that, particularly regarding PLEs<sup>28</sup>, are generally associated with higher prevalence than interview-based measures, although validity and reliability are mostly unchanged<sup>29</sup>.

Secondly, the cross-sectional design of our study precludes firm causal inferences. In this study PTSD/cPTSD were modelled as independent variables largely relying on previous literature reporting stress-related symptoms as mediators in the trauma-psychosis pathways; however, reverse causality could not be excluded given the cross-sectional nature of the data. Further longitudinal studies are required to establish causal relationships among these variables.

### Conclusions

PLEs were highly prevalent among late adolescents endorsing cPTSD. This study adds a relevant piece in the complex literature regarding trauma and psychosis, supporting the importance of a separation of PTSD and cPTSD to achieve a more fine-grained assessment of a potentially intermediate condition on the pathway from trauma towards full-blown psychotic disorders.

Evidence on the relationship between cPTSD and psychosis could be of pivotal clinical importance for the clinical management of at-risk mental states. In this context, specific therapy for cPTSD could be integrated into the management model and possibly reduce the rate of transition in at-risk mental states.

*Ethical standards statement:* the local ethics committee at the University of L'Aquila provided approval to the study (research number 49, 26/09/2019). This study adheres to the declaration of Helsinki.

*Data availability statement:* the datasets generated and/or analyzed during the current study are not publicly available due to privacy regulations, but they may be made available on reasonable request.

*Acknowledgments:* this study was supported by Territori Aperti, a project funded by the Fondo Territori Lavoro e Conoscenza of the Confederazione Generale Italiana del Lavoro,

the Confederazione Italiana Sindacati Lavoratori, and the Unione Italiana del Lavoro.

*Conflict of interests:* the authors have no conflict of interests to declare.

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