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▶ **To cite this version:**

Antoine Yrondi, Guillaume Vaiva, Michel Walter, Thierry D Amato, Frank Bellivier, et al.. Childhood Trauma increases suicidal behaviour in a treatment-resistant depression population: a FACE-DR report. Journal of Psychiatric Research, 2021, 135, pp.20-27. 10.1016/j.jpsychires.2020.12.055 . hal-03271134

HAL Id: hal-03271134
https://hal.umontpellier.fr/hal-03271134

Submitted on 3 Feb 2023

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Version of Record: https://www.sciencedirect.com/science/article/pii/S0022395620311638
Manuscript_e73fb2da20eb1d8cf2093358891fa341

Childhood Trauma increases suicidal behaviour in a treatment-resistant depression population: a FACE-DR report

Running title: Childhood Trauma and suicidal behaviour

Antoine Yrondi, MD, PhD [1,2], Guillaume Vaiva, MD, PhD[1,3] , Michel Walter, MD, PhD [1,4] , Thierry D'Amato MD, PhD[1,5], Frank Bellivier MD, PhD[1,6], Djamila Bennabi MD, PhD[1,7], Thierry Bougerol, MD, PhD[1,8], Vincent Camus, MD, PhD[1,9], Olivier Doumy, MD[1,10], Jean-Baptiste Genty, MD[1,11], Emmanuel Haffen, MD, PhD[1,7], Jérôme Holtzmann, MD[1,8], Mathilde Horn, MD[1,12], Christophe Lancon, MD, PhD[1,13], Marion Leboyer, MD,PhD[1,11], Pierre-Michel Llorca, MD, PhD[1,14], Julia Maruani, MD[1,5], Rémi Moirand, MD [1,5], Fanny Molière, MD[1,15], Jean Petrucci, PhD[1,11], Raphaelle Richieri, MD, PhD[1,13] Ludovic Samalin, MD, PhD[1,14], Laurent Schmitt, MD[1,2], Florian Stephan, MD[1,4], FondaMental Advanced Centers of Expertise in Resistant Depression (FACE-DR), Philippe Courtet, MD, PhD[1,15], Wissam El-Hage, MD, PhD[1,9*], Bruno Aouizerate, MD, PhD[1,10*]
*Co-last author

1. Fondation FondaMental, Creteil France

2. Service de Psychiatrie et de Psychologie Médicale de l'adulte, Centre Expert Dépression Résistante FondaMental, CHU de Toulouse, Hôpital Purpan,ToNIC Toulouse NeuroImaging Center, Université de Toulouse, INSERM, UPS, Toulouse, France

3. Centre National de Ressources et Résilience pour les psychotraumatisme, Lille, France

4. Service Hospitalo-Universitaire de Psychiatrie Générale et de Réhabilitation Psycho Sociale 29G01 et 29G02, Centre Expert Depression Résistante FondaMental, EA 7479, CHRU de Brest, Hôpital de Bohars, Brest, France.

5. INSERM U1028; CNRS UMR5292; University Lyon 1, Villeurbanne, F-69000, France; Lyon Neuroscience Research Center; Psychiatric Disorders: from Resistance to Response ΨR2 Team; Centre Hospitalier Le Vinatier; F-69678, France.

6. AP-HP, GH Saint-Louis - Lariboisière - Fernand Widal, Pôle Neurosciences Tête et Cou, INSERM UMRS 1144, University Paris Diderot, Paris, France

7. Service de Psychiatrie, Centre Expert Dépression Résistante FondaMental, CIC-1431 INSERM, CHU de Besançon, EA 481 Neurosciences, Université de Bourgogne Franche Comté, Besançon, France

8. Université Grenoble Alpes, Inserm, U1216, CHU Grenoble Alpes, Grenoble Institut Neurosciences, 38000 Grenoble, France

9. U1253, iBrain, CIC1415, Inserm, CHRU de Tours, Université de Tours, Tours, France

10. Pôle de Psychiatrie Générale et Universitaire, Centre Expert Dépression Résistante FondaMental, CH Charles Perrens, Bordeaux, Laboratoire Nutrition et Neurobiologie intégrée (UMR INRA 1286), Université de Bordeaux, France

11. Université Paris-Est, UMR_S955, UPEC, Créteil, France Inserm, U955, Equipe 15 Psychiatrie génétique, Créteil, France AP-HP, Hôpital H. Mondor-A. Chenevier, Pôle de psychiatrie, Créteil, France Fondation FondaMental, fondation de cooperation scientifique, Créteil, France

12. Service de Psychiatrie adulte, Centre Expert Dépression Résistante FondaMental, CHRU de Lille, Hôpital Fontan 1, Lille, France

13. Pôle Psychiatrie, Centre Expert Dépression Résistante FondaMental, CHU La Conception, Marseille, France

14. Department of Psychiatry, CHU Clermont-Ferrand, University of Clermont Auvergne, EA 7280, Clermont-Ferrand,, France.

15. Department of Emergency Psychiatry and Acute Care, CHU Montpellier, INSERM U1061, Montpellier University, Montpellier, France

List of FondaMental Advanced Centre of Expertise (FACE-DR) collaborators: FACE-DR Clinical Coordinating Centre (Fondation FondaMental); B. Aouizerate, D. Bennabi, M. Leboyer, E. Haffen and PM Llorca; FACE-DR Data Coordinating Centre (Fondation FondaMental): V. Barteau, S. Bensalem, H. Laouamri, and Karmene Souryis; FACE-DR Clinical Sites and Principal Collaborators in France; AP-HP, DHU PePSY, Pôle de Psychiatrie et d'Addictologie des Hôpitaux

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Universitaires H Mondor, Créteil; L.Mallet, L. Yon, J. Petrucci and JB. Genty; Service de Psychiatrie et de Psychologie Médicale de l'adulte, Centre Expert Dépression Résistante FondaMental, CHRU de Toulouse, Hôpital Purpan, Toulouse, France: A. Yrondi, D Pierre, L Schmitt and M. Sarrail; Service de Psychiatrie clinique, Centre Expert Dépression Résistante FondaMental, EA 481 Neurosciences, Université de Bourgogne Franche Comté, Besançon, France: E. Haffen, Djamila Bennabi, I. Ryff, E. Beuchet, G. Tio, C. Cappe and E. Clerc ;Service de Psychiatrie de l'adulte B, Centre Expert Dépression Résistante FondaMental, CHU de Clermont-Ferrand, Clermont-Ferrand, France: PM. Llorca, M. Garnier, RM Honciuc, E Allauze and O. Blanc ;Service de Psychiatrie adulte, Centre Expert Dépression Résistante FondaMental, Hôpital Fernand-Widal, Paris, France: F. Bellivier, N. Allaili, I. Nieto, J. Meheust, Y. Sunthavy and J. Maruani; Service de Psychiatrie de l'adulte, CS 10217, Centre Expert Dépression Résistante FondaMental, CHU de Grenoble, Hôpital Nord, Grenoble, France: T. Bougerol, M. Polosan, P. Courvoisier, J. Holtzmann, B. Fredembach and S. Foubert-Andreani;Clinique Psychiatrique Universitaire, Centre Expert Dépression Résistante FondaMental, Inserm U1253 imaging and Brain:iBrain, CHRU de Tours, Tours, France: V. Camus and W. El Hage; Service Universitaire de Psychiatrie adulte, Centre Expert Dépression Résistante FondaMental, Centre Hospitalier Le Vinatier, Bron cedex, France: T. D'Amato, F. Haesebaert, C. Dubien, M. Lefebvre, A. Meznad, J. Brunelin and R. Moirand; Pôle de Psychiatrie Générale et Universitaire, Centre Expert Dépression Résistante FondaMental, CH Charles Perrens, Bordeaux, France: B. Aouizerate and O. Doumy; Pôle Psychiatrie, Centre Expert Dépression Résistante FondaMental, CHU La Conception, Marseille, France: C. Lancon, R. Richieri, P. Peri, M. Faugere and C. Faget-Agius; Département des Urgences et Post-Urgences Psychiatriques, Centre Expert Dépression Résistante FondaMental, CHRU Lapeyronie, Montpellier, France: P. Courtet, JP. Boulenger and F. Moliere; Service de Psychiatrie de l'adulte, Centre Expert Dépression Résistante FondaMental, CHU de Brest, Hôpital de Bohars, Bohars, France: F. Stephan, M. Walter and C. Mesmeur ;Service de Psychiatrie adulte, Centre Expert Dépression Résistante FondaMental, CHRU de Lille, Hôpital Fontan 1, Lille, France: G. Vaiva, and M Horn

Corresponding author: Dr Antoine Yrondi, service de psychiatrie et psychologie médicale, CHU Toulouse Purpan, 330 avenue de Grande Bretagne 31059 Toulouse, France.
Tel.: 0033675130806
Email: antoineyrondi@gmail.com

Word count: 3134 words
1 figure, 3 tables

Abstract

Objective: In addition to heredity, exposure to early-life adversity is an important predisposing risk factor of suicidal behaviour. Although the association between Childhood Trauma (CT) and suicide risk is well documented, interactions between CT and suicidal behaviour in Treatment-Resistant Depression (TRD) populations have received little coverage. This study aimed to evaluate i) association between CT and suicidal behaviour in a TRD population, and ii) the role of personality traits and impulsiveness as potential factors of mediation in these associations.

Methods: Patients were recruited from a cohort of the French network of TRD expert centers. Depressive symptom severity, CT, suicidal behaviour, personality traits, and impulsiveness were assessed with the Montgomery-Åsberg Depression Rating Scale (MADRS), the Childhood Trauma Questionnaire (CTQ), the Columbia Suicide Severity Rating Scale (CSSRS), the Structured Clinical Interview for DSM-IV, the Big Five Inventory, and the Barratt Impulsivness Scale (BIS) respectively.

Results: Among the 256 patients with a baseline CTQ, in relation to suicide risk for the current depressive episode, we found an association with the total CTQ scores mediated by the intensity of the current episode in a model adjusted for age and sex (total effect: β=0.171; p=0.011, direct effect: β=0.135; p=0.043; indirect effect: β=0.036; p=0.048). Focusing on CT subtypes, we detected an association between suicide risk and physical neglect in a model adjusted for age and sex (β=0.301; p=0.002), without any mediation by the intensity of the current episode. There was no mediation effect from personality traits nor impulsiveness. With regards to CSSRS to assess suicidal ideation, we did not find any association with the total CTQ score and CT subtype scores.

Conclusion: We report a strong association between suicidal behaviour and CT (in particular childhood physical neglect) in a TRD population.

Keywords: Childhood Trauma; Childhood Abuse; Childhood neglect; Treatment-Resistant Depression; Suicide; Depressive Disorders.

Introduction

Over 800,000 people die of suicide worldwide each year (WHO, 2014), with non-fatal suicidal behaviour substantially outnumbering suicide deaths (Borges et al., 2010; Nock et al., 2013; Turecki & Brent, 2016). The worldwide lifetime prevalence of suicidal ideation and suicide attempts is 9.2% and 2.7%, respectively (Nock et al., 2008; Turecki & Brent, 2016). Individuals who report suicidal ideations within the last 12 months have significantly higher suicide rates achieving between 15% and 20% (Borges et al., 2010; Nock et al., 2013; Turecki & Brent, 2016). Data from emergency departments indicate that people attempting suicide have a 1.6% risk of dying by suicide within the year, and a 16% risk of attempting suicide again with a 5-year suicide risk of around 4% (Carroll et al., 2014).

Most models of suicide risk emphasise the interaction between predisposing and precipitating factors (Turecki & Brent, 2016). Mood disorders are among the most frequent psychiatric disorders contributing to suicide attempts (Georgiades et al., 2019; Nock et al., 2009; Turecki & Brent, 2016). Major Depressive Disorder (MDD) is one of most significant precipitating factors (Turecki et al., 2019). Furthermore, patients experiencing Treatment-Resistant Depression (TRD) are more likely to report a prior suicide attempt compared to individuals showing a favorable treatment response, and treatment resistance rates are higher in patients with severe suicidality (Dold et al., 2018; Malhi et al., 2005; Nelsen & Dunner, 1995). It is reported that approximately 30% of patients with TRD attempt suicide at least once in their lifetime (Dunner et al., 2006; Hantouche et al., 2010; Ozcan et al., 2020). This rate is reported to be at least twice the lifetime suicide rate in patients with non-resistant depression (Bernal et al., 2007; Chen & Dilsaver, 1996).

Among predisposing factors, heredity seems to play an important role. The risk of attempted suicide is 2.0 to 4.8 times higher in relatives of individuals who have died by suicide, and 2 to

7.6 times higher in relatives of individuals with a history of suicide attempts (Brent & Melhem, 2008). Genetic factors appear to be pivotal in the familial transmission of suicidal behaviour with an estimated heritability ranging from 30% to 50% (Turecki & Brent, 2016). Another predisposing risk factor is exposure to early-life adversity such as parental neglect or childhood physical, sexual, and emotional abuse (Castellví et al., 2017). The association between Childhood Trauma (CT) and lifetime suicide risk is well established (Afifi et al., 2008; Brezo et al., 2008; Fergusson et al., 2000a). Several studies report strong associations of childhood sexual abuse with *i)* suicidal ideation, and *ii)* suicidal behaviour (Gomez et al., 2017; Hooven et al., 2012; A. B. Miller et al., 2013; Sit et al., 2015). Physical and emotional abuse is also associated with a high risk of suicidal behaviour (Gomez et al., 2017; Janiri et al., 2018). Moreover, sexual and physical abuse have been closely linked with repeated suicide attempts, independently of other trauma subtypes (emotional abuse and neglect, and physical neglect) (Ystgaard et al., 2004). In a recent meta-analysis, it has been highlighted that all different types of childhood maltreatment were associated with a two- to three-fold increased risk of suicide attempts and suicidal ideation (Angelakis et al., 2019).

Furthermore, CT not only increases the risk of suicide but also precipitates the development of MDD throughout the lifespan, and aggravates its course and chronicity (Bernet & Stein, 1999; Brown et al., 2007; C. Heim & Nemeroff, 2001; Hovens et al., 2010; Liu et al., 2009; Nanni et al., 2012; Wainwright & Surtees, 2002; Wiersma et al., 2009). We highlighted a significant association between CT, mainly regarding physical abuse/neglect, and clinical severity in the TRD population (Yrondi et al., 2020). Moreover, intensity of MDD episode was found to be linked to suicide (McGirr et al., 2008; Turecki et al., 2019).

Key mediating factors between predisposing factors and precipitating factors include personality traits. Among these, those most robustly associated with suicidal behaviour are impulsive-aggressive traits (Fergusson et al., 2000b; Mann et al., 2009; Turecki et al., 2019).

Behavioural disinhibition and impulsiveness have been extensively reported to encourage suicidal behaviours (Carpiniello et al., 2011; Corruble et al., 2003; Ponsoni et al., 2018). Furthermore, individuals who have experienced CT have a greater risk of developing pathological traits and emotional dysregulation thereby increasing the vulnerability to suicide (Turecki et al., 2019).

However, there is little data available focusing on the mediating role of personality traits, impulsiveness, and depressive symptom severity in the relationships between CT and suicidal ideation and behaviours in the specific context of TRD. Indeed, to our knowledge, only one study by Tunnard et al. (2014) has to date documented an association between CT and repeated suicide attempts in a large sample of TRD patients. However, this study did not assess mediating factors or suicidal ideation.

Aims of the study

This study aims to evaluate any potential associations between CT, including different subtypes of trauma, and *i)* suicide attempts, *ii)* suicide risk, and *iii)* suicidal ideation in a TRD population, and the potentially mediating role of personality traits, impulsiveness, and depressive symptoms severity.

Methods

Population

Patients were recruited from a cohort (FACE-DR cohort) of the French network of expert centers for TRD, consisting of 13 specialty care centers located in academic psychiatry departments throughout France (Yrondi et al., 2017).

The patients selected were clinically unresponsive to at least two successive courses of antidepressants from two different pharmacological classes, corresponding to at least stage II of the TRD staging criteria defined by Thase & Rush (Thase & Rush, 1997). At inclusion, all

the patients were treated with an antidepressant medication. Before participating in the full assessment, patients were interviewed by a psychiatrist at the expert center in order to:

– Confirm the diagnosis of MDD according to the DSM-IV (MINI) (Frances et al., 2000) criteria with moderate to severe symptoms, as attested by the Montgomery and Åsberg Rating Scale (MADRS) and a total score above 20 (Taylor et al, 2006), and the level of resistance indicated by, both, the classification of Thase & Rush ≥ 2 (Thase & Rush, 1997) and Antidepressant Treatment History Form (ATHF) (Sackeim, 2001)

– Exclude bipolar disorders, psychotic disorders, obsessive-compulsive disorders, eating disorders (with BMI < 15), somatoform disorders, and mood disorders related to substance abuse or misuse.

– Inform the patient about the formal assessment procedure.

Assessment

For this study, we focused on assessments performed at baseline, after inclusion of TRD patients. Severity of depressive symptoms was assessed with the MADRS (Montgomery & Asberg, 1979). The inter-rater reliability of the MADRS scale was high. Scores on the scale correlated significantly with scores on a standard rating scale for depression, the Hamilton Rating Scale, indicating its validity as a general estimate of severity (Montgomery & Asberg, 1979).

Childhood Trauma was evaluated with the Childhood Trauma Questionnaire (CTQ) based on five major trauma subtypes: emotional abuse (EA)(None:5-8, Low:9-12, Moderate: 13-15, Severe:16+), physical abuse (PA))(None:5-7, Low:8-9, Moderate: 10-12, Severe:13+), sexual abuse (SA) (None:5, Low:6-7, Moderate: 8-12, Severe:13+), emotional neglect (EN))(None:5-9, Low:10-14, Moderate: 15-17, Severe:18+), and physical neglect (PN) (None:5-7,

Low:8-9, Moderate: 10-12, Severe:13+) (Bernstein et al., 1994). Bernstein et al. (1994) highlighted that the CTQ has strong reliability and validity.

Suicide is defined as intentionally ending one's own life, a suicide attempt as self-injurious, non-fatal behaviour with inferred or actual intent to die, and suicidal behaviours as those which may result in ending one's own life, whether fatal or not. This term excludes suicidal ideation. Suicidal ideations are defined as any thoughts about ending one's own life. The risk of acting on suicidal thoughts increases with the frequency, intent, and content of suicidal ideation (Turecki et al., 2019). Suicide risk was assessed with the Structured Clinical Interview for DSM-IV (MINI) (First et al., 2016). A suicidal ideation score is derived from the Columbia Suicide Severity Rating Scale (CSSRS) by adding the severity and intensity sub-scores (Ducasse et al., 2014; Posner et al., 2011). The CSSRS demonstrated good convergent and divergent validity with other multi-informant suicidal ideation and behaviour scales and had high sensitivity and specificity for suicidal behaviour classifications compared with another behaviour scale and an independent suicide evaluation board. Both the ideation and behaviour subscales were sensitive to change over time. The intensity of ideation subscale demonstrated moderate to strong internal consistency (Posner et al., 2011).

Personality traits were assessed with the Big Five Inventory (BFI) (Goldberg, 1990). It assessed five personality traits (neuroticism, extraversion, agreeableness, openness and conscientiousness). The mean internal consistency (0.79) is excellent, providing clear evidence of the psychometric qualities of the tool (internal validity). Internal consistencies of the five personality dimensions were comparable for the BFI and the Revised NEO Personality Inventory (Neuroticism, Extraversion and Openness; NEO-PI-R) (Plaisant et al., 2010).

Impulsiveness was assessed with the Barratt Impulsiveness Scale (BIS) (Patton et al., 1995). Two of the three subtests of the BIS-11 (motor and non-planning) are consistent with those

originally hypothesized by Barratt (Barratt, 1985), but no "pure" cognitive impulsiveness component was evident. The BIS-11 total score was internally consistent across populations and has potential clinical utility for measuring impulsiveness among selected patient and inmate populations.

This assessment protocol was approved by the institutional review board (French CNIL: DR-2015-673) in accordance with French law for non-interventional studies, and requires only an information letter.

Statistics

Sociodemographic and clinical characteristics were presented using means and standard deviations for continuous variables and frequency distributions for categorical variables. First, Linear regression models (enter method) were applied to test the association between dependent variables such as MINI suicide score, CSSRS, and independent variables: CTQ and CT subtypes. We also assessed association between those previous variables and potential mediation factors [depression intensity (MADRS score), personality traits (BFI) and impulsiveness (BIS-11)]. Second, a GLM (general linear model) mediation model (Gallucci, 2019; Rosseel, 2012) was used to assess the association between CTQ and CT subtype (independent variable) and dependent variables such as MINI suicide score and CSSRS. The potential mediation factors showing an association were added in this model. The independent variables are all considered parallel independent variables. The mediators are all inserted in the model as parallel mediators. Mediators were referred to as the related factors that could be used to explain the observed relationship between an exposure variable and an outcome. The exposure variable is CT and the outcome is suicidal behaviour. The GLM mediation model was adjusted based on age and sex. We compared data from patients who did not fill out the CTQ with our sample using the t-test for continuous variables and the Chi2 for categorical

variables. We used one-way ANOVA to compare groups. Statistical analyses were performed with Jamovi 1.2 (R Core Team, 2019; The jamovi project, 2020)

Results

Demographic data

The FACE-DR cohort enrolled 291 patients between 2012 and 2018. Of these, 256 patients (87.7%) had filled out the CTQ at baseline and 91 individuals (31.3%) in this group had attempted suicide prior to baseline. The mean age was 53.21 (SD=12.93) and 62.3% were female. The mean MADRS score was 28.92 (SD=6.90). For emotional abuse, 2.7% of the population had severe intensity and 2% moderate intensity. For physical abuse, 48.8% presented severe intensity and 19.9% moderate intensity. With regard to sexual abuse, 6.6% had a severe score and 33.6% a moderate score. Regarding emotional neglect, the severe and moderate intensities represented 2.7% each, while 25.8% presented severe intensity and 14.5% moderate intensity for physical neglect. The overall characteristics of these 256 patients are summarized in Table 1. We did not find any difference in clinical features between patients who filled out the CTQ and those who did not (Table 2)

Associations between Childhood Trauma and suicidal behaviour in the TRD cohort

With regard to CSSRS to assess suicidal ideation, we did not find any association with total CTQ score (β=0.042; p=0.564) and CT subtype scores (EA score: β=0.16; p=0.084; PA score: β=0.057; p=0.573; SA score: β=-0.11; p=0.193; EN score: β=-0.053; p=0.506; PN score: β=-0.02; p=0.852). However, in relation to suicide risk using the MINI suicide score for the current depressive episode, we found an association with the total CTQ scores mediated by the intensity of the current episode (MADRS score) (Table 3) in a model adjusted for age and

sex (total effect: β=0.171; p=0.011, direct effect: β=0.135; p=0.043; indirect effect: β=0.036; p=0.048) (Figure 1).

Focusing on CT subtypes, we did not find any significant association between the MINI suicide score and the scores of the different CT subtypes such as EA score, PA score, SA score or EN score (EA: β=-0.063; p=0.489; PA: β=-0.06; p=0.522; SA: β=-0.003; p=0.971; EN: β=0.03; p=0.742). However, we observed a strong association between the MINI suicide score and the physical neglect score in a model adjusted for age and sex (β=0.301; p=0.002), without any mediation by the intensity of the current episode (MADRS score) (Table 4; Figure 2).

Assessment of factors mediating the association between Childhood Trauma and suicidal behaviour in the TRD cohort

We examined the putative mediating role of critical factors such as personality traits and impulsiveness in the relationships between CT and suicide risk in our TRD population.

Associations between Childhood Trauma, suicide risk/behaviour, and personality traits in TRD

We found no significant association between CT and personality traits, namely neuroticism (β=0.117; p=0.085), extraversion (β=-0.054; p=0.41), agreeableness (β=0.023; p=0.73), openness (β=-0.002; p=0.98), and conscientiousness (β=0.041; p=0.55). This supports that we could not use a mediation model to assess whether personality traits mediated any relationship between CT and (i) suicide risk and (ii) suicidal behaviour (Supplementary Material S1).

Associations between Childhood Trauma, suicide risk/behaviour, and impulsiveness in TRD

We did not find any significant association between impulsiveness (BIS) and CT or CT subtypes (CTQ: β=0.079; p=0.233; EA score: β=0.108; p=0.51; PA score: β=0.085; p=0.98;

SA score: β=0.054; p=0.999; EN score: β=0.053; p=0.999; PN score: β=0.012; p=0.999). This supports that a mediation model could not be used to assess whether impulsiveness mediated any relationship between CT and (i) suicide risk and (ii) suicidal behaviour.

Discussion

To our knowledge, our study is the first to specifically investigate associations between childhood adversities and suicidal risk and ideation in a TRD population.

Regarding suicide risk, we showed that depressive symptoms (MADRS) significantly mediated the effect of CT on suicide risk. However, when suicidal ideation was assessed with CSSRS, we did not observe any association with CT (or subtypes). Finally, there was no relationship between CT and *i)* personality traits and *ii)* impulsiveness.

In terms of the TRD literature, our results are in line with those reported by Tunnard et al. showing that CT was associated with an increased risk of suicidal behaviours (Tunnard et al., 2014). In addition, we specifically found an association between childhood physical neglect and suicide risk. However, our findings are not consistent with the previously published studies on non-resistant MDD documenting that physical abuse, sexual abuse, and emotional abuse are associated with an increased risk of suicidal behaviour (Gomez et al., 2017; Hooven et al., 2012; Janiri et al., 2018; A. B. Miller et al., 2013; Ystgaard et al., 2004). Moreover, Norman's meta-analysis supported a clear relationship between physical abuse and emotional abuse and neglect with suicidal behaviour (Norman et al., 2012). Surprisingly, in relation to impulsiveness, which is a well-established risk factor for suicide, our results were not consistent with those of Brodsky et al. reporting that patients with a childhood history of abuse had significantly higher impulsiveness and aggression scores than those who did not report any previous history of abuse (Brodsky et al., 2001). Moreover, while Zhang et al. have shown that personality traits could be potential mediators in the relationships between CT and

depressive symptoms, we did not find any association between CT and personality profiles (Zhang et al., 2018). In our study, personality traits and impulsiveness were not reported to mediate the influence of CT on suicidal behaviour and risk. This may be due to the fact that TRD participants were currently treated with antidepressant medication which could improve impulsiveness and change personality components although having no significant effect on overall clinical severity (Bond, 2005; Jylhä et al., 2020).

To summarize, we report strong associations between CT (mainly physical neglect) with suicidal risk in the TRD population. This could be explained by the pathophysiology of TRD and biological mechanisms related to Childhood Trauma. The hypothalamic-pituitary-adrenal (HPA) axis regulates physiological responses to stress and allows individuals to cope with a changing environment or specific events by regulating cortisol levels (Lutz et al., 2017; Turecki & Brent, 2016). Individuals who experience early-life adversity often have a overactive HPA axis and an increased stress response (Christine Heim et al., 2010). This is partly due to lowered hippocampal expression of glucocorticoid receptors (GRs) caused by increased receptor promoter methylation in both central nervous and peripheral tissues (McGowan et al., 2009; Turecki & Meaney, 2016). CT was recently demonstrated to be associated with elevated peripheral concentrations of pro-inflammatory cytokines (Coelho et al., 2011, 2014; Müller et al., 2019). Moreover, MDD and TRD appear to be related to dysfunction of the immune and inflammatory responses (A. H. Miller & Raison, 2016). In the context of MDD, external stress can be a precipitating factor, which can increase levels of circulating cytokines (TNFα and IL-6), both peripherally and systemically (A. H. Miller, 2009; A. H. Miller et al., 2009). Increased expression of these central nervous system (CNS) cytokines appears to result from activation of the microglia by external stress factors (A. H. Miller et al., 2009). Proinflammatory cytokines contribute to the overactive HPA axis observed in MDD. These cytokine changes also alter the metabolism of serotonin,

norepinephrine, and dopamine in brain regions essential for regulating emotions and behaviours, such as the limbic system (amygdala, hippocampus, and nucleus accumbens) (Raison et al., 2006). Indeed, inflammation has largely been documented to generate brain monoamine deficits (Raison et al., 2006). Furthermore, the impairment of the serotonin, norepinephrine, and dopamine pathways is pivotal in precipitating MDD and/or suicidal behaviour (Belmaker & Agam, 2008; Lutz et al., 2017). In addition, monoaminergic, inflammatory, and immune pathways underpin the mechanisms of TRD. Antidepressant treatments that primarily target monoamine transmissions are presumably unable to compensate for the monoamine deficit generated by inflammatory conditions (Capuron & Aouizerate, 2017; Capuron & Miller, 2011; Coplan et al., 2014; Lutz et al., 2017; A. H. Miller et al., 2009). Taken together, these observations plead for the pivotal role of these biological pathways in the relationships between CT and suicidal behaviour and suicide risk in the TRD population.

Limitations

Our cohort excluded mood disorders related to substance abuse and/or misuse, even though substance abuse/misuse is a major suicide risk factor (Turecki & Brent, 2016). This exclusion may underestimate the association between CT and suicide risk and/or suicidal behaviour in our study. In addition, we only assessed suicidal ideation with CSSRS at a single point in time. A more complex assessment based on measurements at regular time intervals would be informative to detect any potential associations between CT and suicidal ideation over time. Moreover, the CTQ asks questions retrospectively, which could induce a memory bias. Finally, we did not take into account any of the biological mechanisms that are thought to underpin the associations between CT and suicidal behaviour and suicide risk in TRD.

Conclusion

Here, we found a significant association between suicidal behaviour and Childhood Trauma, predominantly with respect to physical neglect, in our TRD population. This is consistent with the previously reported relationships between CT and suicidal behaviour in MDD populations. In clinical practice, information about a history of childhood abuse could therefore help to identify individuals at risk of suicidal behaviour. However, the significance of our findings would need to be confirmed in a larger prospective TRD cohort designed to evaluate suicide attempts in relation to biological assessments including especially HPA axis-immune functions. Better characterization and understanding of the clinical and biological features involved in TRD, through a better determination of the long-term impact of CT for the early identification and efficient prevention of suicidal behaviour, may uncover useful parameters for mental health providers in everyday clinical practice.

Data Availability Statement

To get the available data, please contact the corresponding author:

antoineyrondi@gmail.com

Acknowledgments: This research was supported by the *FondaMental* Foundation, *Institut National de la Santé et de la Recherche Médicale* (INSERM), AP-HP, Astra Zeneca, and by the *Investissements d'Avenir* programme managed by the ANR under reference ANR-11-IDEX-0004-02. This funding source had no role in the study design, data collection, analysis, preparation of the manuscript, or decision to submit the manuscript for publication.

All authors have approved the manuscript.

Conflict of interest statement

Antoine Yrondi received speaker's honoraria (AstraZeneca, Janssen, Lundbeck, Otsuka, Servier) and carried out clinical studies in relation to the development of a medicine (Janssen, Lundbeck) unrelated to this work.

Olivier Doumy received honoraria from Lilly, Astra-Zeneca, Janssen, Servier, and Lundbeck.

Jean Baptiste Genty received a speaker's honorarium from Servier.

Pierre Michel Llorca received grants, honoraria, and consulting fees from Allergan, Gedeon Richter, Janssen-Cilag, Lundbeck, Otsuka, Recordati, Sanofi-Aventis, and Teva.

Raphael Richieri received a speaker's honorarium from Janssen Cilag.

Ludovic Samalin received grants, honoraria, and consulting fees from Janssen-Cilag, Lundbeck, and Otsuka.

Florian Stephan received honoraria from Otsuka.

Emmanuel Haffen: acted in advisory capacities, carried out clinical studies in relation to the development of a medicine, received personal researches, studies, or travel allowance, gave presentations at meetings, and received remuneration for input from the following pharmaceutical organisations: AstraZeneca, BMS, Cellgene, Euthérapie - Servier, Janssen, Elli Lilly, Lundbeck, LivaNova, Otsuka, Pfizer, Sanofi. He also held a managerial position in the FondaMental Foundation (Créteil) and the French Association of Biological Psychiatry and Neuropsychopharmacology.

Wissam El-Hage reports receiving speaker's honoraria from Chugai, Eisai, Lundbeck, Janssen-Cilag, Otsuka, and UCB unrelated to this work.

Bruno Aouizerate: received speaker's honoraria and/or a travel allowance from Lundbeck, Janssen-Cilag, and Eli Lilly. He has served on the advisory board of Janssen-Cilag.

Thierry d'Amato, Franck Bellivier, Djamila Bennabi, Thierry Bougerol, Vincent Camus, Philippe Courtet, Jérôme Holtzmann, Christophe Lançon, Marion Leboyer, Julia Maruani, Rémi Moirand, Fanny Molière, Michel Walter Jean Petrucci, Laurent Schmitt and Guillaume Vaiva declare having no conflicts of interest.

Contributions: All authors were involved in the identification and selection of patients, in the clinical assessment, and co-wrote the paper. A. Yrondi, G. Vaiva, M. Walter, P. Courtet, W. El-Hage, and B. Aouizerate were also involved in choosing the data set for this project and the statistical analysis.

Funding: This research was funded by the *FondaMental* Foundation, *Institut National de la Santé et de la Recherche Médicale* (INSERM), AP-HP, Astra Zeneca, and by the *Investissements d'Avenir* programme managed by the ANR under reference ANR-11-IDEX-0004-02. This funding source had no role in the study design, data collection, analysis, preparation of the manuscript, or decision to submit the manuscript for publication.

All authors have approved the manuscript.

Ethical standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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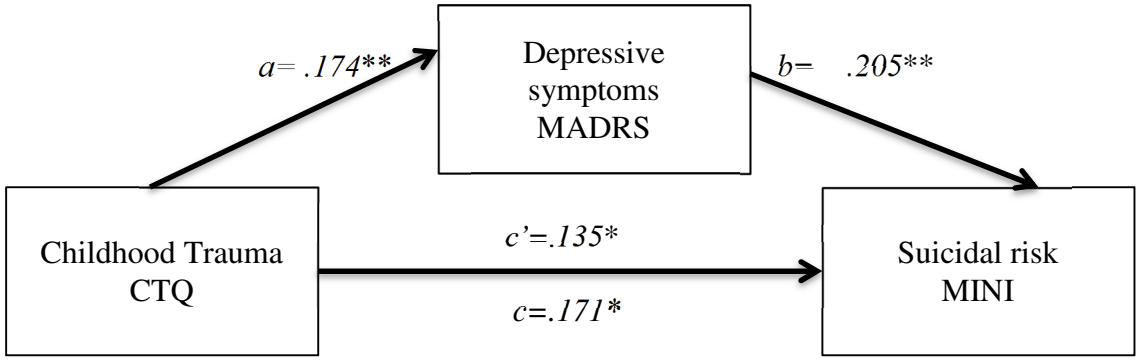
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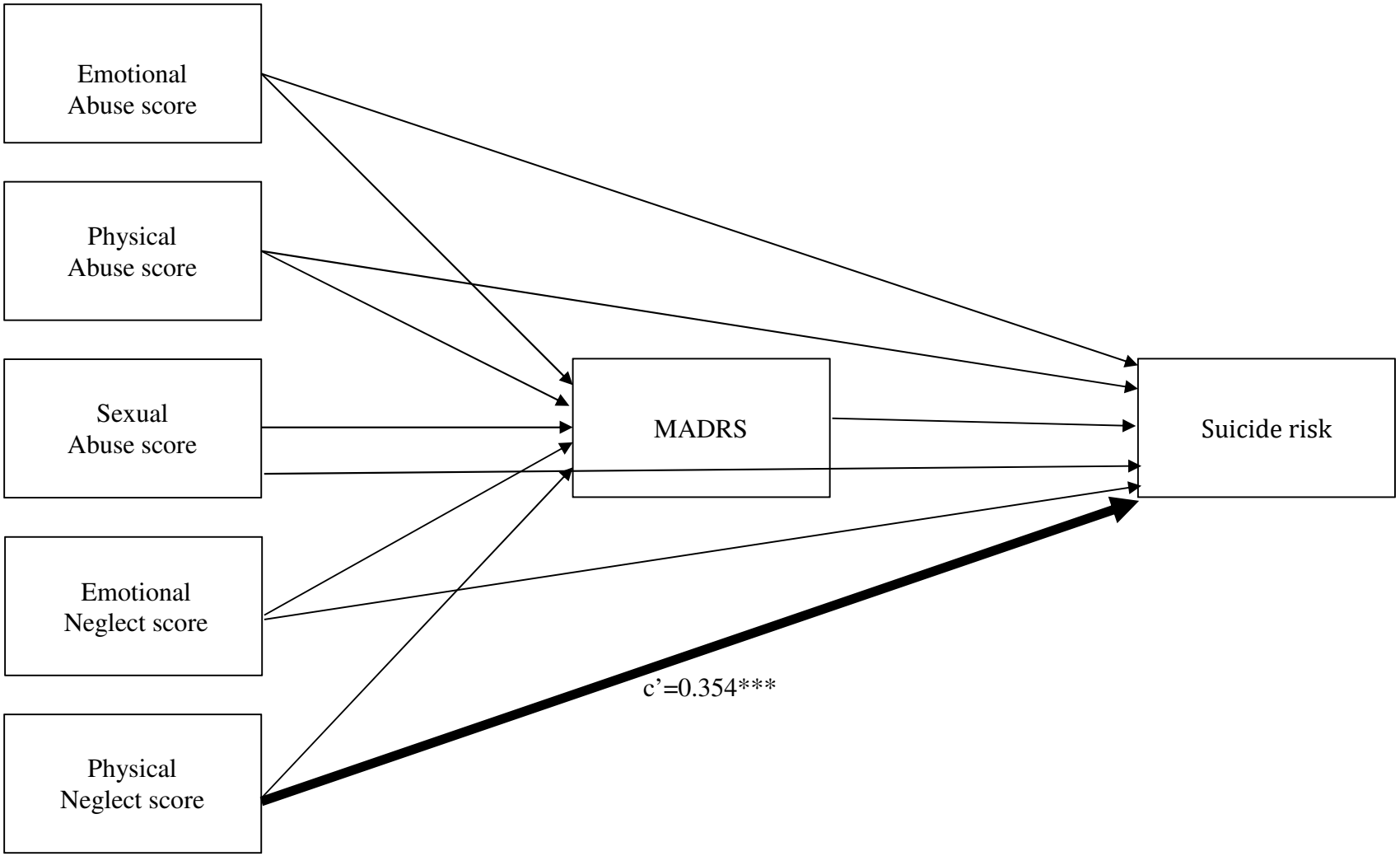
Figure 1 : Depressive symptoms as mediator of childhood trauma on suicidal risk
Figure 2 : Association between childhood trauma subtype and suicidal risk

Figure 1 : Depressive symptoms as mediator of childhood trauma on suicidal risk



*MADRS : Montgomery and Asberg Depression Rating Scale ; CTQ : Childhood Trauma Questionnaire ; axb : indirect effect ; c' : direct effect ; c : total effect * : p<.05, **p<=.01, ns : non significant*

Figure 2 : Association between childhood trauma subtype and suicidal risk



*MADRS : Montgomery and Asberg Depression Rating Scale, arrow in bold: association statistically significant; c'= direct effect; ***=<0.001*

Table 1. Population characteristics.

		N	Mean (SD)
Age, years		291	53.21 (12.93)
Females, %		181 (62.2%)	
ATHF		239	4.03 (.51)
CTQ, total score		256	42.57 (14.51)
Emotional abuse, score		256	6.46 (2.88)
	None (5-8)	216 (84.4%)	
	Low (9-12)	28 (10.9%)	
	Moderate (13-15)	5 (2%)	
	Severe (16+)	7 (2.7%)	
Physical abuse, score		256	12.77 (5.06)
	None (5-7)	40 (15.6%)	
	Low (8-9)	42 (16.4%)	
	Moderate (10-12)	51 (19.9%)	
	Severe (13+)	123 (48.8%)	
Sexual abuse, score		256	7.42 (2.72)
	None (5)	84 (32.8%)	
	Low (6-7)	69 (27%)	
	Moderate (8-12)	86 (33.6%)	
	Severe (13+)	17 (6.6%)	
Emotional neglect, score		256	6.27 (3.46)
	None (5-9)	230 (89.8%)	
	Low (10-14)	12 (4.7%)	
	Moderate (15-17)	7 (2.7%)	
	Severe (18+)	7 (2.7%)	
Physical neglect, score		256	9.66 (5.07)
	None (5-7)	121 (47.3%)	
	Low (8-9)	32 (12.5%)	
	Moderate (10-12)	37 (14.5%)	
	Severe (13+)	66 (25.8%)	

BFI extraversion	252	2.26 (.83)
BFI agreeableness	252	4.11 (.48)
BFI neuroticism	231	3.94 (.62)
BFI conscientiousness	231	3.46 (.76)
BFI openness	252	2.85 (.81)
BIS	247	64.26 (9.6)
MADRS	282	28.92 (6 .90)
CSSRS	202	12.91 (7.63)
MINI suicide score	244	8.85 (10.4)

ATHF: Antidepressant Treatment History Form; BFI: Big Five Inventory; BIS: Barratt Impulsivity Scale; CSSRS: Columbia Severity Suicide Rating Scale; CTQ: Child Trauma Questionnaire; MADRS: Montgomery-Åsberg Depression Rating Scale; MINI: Mini International Neuropsychiatric Interview; N: Number; SD: Standard Deviation.

Table 2. Comparison between patients filling CTQ and non-filling CTQ

Variables	group	N	Mean (SD)	p
Age	CTQ	256	52.73 (12.95)	0.085[t]
	No CTQ	35		
Sex (F)	CTQ	158		0.648[c]
	No CTQ	23		
MADRS	CTQ	253	28.99 (6.73)	0.617[t]
	No CTQ	29	28.31 (8.35)	
MINI suicide risk	CTQ	217	9.02 (10.62)	0.458[t]
	No CTQ	27	7.44(8.47)	
CSSRS	CTQ	181	16 (9.03)	0.303[t]
	No CTQ	21	14 (8.31)	

[C] *: Chi2 ; CSSRS : Columbia Suicide Severity Rating Scale* suicidal ideation score; *CTQ : Childhood Trauma Questionnaire score ; MADRS : Montgomery Asberg Depression Rating Scale ;MINI : Mini International Neuropsychiatric Interview ; p : p-value, SD : Standard Deviation ;* [t] *: t-test*

Table 3. Results of general linear model with mediation model (CTQ)

Interactions		
		95% C.I.

Type	Effect	Lower	Upper	β	p
Indirect	CTQ ⇒ MADRS ⇒ MINI suicide score	2.6e-4	0.052	0.036	0.048
Component	CTQ ⇒ MADRS	0.019	0.137	0.174	0.010
	MADRS ⇒ MINI suicide score	0.12	0.546	0.205	0.002
Direct	CTQ ⇒ MINI suicide score	0.003	0.194	0.135	0.043
Total	CTQ ⇒ MINI suicide score	0.028	0.22	0.171	0.011

β: β value ; CI : confident Interval ; CTQ : Childhood Trauma Questionnaire score ; MADRS : Montgomery Asberg Depression Rating Scale ;MINI : Mini International Neuropsychiatric Interview ; p : p-value

Table 4. Results of general linear model with mediation model (sub-type of childhood trauma)

Interactions

		95% C.I.			
Type	**Effect**	**Lower**	**Upper**	**β**	**p**
Indirect	Emotional Abuse ⇒ MADRS ⇒ MINI suicide score	-0.156	0.161	7.1e-4	0.975
	Physical Abuse ⇒ MADRS ⇒ MINI suicide score	0.002	0.226	0.055	0.047
	Sexual Abuse ⇒ MADRS ⇒ MINI suicide score	0.008	0.382	0.050	0.041
	Emotional Neglect ⇒ MADRS ⇒ MINI suicide score	-0.072	0.171	0.016	0.428
	Physical Neglect ⇒ MADRS M0 ⇒ MINI suicide score	-0.228	0.004	-0.053	0.059
Component	Emotional Abuse ⇒ MADRS	-0.377	0.389	0.003	0.975
	MADRS ⇒ MINI suicide score	0.2	0.627	0.255	< .001

Interactions					
		95% C.I.			
Type	**Effect**	**Lower**	**Upper**	**β**	**p**
	Physical Abuse ⇒ MADRS	0.044	0.505	0.215	0.020
	Sexual Abuse ⇒ MADRS	0.091	0.853	0.198	0.015
	Emotional Neglect ⇒ MADRS	-0.169	0.405	0.062	0.418
	Physical Neglect ⇒ MADRS	-0.515	-0.027	-0.208	0.029
Direct	Emotional Abuse ⇒ MINI suicide score	-0.838	0.386	-0.064	0.469
	Physical Abuse ⇒ MINI suicide score	-0.611	0.134	-0.115	0.210
	Sexual Abuse ⇒ MINI suicide score	-0.823	0.409	-0.053	0.511
	Emotional Neglect ⇒ MINI suicide score	-0.428	0.489	0.01	0.896
	Physical Neglect ⇒ MINI suicide score	0.354	1.141	0.354	< .001
Total	Emotional Abuse ⇒ MINI suicide score	-0.857	0.410	-0.063	0.489
	Physical Abuse ⇒ MINI suicide score	-0.506	0.257	-0.060	0.522
	Sexual Abuse ⇒ MINI suicide score	-0.641	0.617	-0.003	0.971
	Emotional Neglect ⇒ MINI suicide score	-0.395	0.554	0.025	0.742
	Physical Neglect ⇒ MINI suicide score	0.232	1.038	0.301	0.002

β: β value ; CI : confident Interval ; CTQ : Childhood Trauma Questionnaire score ; MADRS : Montgomery Asberg Depression Rating Scale ;MINI : Mini International Neuropsychiatric Interview ; p : p-value