

# Relationship between Childhood Physical Abuse and Clinical Severity of Treatment-Resistant Depression in a Geriatric Population

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# Abstract

**Background:** We assessed the correlation between childhood maltreatment (CM) and severity of depression in an elderly unipolar Treatment-Resistant Depression (TRD) sample.

**Methods:** Patients were enrolled from a longitudinal cohort (FACE-DR) of the French Network of Expert TRD Centres.

**Results:** Our sample included 96 patients (33% of the overall cohort) aged 60 years or above, with a mean age of 67.2 (SD = 5.7). Most of the patients were female (62.5%). The Montgomery and Asberg Depression Rating Scale (MADRS) and Quick Inventory Depression Scale-Self Report (QIDS-SR) mean scores were high, 28.2 (SD = 7.49) [MADRS score range: 0-60; moderate severity  $\geq 20$ , high severity  $\geq 35$ ] and 16.5 (SD=4.94) [QIDS-SR score range: 0-27; moderate severity  $\geq 11$ , high severity  $\geq 16$ ], respectively. Mean self-esteem scores were 22.47 (SD=6.26) [range 0-30]. In an age and sex-adjusted model, we found a positive correlation between childhood trauma (CTQ scores) and depressive symptom severity [MADRS ( $\beta=0.274$ ;  $p=0.07$ ) and QIDS-SR ( $\beta=0.302$ ;  $p=0.005$ ) scores]. We detected a statistically significant correlation between physical abuse and depressive symptom severity [MADRS ( $\beta=0.304$ ;  $p=0.03$ ) and QIDS-SR ( $\beta=0.362$ ;  $p=0.005$ ) scores]. We did not observe any significant correlation between other types of trauma and depressive symptom severity. We showed that self-esteem (Rosenberg scale) mediated the effect of physical abuse (PA) on the intensity of depressive symptoms [MADRS:  $b=0.318$ , 95% *BCa* C.I. [0.07, 0.62]; QIDS-SR:  $b=0.177$ , 95% *BCa* C.I. [0.04, 0.37]]. Preacher & Kelly's Kappa Squared values of 19.1% ( $k^2=0.191$ ) and 16% ( $k^2=0.16$ ), respectively, indicate a moderate effect.

**Conclusion:** To our knowledge, this is the first study conducted in a geriatric TRD population documenting an association between childhood trauma (mainly relating to PA) and the intensity of depressive symptoms.

## Background

Depression is a very common disorder in the elderly, with a prevalence of up to 30% [1]. Geriatric depression is currently defined as the occurrence of depressive episodes in the elderly, although the age at onset is critical with early- (EOD; first episode before the age of 60) or late-onset depression (LOD; first episode after the age of 60). Some differences have been reported between EOD and LOD [2–4]. For instance, personality abnormalities and a family history of psychiatric illness were significantly more common in EOD [3, 4]. However, considering the severity, phenomenology, history of previous episode, and neuropsychological performance, there is no difference between EOD and LOD in elderly people [3, 4]. Half of the elderly depressed adults report some form of childhood abuse [5]. However, childhood mistreatment is associated with the development of geriatric depression, albeit more frequently in EOD [1, 5]. There is also a link between childhood abuse and EOD in older populations [6]. In addition, the relationship between childhood maltreatment and geriatric depression (EOD or LOD) is mediated by certain personality traits. Neuroticism and extraversion seem to be more direct mediators while

agreeableness and conscientiousness are rather indirect mediators [1]. However, none of these previous studies specifically examined the link between childhood trauma and treatment-resistant depression (TRD) in the context of a geriatric population. TRD is currently defined by the failure of at least two attempted antidepressant treatments administered sequentially, at adequate dose, and for an adequate duration [7]. It can be assumed that approximately 20 to 30% of depressed patients experience TRD, as reported in Anglo-Saxon countries [8], and up to one-half of patients respond only partially [7]. TRD has been estimated to represent half of the overall treatment costs for MDD [9, 10]. There are specific care for TRD in elderly population[11]. To date, there has been little investigation examining the associations between childhood adversity and TRD. Kaplan & Klinetob [12] compared the TRD population to the population that responded successfully to antidepressants. They reported greater levels of childhood emotional abuse in the TRD group. Tunnard et al. [13] focused on TRD, although unipolar and bipolar populations were mixed. They showed that childhood adversity was common among these TRD patients (62%) and was associated with poor clinical progression, characteristics of psychosis, and suicide attempts. However, to our knowledge, there was no study focusing on childhood trauma and TRD in geriatric population.

Moreover, self-esteem is associated with the clinical symptomatology and prognosis in geriatric depression. Indeed, it has been found that low self-esteem significantly increases the risk of suicidal behaviour [14]. In addition, patients with low self-esteem respond more slowly to antidepressant treatment compared to their counterparts with higher self-esteem [15].

Thus, given the frequent history of childhood trauma in elderly depressed patients, we aim to assess the correlation between childhood maltreatment (CM) and the severity of depression specifically in an elderly TRD sample. Moreover, given the role of personality traits as well as self-esteem in the symptomatology and course of the depressive disorder, we intend to assess whether personality traits and self-esteem could influence the association between CM and the severity of depressive symptoms.

## Methods

**Populations:** Patients were recruited for a prospective cohort (FACE-DR cohort) from the French Network of Expert Centres for Resistant Depression, consisting of 13 specialist care centre hosted within academic psychiatry departments across France [16].

Patients were clinically unresponsive to at least two successive, adequate courses of antidepressants from two different pharmacological classes corresponding to at least stage II of the staging criteria proposed by Thase & Rush for defining TRD [17]. We selected all cohort patients over 60 years of age for this study. Although the cut-off between geriatric and non-geriatric depression remains unclear, ranging from 60 [1, 6, 18, 19] to 65 years old [20, 21], we chose the age of 60 in order to compare our findings with

those of most studies focusing on the impact of CM in depressive disorders [1, 6, 18, 19]. Before participating in the full assessment, patients were interviewed by a psychiatrist at the expert centre in order to:

- Confirm the diagnosis of TRD according to the DSM-IV (MINI) [22] criteria with moderate to severe symptoms, the level of resistance indicated by the classification of Thase & Rush  $\geq 2$  [17].
- 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: We selected patients who were 60 or over, and clinically resistant to medication as determined by the Thase & Rush staging criteria (i.e. level II) [16, 17]. The severity of depressive symptoms, CM, self-esteem and personality traits were assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS) [23], the Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR) [24], the Childhood Trauma Questionnaire (CTQ) [25], the Rosenberg scale [26] and the Big Five Inventory (BFI) [27]. The MADRS is a ten-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders. Scores range from 0 to 60 [23]. The QIDS-SR is derived from the 30-item Inventory of Depressive Symptomatology. It asks 16 questions in order to assess the severity of the nine diagnostic symptom criteria used in DSM. These nine criterion-related symptoms do not assess anxious, atypical or melancholic features or other commonly associated symptoms such as pain or gastrointestinal disturbances. Scores range from 0 to 27 [24]. **The CTQ** is a screening tool for histories of abuse and neglect. The self-report includes a 28-item scale that measures 5 types of maltreatment – emotional, physical and sexual abuse, and emotional and physical neglect [25]. The Rosenberg scale determines global self-worth by measuring both positive and negative feelings about oneself. Scores range from 0 to 30 [26]. The BFI is a self-report inventory designed to measure the Big Five dimensions including neuroticism, extraversion, agreeableness, openness and conscientiousness. It is a 44-item multidimensional personality inventory [27].

The assessment protocol was approved by the relevant institutional review board [French CNIL (French Data Protection Authority): DR-2015-673].

Statistical analysis: Sociodemographic and clinical characteristics were presented using means and standard deviations for continuous variables and frequency distributions for categorical variables. The chi<sup>2</sup> test was used to compare categorical variables and the t-test and ANOVA to compare continuous variables. Linear regression models were applied to test the association between dependent variables (MADRS, QIDS-SR) and independent variables (CTQ and subtypes, BFI subtypes, Rosenberg scale). Linear regression models were adjusted for age and sex. We used the Hayes mediation model [28] in the cross-sectional study to assess the influence of one variable on the association between CM and intensity of

depressive symptoms at a specific time point. Mediation was deemed partial when indirect and direct effects were both statistically significant and considered to be complete with only the indirect effect being statistically significant. Bonferroni correction was applied for multiple comparisons (CM subtypes). Statistical analyses were performed with SPSS 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Mac, Version 25.0. Armonk, NY: IBM Corp.).

## Results

### *Demographic and clinical data*

Our study included 96 patients (*Table 1*) (33% of the overall cohort) with a mean age of 67.2 [standard deviation (SD): 5.7] and mostly women (62.5%). In our sample, 82 patients (85.4%) completed the CTQ – with a mean score of 37.35 (SD: 9.69). The MADRS and QIDS-SR mean scores were high, 28.2 (SD: 7.49) [No Depression: MADRS=0-6, mild severity=7-19 moderate severity: MADRS score=20-34, high severity: MADRS score  $\geq$ 35 [29]] and 16.53 (SD: 4.94) [No Depression: QIDS-SR=0-5, mild severity= 6-10 moderate severity: QIDS-SR score=11-15; high severity: QIDS score  $\geq$ 16 [30]], respectively. There was no difference in the intensity of depression symptoms on comparing the difference in terms of marital status [MADRS: married=28.4 (SD=7.2), single=25 (SD=9.41), separated=31.5 (SD=13.44), divorced=31.63 (SD=7.13), widowed=29 (SD=5.67),  $F=0.879$ ,  $p=0.481$ ; QIDS-SR: married=16.7 (SD=4.4), single=4.25 (SD=8.48), separated=17.5 (SD=7.78), divorced=17.6 (SD=4.53), widowed=15.33 (SD=8.62)  $F= 0.583$ ,  $p=0.676$ ]. A Rosenberg mean score of 22.47 (SD: 6.26) was documented. BFI scores were neuroticism [mean: 3.85 (SD: .63)], extraversion [mean: 2.37 (SD: .83)], agreeableness [mean: 4.14 (SD: .46)], openness [mean: 2.8 (SD: .86)] and conscientiousness [mean: 3.5 (SD: .75)], respectively. LOD (i.e. the first episode after 60 years of age) affected 25 patients (26%). A difference between EOD [8.66 (SD: 4.44)] and LOD [6.48 (SD: 1.54)] was noted in relation to PN ( $p=0.025$ ) (Figure 1). We did not find any difference between LOD and EOD in relation to (i) other CM (table 1); (ii) the severity of depressive symptoms (MADRS scores:  $p=0.267$ ; QIDS-SR scores:  $p=0.646$ ) and (iii) self-esteem (Rosenberg scale scores:  $p=0.966$ ) (Table 1).

Consequently, our study subjects exhibited moderate to severe depressive symptoms. Their marital status had no impact on the intensity of depressive symptoms. Finally, more PN was found in EOD as opposed to LOD patients.

### *Association between Childhood Trauma and intensity of depressive symptoms*

We found a significant positive correlation between CM and the intensity of depressive symptoms throughout our study sample of elderly TRD patients (*Table 2.*). In an adjusted model (age and gender), CTQ scores were positively associated with MADRS ( $\beta=0.274$ ;  $p=0.07$ ) and QIDS-SR ( $\beta=0.302$ ;  $p=0.005$ ) scores (Figure 2.). In relation to physical abuse (PA), we highlighted a significant correlation with MADRS ( $\beta=0.304$ ;  $p=0.03$ ) and QIDS-SR ( $\beta=0.362$ ;  $p=0.005$ ) scores (Figure 3.). We did not, however, detect any

significant correlations between others types of trauma and the intensity of depressive symptoms (Table 2.). A correlation between childhood maltreatment, mainly physical abuse, and intensity of depressive symptoms was documented.

### *Influence of personality traits on the association between Childhood Trauma and intensity of depressive symptoms*

We found no significant correlation between CM and personality traits, namely neuroticism ( $\beta=0.223$ ;  $p=0.07$ ), extraversion ( $\beta=-0.191$ ;  $p=0.13$ ), agreeableness ( $\beta=0.052$ ;  $p=0.68$ ), openness ( $\beta=-0.058$ ;  $p=0.63$ ) and conscientiousness ( $\beta=-0.204$ ;  $p=0.11$ ). We found no significant associations between distinct subtypes of CM and personality traits: neuroticism (EA, PA, SA, EN, PN), extraversion (EA, PA, SA, EN, PN), agreeableness (EA, PA, SA, EN, PN), openness (EA, PA, SA, EN, PN) and conscientiousness (EA, PA, SA, EN, PN).

### *Influence of self-esteem on the correlation between Childhood Trauma and intensity of depressive symptoms*

In an adjusted model, we found a negative correlation between CM (CTQ total) and self-esteem ( $\beta=-0.25$ ;  $p=0.036$ ), specifically in cases reporting PA ( $\beta=-0.32$ ;  $p=0.04$ ) (Table 3.). Our objective was to assess the potential role of self-esteem on the correlation between CM (mainly PA subtype) and intensity of depression. We therefore had to consider a potential correlation between self-esteem and (i) CM mainly PA and (ii) intensity of depression. The correlation between PA and self-esteem levels (Rosenberg score) was significant ( $\beta = -0.472$ ,  $p < 0.01$ ). Self-esteem levels (Rosenberg score) were associated with the intensity of depression symptoms (MADRS:  $\beta = -0.675$ ,  $p < 0.001$ ; QIDS:  $\beta = -0.375$ ,  $p < 0.001$ ). Therefore, we looked at a potential mediator effect of self-esteem on the correlation between PA and intensity of depression (Hayes' model). We showed that self-esteem (Rosenberg scale) significantly mediated the effect of PA on the severity of depressive symptoms: MADRS:  $b=0.318$ , 95% *BCa C.I.* [0.07, 0.62]; QIDS-SR:  $b=0.177$ , 95% *BCa C.I.* [0.04, 0.37]. Preacher & Kelly's Kappa Squared values of 19.1% ( $k^2=0.191$ ) and 16% ( $k^2=0.16$ ), respectively, were documented indicating a moderate effect of the mediation (Figure 4). The mediation indices were found to be 0.182 [95% CI: 0.042; 0.338] for MADRS and 0.148 [95% CI: 0.031; 0.292] for QIDS-SR respectively. Therefore, self-esteem had a moderate total mediation effect. The indirect effect of PA on depressive symptom intensity was significant (MADRS:  $\beta = 0.318$ , 95%CI [0.07; 0.624], QIDS:  $\beta = 0.177$ : 95%CI [0.036; 0.377]). The direct effect of PA on depression symptom severity was a positive correlation but insignificant on the basis of MADRS ( $\beta = 0.263$ ,  $p = 0.132$ ). However, the correlation was both positive and significant focusing on QIDS-SR ( $\beta = 0.285$ ,  $p < 0.05$ ). The full model effect of PA on intensity of depression symptoms was significant (MADRS:  $\beta = 0.582$ ,  $p < 0.01$ ; QIDS:  $\beta =$

0.463,  $p < 0.001$ ) (Figure 4). Self-esteem appeared to mediate the association between PA in childhood and depression symptom severity.

## Discussion

To our knowledge, this is the first study in a geriatric TRD population to document an association between CM, specifically relating to PA and the intensity of depressive symptoms using either self- or hetero evaluations. It seems that self-esteem mediates this association between PA in childhood and depression symptom severity.

To our knowledge, Tunnard *et al.* [13] was the only study to focus on the correlation between CM and TRD. However, this study was not conducted in the area of geriatric depression as the recruited population was particularly heterogeneous and included both unipolar and bipolar patients. They reported that CM is common, affecting up to 62% of TRD patients. However, they failed to show any significant correlation between childhood trauma and clinical severity.

Self-esteem is associated with geriatric depression symptoms [14] and prognosis [15]. Moreover, numerous studies have documented a strong positive correlation between maltreatment and low self-esteem [31–33]. This correlation could be explained by the fact that early maltreatment can negatively affect the cognitive, social and emotional development of child. In addition, it is well-established that low self-esteem and depression are closely linked [31–33]. Finally, self-esteem was found to peak in people in their fifties or sixties before decreasing dramatically thereafter. Two explanations for this decline have been put forward [34, 35]. The first refers to losing things associated with self-esteem (i.e. socioeconomic positions or social roles due to retirement, abilities such as physical and cognitive performances, etc.). The second relates to profound changes in attitudes toward oneself (elderly people tend to accept their limitations as they get older, which leads them to take a more modest view of themselves.). Because of the known correlations between self-esteem and (i) CM and (ii) depression, as well as diminished self-esteem from the age of 60, we endeavoured to assess the potential impact of self-esteem on the correlation between CM (mainly PA subtype) and the intensity of depression. We found that self-esteem could influence this effect (complete mediation with MADRS and partial mediation with QIDS-SR). Our findings suggest that low self-esteem is an important factor in geriatric depression especially in individuals with a previous history of physical abuse. In contrast to previously published studies [1, 5, 6], we found no significant correlation with personality traits, while our work focused specifically on TRD in the geriatric population. Our study sample was selected from highly specialised care centres in contrast to other published studies which focused on samples identified in the general population [1, 5, 6]. There were some limitations. Firstly, our sample was smaller than that of other studies carried out in geriatric populations [1, 5, 6]. This could account for the lack of correlation between personality traits and CM. Moreover, we did not compare our results to a control group of depressed patients with no resistance to treatment, in order to assess whether mediation through self-esteem is closely related to TRD. In addition to this, the cut-off age we used for geriatric depression was relatively young (60 years of age and above). However, this cut-off is the same as that used in other studies [1, 5, 6]. In addition, the diagnosis of EOD

and LOD was determined retrospectively. This may introduce a bias and may explain the lack of data in relation to the first major depressive episode. There could also be a recall bias regarding CTQ. Indeed, recall bias, or greater likelihood of reporting exposure in participants with MDD, has been highlighted (probably linked to negative bias in autobiographical memory) [36]. Moreover, the mediation analysis should be interpreted with caution given the fact that this was a cross-sectional study. Finally, the involvement of other factors such as cognitive decline and traumatic events occurring in adulthood, which could be linked to the intensity of depressive symptoms, at least in part, would require further investigation in future research involving geriatric TRD populations. Despite the need for future studies to confirm our findings, it seems important to take the mediation effect of self-esteem into account in routine clinical practice. Indeed, relevant data indicate the positive effect of psychotherapy, such as cognitive-behavioural therapy (CBT), on low self-esteem [37–41]. Therefore, CBT focused on self-esteem could be particularly useful for the management of TRD, especially in patients with early negative life experiences. In fact, given that higher self-esteem is significantly correlated with better treatment outcomes, increased self-esteem could improve the medical care outcome [42, 43].

## Conclusions

We highlighted a correlation between childhood trauma (mainly relating to PA) and the intensity of depressive symptoms in a geriatric TRD population. Our findings must be confirmed in well-designed prospective studies involving larger pathological populations. However, these results underpin the potential relevance of CBT predominantly focused on self-esteem as add-on treatment in the management of TRD in geriatric populations, especially in cases reporting CM.

## Abbreviations

BFI: Big Five Inventory

BMI: Body Mass Index

CM: Childhood Maltreatment

CTQ: Childhood Trauma Questionnaire

DSM: Diagnostic and Statistical Manual of Mental disorders

EA: Emotional Abuse

EN: Emotional Neglect

EOD : Early Onset Depression

FACE-DR: French Network of Expert Centres for Resistant Depression

LOD : Late Onset Depression

MADRS: Montgomery-Åsberg Depression Rating Scale

MDD: Major Depressive Disorder

MINI: Mini International Neuropsychiatric Interview

PA : Physical Abuse

PN: Physical Neglect

QIDS-SR: Quick Inventory of Depressive Symptomatology Self-

SA : Sexual Abuse

SD: Standard Deviation

TRD: Treatment Resistant Depression

## **Declarations**

### **Ethics approval and consent to participate**

The authors hereby confirm that all work-related procedures 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. The assessment protocol was approved by the relevant institutional review board [French CNIL (French Data Protection Authority): DR-2015-673]. The consent obtained from study participants was written and verbal.

### **Consent for publication**

Not Applicable

### **Availability of data and materials**

To get available data, please contact correspondent author: [antoineyrondi@gmail.com](mailto:antoineyrondi@gmail.com)

### **Competing interests**

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.

Christophe Arbus received honoraria (Janssen, Lundbeck, Otsuka) and carried out clinical studies in relation to the development of a medicine (Janssen).

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

Jean Baptiste Genty received speaker's honoraria 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 Rachieri received speaker's honoraria from Janssen Cilag.

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

Florian Stephan received honoraria from Otsuka.

Guillaume Vaiva received speaker's honoraria from Otsuka/Lundbeck (Annual participation at the reception day for new professors of psychiatry).

Emmanuel Haffen: acted in an advisory capacity, carried out clinical studies in relation to the development of a medicine, received personal research, study or travel allowances, 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 and Sanofi. He also held a managerial position at the FondaMental Foundation (Créteil) and the French Association of Biological Psychiatry and Neuropsychopharmacology.

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

Bruno Aouizerate received speaker's honoraria and 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, Pierre Michel Llorca, Julia Maruani, Fanny Molière, Michel Walter and Jean Petrucci have no conflicts of interest to declare.

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All authors have approved the manuscript.

### **Author's contributions:**

All authors were involved in patient selection and enrolment, clinical assessment and drafting of this paper.

AY, CA, DB, EH, WEH and BA were also involved in choosing the data set for this project and the statistical analysis.

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FondaMental Advanced Centres of Expertise (FACE-DR) collaborators

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## Tables

**Table 1.** Population characteristics.

	General population				EOD		LOD		p
	N	Min.	Max.	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
AGE, years	96	60	84	67.25 (5.67)	50 (52.1%)	65.66 (5.44)	25 (26%)	69.8 (5.77)	.003 <sup>t</sup>
Female(%)	60 (62.5%)				34		12		.094
Marital status (%)									.017 <sup>c</sup>
Single	8 (8.3%)				7		0		
Married	62 (64.6%)				27		20		
Seprared	2 (2.1%)				2		0		
Divorced	10 (10.4%)				8		1		
Widowed	3 (3.1%)				0		2		
Educational level									.429 <sup>c</sup>
Elementary school degree	23 (23.8%)				10		9		
High school degree	11 (11.5%)				4		3		
Youth training (National Vocational Qualification - Level 1, 2)	7 (7.3%)				3		1		
Business and Technology Education Council first diploma	10 (10.4%)				4		3		
High school degre+1	3 (3.1%)				3		0		
High school degre+2	9 (9.4%)				7		2		
High school degre+3	6 (6.3%)				2		2		
High school degre+4	4 (4.2%)				4		0		
High school degre+5	5 (5.2%)				3		1		
Doctoral Degree	6 (6.3%)				4		1		
LOD	25 (26%)								
MADRS score M0	92	8	44	28.2 (7.49)	47	29.34 (8.02)	25	27.28 (6.16)	.23 <sup>t</sup>
QIDS-SR M0	89	1	26	16.53 (4.94)	47	17 (4.95)	23	16.43 (4.5)	.646 <sup>t</sup>
Rosemberg score M0	79	10	36	22.47 (6.26)	39	22.31 (6.25)	21	22.38 (6.43)	.966 <sup>t</sup>
BFI extraversion	78	1	4.25	2.37 (.83)	41	2.28 (.77)	20	2.47 (.73)	.384 <sup>t</sup>
BFI agreeableness	78	3.20	5	4.14 (.46)	41	4.25 (.42)	20	3.97 (.45)	.02 <sup>t</sup>
BFI neuroticism	73	2	5	3.85 (.63)	40	3.96 (.53)	20	3.7 (.72)	.119 <sup>t</sup>
BFI conscientiousness	73	1.22	4.89	3.5 (.75)	40	3.7 (.73)	20	3.31 (.75)	.061 <sup>t</sup>
BFI openess	78	1.10	4.80	2.8 (.86)	41	2.96 (.83)	20	2.45 (.84)	.027 <sup>t</sup>
CTQ total score	82	25	78	37.35 (9.69)	44	38.86 (11.62)	21	35.57 (5.57)	.128 <sup>t</sup>
Emotional Abuse	82	5	10	5.51 (1.07)	44	5.55 (1.23)	21	5.52 (.75)	.999 <sup>t</sup>

Physical Abuse	82	5	22	11.48 (4.28)	44	12.18 (4.68)	21	11 (3.42)	.999 <sup>t</sup>
Sexual Abuse	82	5	15	7.2 (2.51)	44	7.05 (2.52)	21	7.38 (2.4)	.999 <sup>t</sup>
Emotional Neglect	82	5		5.35 (1.85)	44	5.43 (2.44)	21	5.19 (.68)	.999 <sup>t</sup>
Physical Neglect	82	5		7.82 (3.65)	44	8.66 (4.44)	21	6.48 (1.54)	.025 <sup>t</sup>

*BFI : Big Five Inventory ; <sup>C</sup> : Chi2 test ; CTQ : Childhood Trauma Inventory ; EOD : Early On Set Depression ; LOD : Late On Set Depression ; M0 : Month 0 ; MADRS : Montgomery-Asberg Depression Rating Scale ; Max. : Maximum ; Min. : Minimum ; N : Number ; QIDS-SR : Quick Inventory Depression Scale-Self Rated ; SD : Standard Deviation ; <sup>t</sup> : t-test*

**Table 2.** Association between the intensity of depressive disorder and childhood trauma at baseline.

		Unadjusted		Adjusted <sup>a</sup>	
		$\beta$	p-value*	$\beta$	p-value*
MADRS, score	CTQ, total score	0.3	0.04	0.274	0.07
	Emotional abuse, score	0.049	0.999	0.032	0.999
	Physical abuse, score	0.328	0.02	0.304	0.03
	Sexual abuse, score	0.263	0.09	0.251	0.11
	Emotional neglect, score	0.176	0.59	0.190	0.42
	Physical neglect, score	0.113	0.999	0.082	0.999
QIDS, score	CTQ, total score	0.338	0.002	0.302	0.005
	Emotional abuse, score	0.105	0.999	0.075	0.999
	Physical abuse, score	0.392	0.002	0.362	0.005
	Sexual abuse, score	0.199	0.37	0.184	0.45
	Emotional neglect, score	-0.037	0.999	-0.055	0.999
	Physical neglect, score	0.293	0.04	0.251	0.11

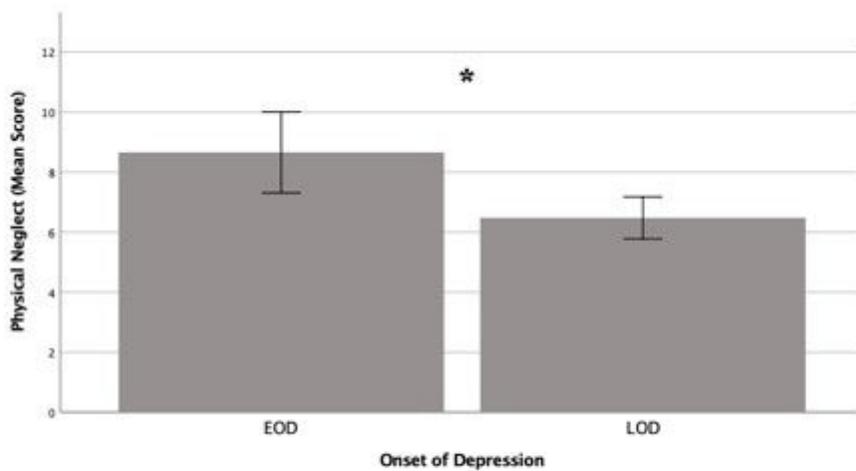
*CTQ: Child Trauma Questionnaire; MADRS: Montgomery-Asberg Depression Rating Scale; QIDS: Quick Inventory of Depressive Symptomatology; <sup>a</sup> Age and sex; \* Bonferroni corrections.*

**Table 3.** Association between self-esteem and childhood trauma at baseline.

		Unadjusted		Adjusted <sup>a</sup>	
		$\beta$	p-value*	$\beta$	p-value*
Rosenberg, score	CTQ, total score	-0.25	0.035	-0.25	0.036
	Emotional abuse, score	0.11	0.99	0.11	0.99
	Physical abuse, score	-0.31	0.04	-0.32	0.04
	Sexual abuse, score	-0.27	0.12	-0.27	0.1
	Emotional neglect, score	-0.06	0.999	-0.05	0.999
	Physical neglect, score	-0.12	0.999	-0.11	0.999

*CTQ: Child Trauma Questionnaire; MADRS: Montgomery-Åsberg Depression Rating Scale; QIDS: Quick Inventory of Depressive Symptomatology; STAI: State-Trait Anxiety Inventory; <sup>a</sup> Age and sex; \* Bonferroni corrections.*

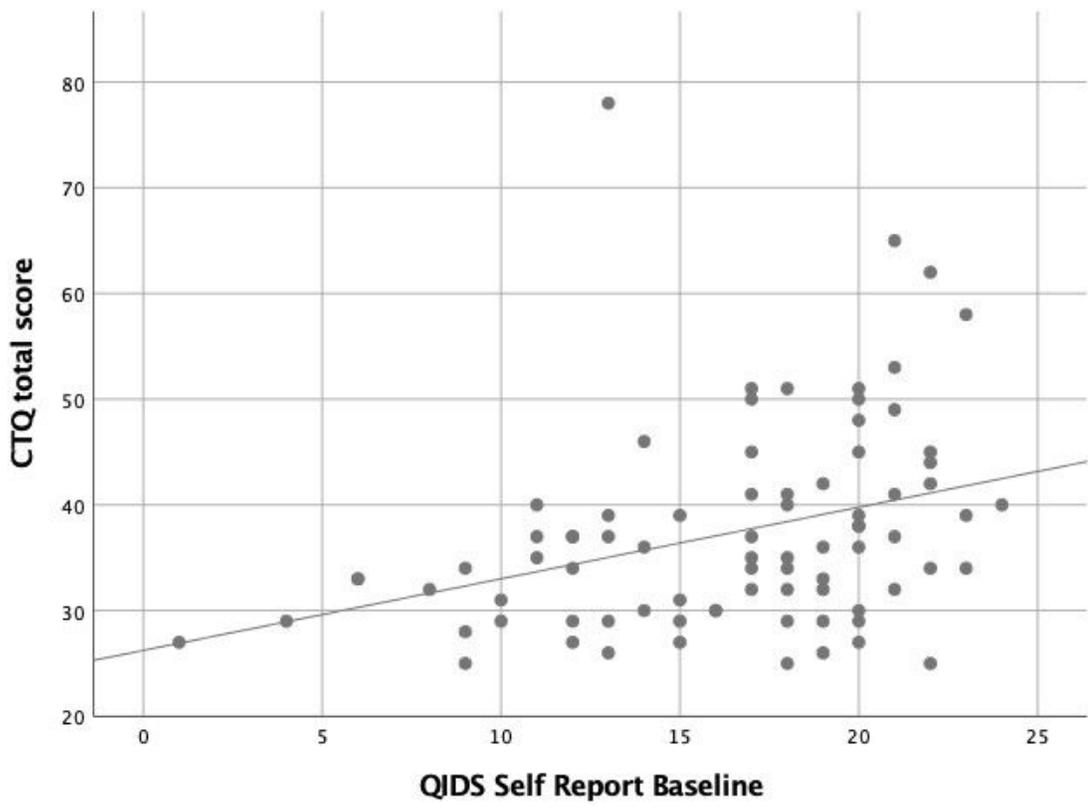
## Figures



*EOD: Early Onset Depression; LOD: Late Onset Depression; \*: p < .05*

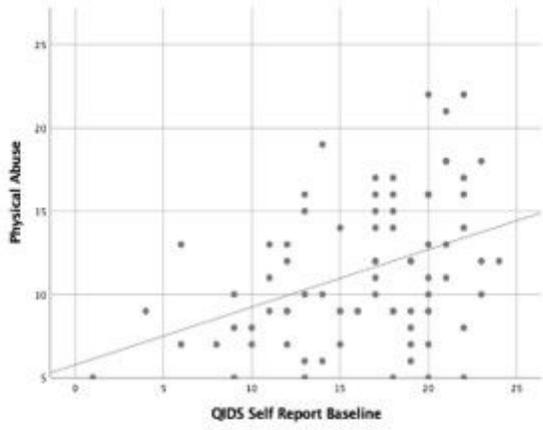
**Figure 1**

Difference of Physical Neglect between patients with Early Onset Depression (EOD) and Late Onset Depression (LOD)

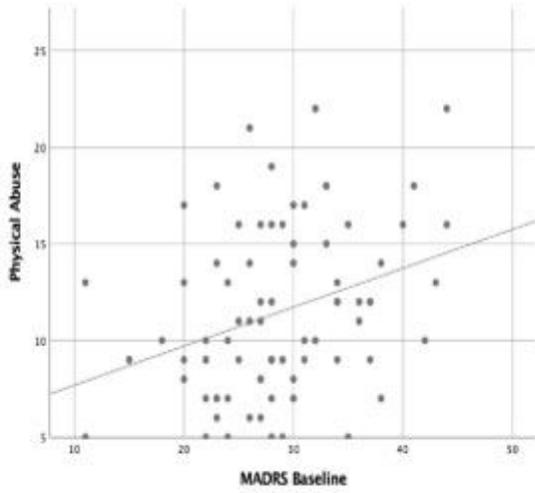


**Figure 2**

Association between Childhood trauma and intensity of self-reported depressive symptoms



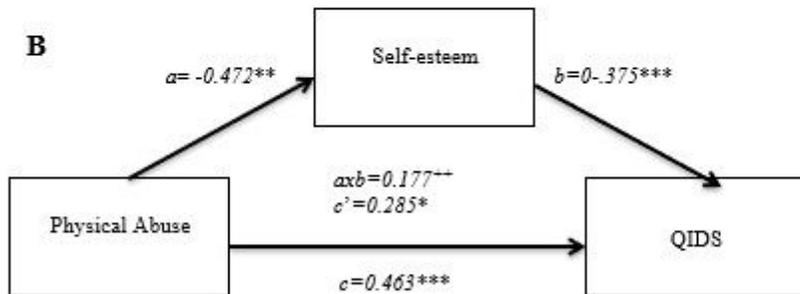
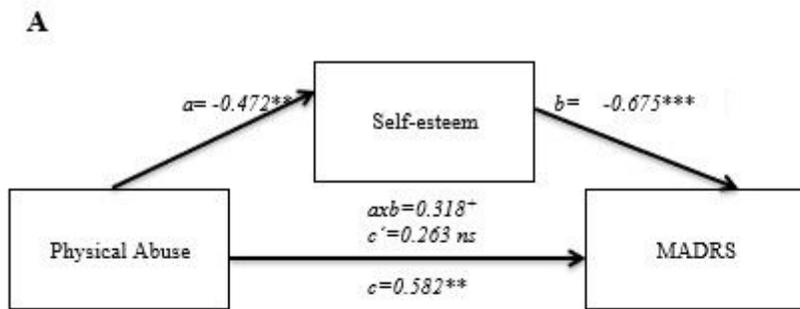
A



B

**Figure 3**

Association between Physical Abuse and intensity of depressive symptoms (A: QIDS-SR; B: MADRS)



*MADRS : Montgomery and Asberg Depression Rating Scale ; QIDS : Quick Inventory Depressive Symptomatology ; axb : indirect effect ; c' : direct effect ; c : total effect \* :  $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ , + : CI95% [0.07 ; 0.624], ++ : CI95% [0.036 ; 0.377], ns : non significant*

**Figure 4**

Self-esteem as mediator of Physical Abuse on intensity of depressive symptoms: A : MADRS ; B : QIDS