

Childhood adversities as specific contributors to the co-occurrence of posttraumatic stress and alcohol use disorders

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Abstract

There is much evidence that alcohol use disorders (AUD) often co-occur with posttraumatic stress disorders (PTSD), and that the comorbid condition is associated with a more severe clinical profile than that of PTSD without AUD. However, little is known about the role of childhood adversities as specific risk factors for the development of AUD in individuals presenting with PTSD. The aim of the study was to explore whether specific stressors from the spectrum of trauma and childhood adversities contribute to the development of AUD among subjects with PTSD. From a large community sample, of N=140 individuals with PTSD, N=24 (17.14%) received an additional diagnosis of AUD with an onset after the onset of PTSD. Those with comorbid PTSD/AUD and those with PTSD only were compared regarding type and features of their trauma, childhood adversities and psychiatric comorbidity. Compared to PTSD alone, PTSD/AUD was associated with higher levels of stress in terms of childhood adversities; in particular, sexual abuse below the age of 16, but also with having been brought up in a foster home. PTSD/AUD was also associated with an earlier age of adverse events. Treatment of AUD should include standardized assessments of trauma, especially of trauma experienced during childhood.

Keywords: Posttraumatic stress disorder; Alcohol use disorder; Comorbidity; Childhood trauma and adversity; Sexual abuse

1. Introduction

The DSM-IV defines posttraumatic stress disorder (PTSD) as a psychological reaction following exposure to a traumatic event characterized by symptoms of re-experiencing, avoidance and increased arousal for at least one month (American Psychiatric Association, 1994). PTSD is frequently associated with a considerable amount of comorbid conditions and suicidality (Galatzer-Levy et al., 2013; Müller et al., 2014). Previous research suggests that the course and clinical profile of PTSD might be especially complicated by comorbid alcohol use disorders (AUD) (Carter et al., 2011; Saladin et al., 1995). Indeed, the co-occurrence of PTSD and AUD is well documented by a number of studies (for a review Debell et al., 2014; Stewart et al., 1998). The prevalence of AUD in individuals with PTSD was estimated from 10% in a community sample up to 61% in Vietnam veterans (Debell et al., 2014). In the general population PTSD, defined according to the DSM-IV, was the anxiety disorder that was most strongly associated with AUD (Leray et al., 2011; Norman et al., 2012). Although the epidemiological prevalence of PTSD/AUD is rather low compared to other co-occurring common mental disorders, this condition has been associated with some of the poorest treatment outcomes, a higher number of comorbid psychiatric conditions, functional impairment as well as lower quality of life (Blanco et al., 2013; Sartor et al., 2010).

The awareness of the negative consequences of co-occurring PTSD and AUD has led to a sizeable amount of research on its etiology in order to develop appropriate prevention and treatment strategies (Pennington et al., 2014; Schaumberg et al., 2015). Thereby, some research has focused on the role of adverse environmental factors in the etiology and functional association of these conditions (Maniglio, 2012; Norman et al., 2012; Stewart et al., 1998). Epidemiological data suggest that approximately three quarters of individuals with AUD have experienced at least one traumatic event during their lives (Mills et al., 2006).

There is evidence that certain trauma types, specifically childhood traumatic experiences, are outstanding determinants in the development of AUD in individuals with PTSD (Khoury et al., 2010). From those, sexual abuse appeared to be the most specific risk factor for a PTSD/AUD comorbidity in clinical as well as epidemiological samples (Langeland et al., 2004; Sartor et al., 2010). A recent epidemiological study also found that other adverse environmental factors during childhood, which refer to familial dysfunction such as parental mental health problems or familial instability, were more likely in individuals with PTSD and AUD than in those with PTSD alone (Blanco et al., 2013). Even although these findings are based on bi-variate associations, they raise an interesting point since no other data on this topic are currently available. Previous research has shown that adversities in childhood, such as unstable family structures, parental mental health and overall unhappy childhood increase the risk for both PTSD (Peleikis et al., 2004) and AUD (Kauhanen et al., 2011; Kestila et al., 2008), independently from adversities experienced during adulthood. However, it is not well known whether childhood adversities constitute a unique risk in comorbid cases (PTSD/AUD) after accounting for background variables such as sociodemographic and clinical factors. Accordingly, a number of individual level determinants that were found to be associated with an increased risk of having both PTSD and AUD have been taken into account. These factors comprise male gender, older age, lower educational attainment and lower socio-economic status, or having more psychiatric comorbidities including other substance use disorders and suicide attempts (Blanco et al., 2013; Leeies et al., 2010; Sonne et al., 2003).

While most research on the comorbidity of PTSD/AUD focused on clinical samples the current study provides the opportunity to examine environmental factors associated with this condition in a community sample. Notably, relatively few epidemiological data on trauma and PTSD are available for Switzerland (Hepp et al., 2006; Perrin et al., 2014). Compared to most other Western countries, Switzerland is a relatively secure environment with rather low rates

of trauma exposure (Hepp et al., 2006; Perrin et al., 2014). On the other hand there were quite high rates of PTSD in the current sample compared to other populations with similar or even higher rates of exposure (Kawakami et al., 2014; Müller et al., 2014; Olaya et al., 2014), which makes this sample somewhat unique in the general population.

The current study aims to examine how trauma characteristics (type and age of trauma), and other environmental adversities that occurred during childhood (dysfunctional familial environment) are related to comorbid AUD in our community sample of individuals with PTSD. First, we hypothesized that sexual abuse would be more likely in the comorbid condition group than in the group with PTSD alone while we expected no such associations for other trauma types. Second, we expected trauma exposure below the age of 16, in particular sexual abuse, to be more strongly related to the comorbid condition than to PTSD alone. We also expected the comorbid group to report a younger recalled age of exposure to sexual trauma in particular than the group with PTSD alone. Finally, we sought to replicate earlier preliminary findings of high associations between childhood environmental adversities and comorbid PTSD/AUD. Thus, we hypothesized that the comorbid group were more likely to have experienced an adverse childhood environment than the group with PTSD alone.

2. Method

2.1 Sample and procedure

All data were collected within the PsyCoLaus study, a subsample from the larger CoLaus study, a randomly selected population-based cohort study in Lausanne, i.e. in the French-speaking part of Switzerland. From 2003 to 2006, a community sample of N=6,734 subjects aged between 35 and 75 years was recruited for the first wave of CoLaus, an epidemiological study designed to assess the prevalence of cardiovascular risk factors and diseases. From a

total of 5,535 individuals that finally participated in the CoLaus study, two thirds (N=3,720; 67.00%) agreed to take part in the additional psychiatric (PsyCoLaus) assessment. For the purpose of the current study, only those subjects with a lifetime diagnosis of PTSD (N=147; 3.95%) were selected. In order to explore comorbid AUD as a specific consequence of trauma and adversity or subtype of PTSD, respectively, those with a recalled age of AUD onset prior to the age of trauma (N=7) were excluded from the current analyses.

From the final study sample (N=140) about three quarters (72.14%) were females and the mean age was 48.39 years (SD=8.71). More than half of the study sample (56.39%) had basic education (compulsory school degree only), 25.56% higher education and 18.05% had a university-like degree. Socio-economic status (SES) was assessed according to the Hollingshead's index (Hollingshead, 1975). The mean SES was 3.01 (SD=1.35), the average sample therefore belonged to the middle class.

All interviews were conducted either by psychologists or by psychiatrists, who had been trained over a period of two months. Each interview and diagnostic assessment was reviewed by an experienced senior psychologist.

The study was approved by the Ethics Committee of the University of Lausanne, Switzerland. All participants provided written consent after being informed of the goal and funding of the study.

2.2 Measures

The data of the PsyCoLaus study were derived from the French version (Leboyer et al., 1995) of the semi-structured Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994). In addition to demographic features, the French version of the DIGS comprises information on a broad spectrum of DSM-IV Axis I and Axis II criteria (including AUD,

which comprised both abuse and dependence) as well as on suicide behavior (Preisig et al., 2009). PTSD and generalized anxiety disorders were assessed using the relevant sections of the French version (Leboyer et al., 1991) of the Schedule for Affective Disorders and Schizophrenia – Lifetime and Anxiety disorder version (Endicott and Spitzer, 1978).

In addition to AUD, the following categories, based on the DSM-IV criteria, were considered as further comorbid conditions of PTSD: major depressive disorder (MDD), generalized anxiety disorder (GAD), simple phobia, social phobia, agoraphobia, obsessive-compulsive disorder (OCD), panic disorder, antisocial personality disorder, other substance-related disorders (cannabis, solvent, hallucinogens, stimulants, cocaine, sedatives, or narcotics abuse or dependence), and suicide attempts.

Exposure to potentially traumatizing events was assessed using five separate questions: 1.) accident, 2.) physical assault, 3.) combat and/or war, 4.) witness of murder, violence or death by an accident, and 5.) sexual abuse. Subsequently, all distinct events reported by the respondent were repeated by the interviewer and the respondent was asked to identify the most upsetting event and the recalled age of first exposure to this event. Age of first sexual abuse was asked separately. Events below the age of 16 years were double-coded as “childhood trauma”, which was further divided into “childhood sexual abuse” and “other childhood trauma”. The category “other childhood trauma” included all previously mentioned events from categories 1 to 4 (i.e. except for sexual abuse) that were experienced below the age of 16. Furthermore, participants were asked about other chronically adverse or dysfunctional environments during childhood that might have negatively impacted their development, namely: being placed in a foster home, having divorced parents, not being raised by biological parents, having had an overall unhappy childhood, and having parents with mental health problems.

The French version of the DIGS as well as the anxiety sections of the SADS-LA revealed excellent inter-rater and fair to good test-retest reliability for mood (Preisig et al., 1999), substance use (Berney et al., 2002) and anxiety disorders (Leboyer et al., 1991). To test the reliability of the PTSD section of the French version of the SADS-LA a three-year follow-up study on 176 psychiatric patients was conducted, which revealed test-retest reliability of 0.69 for the PTSD diagnosis (unpublished). Furthermore, the test-retest coefficients for exposure to violent crime and sexual trauma in this sample were as high as 0.84 and 0.57, respectively, although those for exposure to accidents and witnessing trauma to others were only 0.30 and 0.22, respectively. The test-retest reliability for exposure to war could not be tested in this sample given its rareness.

2.3 Statistical analysis

The study sample consisted of two diagnostic conditions: 1.) individuals with a diagnosis of PTSD but no additional AUD, and 2.) individuals with a diagnosis of PTSD and (later onset) comorbid AUD.

Descriptive statistics are provided for socio-demographic features, comorbid conditions and PTSD symptom types. Frequencies and percentages are given for categorical variables, and means (M) and standard deviations (SD) for continuous variables. To examine for differences between groups we calculated Chi-square statistics for categorical variables and one-way ANOVAs for continuous variables.

Then, we assessed whether specific trauma type or adversity variables were associated with the co-occurrence of PTSD and AUD compared to the occurrence of PTSD alone. Furthermore, we tested whether these associations were confounded by other variables, such as socio-demographic features, PTSD symptom types as well as other psychiatric

comorbidities. A series of binary logistic regression models were calculated, in which, starting with an unadjusted model, the aforementioned confounders were included using a stepwise procedure. Odd's ratios (OR) and 95% Confidence Intervals (95%CI) were computed to examine for differences between conditions. Since multiple tests were performed for: 1) type of lifetime trauma, 2) type of childhood trauma, and 3) adverse childhood environment, the rate of Type I error might be inflated. Therefore, p-values were corrected using the Bonferroni method by dividing the p-value (<0.05) by the number of tests within each of these categories. Accordingly, a certain predictor was identified as clinically relevant if it reached the level of statistical significance after adjusting for multiplicity.

All analyses were conducted using Stata/SE 12 (StataCorp, 2011).

3. Results

Table 1 shows the distribution of socio-demographic and clinical variables for the total sample and the subsamples of subjects with PTSD/AUD (17.14%) and PTSD alone (82.86%), respectively. The comorbid group did not differ from those with PTSD alone regarding any socio-demographic characteristics. However, compared to PTSD alone, comorbid PTSD/AUD was associated with higher rates of antisocial personality disorder, other substance-related disorders, lifetime suicide attempts as well as with a higher occurrence of PTSD avoidance symptoms.

- insert Table 1 -

Table 2 displays the results of the logistic regression models with estimated conditional probabilities for comorbid PTSD/AUD versus PTSD alone by different trauma types and other childhood factors. Models were serially adjusted for socio-demographic features, PTSD symptom types and comorbidity, and were corrected for multiple testing in categories with multiple predictors (lifetime trauma, type of childhood trauma, and adverse childhood environment). Accordingly, compared to the category of PTSD alone, lifetime sexual abuse was initially positively associated with comorbid PTSD/AUD, when unadjusted and adjusted for socio-demographic features, but this association only reached statistical significance after the type I error correction procedure in the latter model. In the models with higher order adjustments (i.e. PTSD symptom types and comorbidity), the risk of lifetime sexual abuse no longer reached statistical significance. In contrast, sexual abuse that occurred below the age of 16 and younger age of trauma exposure in general were strongly associated with comorbid PTSD/AUD, even when fully adjusted. Similarly, overall childhood adversities, in particular having been brought up in a foster home and having had an unhappy childhood were associated with comorbid PTSD/AUD in all the models, although the latter association no longer reached statistical significance in the final model after correction for type I error. The other childhood factors were not linked to comorbid PTSD-AUD in any model after correction for type I error.

- insert Table 2 -

4. Discussion

The present study aimed to examine environmental factors that potentially contribute to the development of comorbid AUD in subjects with pre-existing PTSD. For this analysis, individuals with a lifetime diagnosis of PTSD were chosen from a large representative sample from the Swiss community. Lifetime and childhood traumatic events as well as markers of

adverse or dysfunctional childhood environments were examined for their association with the development of AUD.

As expected, our results strongly suggest that both traumatic and adverse events in childhood might be important etiological factors for the co-occurrence of PTSD and AUD. Approximately three quarters of subjects with comorbid PTSD/AUD (versus one third of those with PTSD only) experienced at least one childhood trauma, mostly as sexual abuse. Furthermore, those with both conditions were on average 10 years younger (14 vs. 24 years) at first trauma exposure and approximately 5 years younger in case of sexual abuse (10 vs. 15 years), although the latter difference did not reach statistical significance. These findings are supported by earlier research. For example, Khoury et al. (2010) found that higher loads of childhood trauma generally had a progressive effect on both levels of alcohol use and PTSD symptom severity. Another study found sexual abuse before age of 16 to be independently associated with comorbid PTSD in a sample of treatment-seeking alcoholics (Langeland et al., 2004). Similarly, sexual abuse below the age of 14 strongly contributed to the development of AUD in women with PTSD (Sartor et al., 2010). Our findings expand on those of previous research by including additional types of childhood adversities that might be associated with comorbid AUD in individuals with PTSD. Associations were found for overall childhood adversities and particularly for growing up in a foster home or having had an overall unhappy childhood, although the latter association did not remain significant in the fully adjusted model after correction for type I error. Nevertheless, it can be suggested that both exposure to childhood trauma and early adversities may provoke important changes in biological stress response systems that increase the risk of PTSD and possibly an attempt to “self-medicate” negative affective symptoms with higher alcohol use. In particular, the experience of sexual abuse during childhood can be regarded as one of the most pervading interpersonal traumatic events that a child can experience, which might have long-term effects on the affected person’s life (Gaon et al., 2013).

Actually, our findings further suggest that individuals with PTSD/AUD presented with a more severe clinical profile in relation to the number of comorbid disorders compared to those with PTSD only. Congruently, previous research has suggested that greater illness severity among individuals with PTSD/AUD was more likely among those with adverse childhood experiences (Blanco et al., 2013; Ouimette et al., 1996). Our findings further suggest that the comorbid group experienced a more severe form of PTSD than those with PTSD alone, indicated by at least a greater number of avoidance symptoms. There is evidence showing that avoidance symptoms were most consistently associated with alcohol misuse (Debell et al., 2014; Müller et al., 2015) as well as with higher rates of posttraumatic comorbidity and greater impairment (Jakupcak et al., 2010; North et al., 1999). More severe experiences, such as childhood and/or sexual abuse appear to play a central role in maintaining this association (Müller et al., 2015). Thus, as an effective behavioral strategy to avoid unpleasant emotions or thoughts linked to the adverse experience, avoidance symptoms increase the risk of PTSD chronification, which might be linked to higher alcohol misuse, more withdrawal and lower remission rates (Rosenthal et al., 2005).

The current study has some limitations that have to be acknowledged. First, the study was based on cross-sectional data; therefore causal relations cannot be proven. Although relationships have been shown to exist between early life adversities assessed retrospectively and later comorbid PTSD/AUD conditions further prospective research is needed to confirm our important findings. Furthermore, due to a lack of corresponding data we could not test whether associations between childhood adversities and PTSD/AUD might still exist after controlling for parental substance abuse. However, in a review other authors have concluded that later life risky substance consumption may specifically arise from adverse childhood experiences while parental substance abuse was not found to contribute significantly to this association (Downs and Harrison, 1998). Furthermore, the structured interview that was used to determine diagnoses of PTSD and other Axis I and II disorders was based on the diagnostic

criteria of DSM-IV while DSM-5 is now currently in use. Therefore, the presence of DSM-5 PTSD and its association with AUD needs to be determined in further research. And finally, findings on significant associations between trauma or adversities and PTSD/AUD comorbidity should be interpreted with caution due to the large confidence intervals. This might be due to the small number of individuals with comorbid PTSD/AUD, which, however, reflect the given prevalence of this condition. Therefore, our findings need to be replicated in larger samples.

In summary, our study suggests that the co-occurrence of PTSD and AUD remains frequent even in a sample with lower rates of PTSD and AUD, indicating a strong relationship between both disorders. Our results are among the first to provide clear evidence, after controlling for potential confounders, that this condition is clearly linked to childhood trauma, in particular to experiences of sexual abuse and, moreover, to other childhood environmental adversities. They have important implications for early identification, prevention and treatment. Early identification and treatment of individuals exposed to childhood trauma and adversity could reduce the probable co-occurrence of PTSD and AUD, related impairment and societal burden. Therefore, it seems important to develop uniform and standardized screening methods not only for trauma but also for other adversities during childhood to identify individuals that are at increased risk for the development of AUD. Similarly, treatment of AUD would benefit from such an assessment since it allows health care providers to identify potential triggers of AUD and therefore to improve long-term outcomes. Thus, integrated treatment should be provided that specifically focuses on comorbid substance abuse in those who report severe traumatization. To further enhance long-term remission after AUD treatment, subsequent interventions should focus on PTSD treatment. Since PTSD symptoms were found to trigger AUD, they might likewise play an important role in the remission of AUD (Bradizza et al., 2006). Unfortunately, the majority of dually diagnosed patients were never previously referred to any trauma-focused treatment (Brown et al., 1998).

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Tab 1. Socio-demographic characteristics, comorbidity and PTSD symptom types in the overall study sample and in subsamples stratified by diagnostic status

		Study sample (N=140)		Group comparison		
				PTSD alone (N=116)	PTSD/AUD (N=24)	
		N	%	%	%	p-value
Sex	Female	101	72.14	75.00	58.33	0.097
Age	Years (M±SD)		48.39±8.71	49.26±8.60	50.04±9.42	0.690
Education	Low	75	56.39	52.29	75.00	0.073
	Medium	34	25.56	29.36	8.33	
	High	24	18.05	18.35	16.67	
SES	Hollingshead Index (M±SD)		3.01±1.35	3.01±1.34	3.00±1.44	0.978
Comorbid disorders	MDD	103	73.57	74.14	70.83	0.738
	GAD	16	11.43	9.48	20.83	0.112
	Agoraphobia	16	11.43	9.48	20.83	0.112
	Simple phobia	32	22.86	22.41	25.00	0.784
	Social phobia	32	22.86	20.69	33.33	0.179
	OCD	7	5.00	3.45	12.50	0.064
	Panic disorder	21	15.11	14.66	17.39	0.738
	Antisocial PD	11	7.91	5.22	20.83	0.010
	SUD	13	9.29	5.17	29.17	<0.001
	Suicide attempts	41	29.29	25.86	45.83	0.050

PTSD symptoms	Re-experience	3.66±1.32	3.70±1.25	3.50±1.62	0.504
	Avoidance	4.71±1.38	4.55±1.33	5.46±1.38	0.003
	Hyperarousal	3.28±1.10	3.22±1.07	3.54±1.22	0.199

Note: PTSD=Posttraumatic stress disorder; AUD=Alcohol use disorder; SES=Socio-economic status; M±SD=Mean±standard deviation; MDD=major depressive disorder; GAD=generalized anxiety disorder; OCD=obsessive-compulsive disorder; Antisocial PD=antisocial personality disorder; SUD=substance use disorders.

		PTSD alone (N=116)	PTSD + AUD (N=24)	PTSD/AUD versus PTSD alone			
				Unadjusted	Adjusted for socio-demographic features	Adjusted for socio-demographic features & PTSD symptom types	Adjusted for socio-demographic features, PTSD symptom types & psychiatric comorbidity
	%	%	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Type of lifetime trauma ^a	Accident	13.79	8.33	0.57 (0.12-2.65)	0.59 (0.12-2.90)	0.92 (0.16-5.28)	0.72 (0.07-7.36)
	Crime	21.55	12.50	0.52 (0.14-1.89)	0.58 (0.15-2.20)	0.75 (0.18-3.20)	1.07 (0.18-6.29)
	War	3.45	4.17	1.22 (0.13-11.40)	0.53 (0.05-5.80)	0.65 (0.05-7.73)	0.71 (0.04-11.48)
	Witnessing Violence	32.76	25.00	0.68 (0.25-1.86)	0.48 (0.16-1.46)	0.41 (0.12-1.44)	0.42 (0.09-2.01)
	Lifetime sexual abuse	28.45	50.00	2.52 (1.03-6.16)* ns	4.54 (1.52-13.58)** ¹	3.16 (0.98-10.18)	3.36 (0.64-17.73)
Any childhood trauma		32.76	70.83	4.98 (1.91-13.04)***	7.94 (2.46-25.59)***	7.80 (2.09-29.10)**	20.48 (2.81-149.12)**
Type of childhood trauma ^a	Childhood sexual abuse	18.10	45.83	3.83 (1.51-9.72)** ²	6.21 (1.95-19.77)** ²	4.47 (1.30-15.36)* ²	7.81 (1.38-44.28)* ²
	Other childhood trauma	14.66	25.00	1.94 (0.67-5.59)	1.89 (0.61-5.87)	2.34 (0.64-8.51)	2.94 (0.58-14.91)
Number of events (M±SD)		1.33±0.59	1.21±0.51	0.66 (0.27-1.61)	0.65 (0.25-1.66)	0.51 (0.18-1.46)	0.52 (0.12-2.31)
Age of event (M±SD) ^b		24.01±14.16	14.00±8.68	0.35 (0.17-0.68)**	0.28 (0.13-0.62)**	0.33 (0.15-0.74)**	0.25 (0.09-0.72)*
Age of first sexual abuse (M±SD) ^b		14.74±8.60	10.00±4.43	0.41 (0.16-1.08)	0.49 (0.16-1.51)	0.53 (0.13-2.25)	- ^c
Adverse childhood environment ^a	Foster home	17.24	45.83	4.06 (1.59-10.36)** ¹	4.28 (1.51-12.09)** ¹	7.68 (2.08-28.32)** ¹	8.78 (1.84-41.78)** ¹
	Parents divorced or separated	22.41	37.50	2.08 (0.82-5.29)	2.14 (0.79-5.82)	2.05 (0.65-6.45)	1.28 (0.28-5.88)
	Not raised by biological parents	42.24	66.67	2.73 (1.08-6.90)* ns	3.38 (1.22-9.34)* ns	4.55 (1.40-14.79)* ns	3.65 (0.83-15.92)
	Unhappy childhood	25.86	45.83	2.43 (0.98-5.99)	4.74 (1.54-14.58)** ¹	7.72 (1.97-30.31)** ¹	9.61 (1.63-56.57)* ns
	Parental mental health problems	33.33	54.17	2.36 (0.97-5.78)	3.32 (1.20-9.22)* ns	3.78 (1.18-12.08)* ns	2.60 (0.61-11.10)

Any adverse childhood condition	62.07	79.17	2.32 (0.81-6.66)	3.33 (1.02-10.89)*	4.36 (1.18-16.16)*	2.27 (0.49-10.50)
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Tab 2. Conditional probabilities of PTSD/AUD comorbidity versus PTSD alone

Note: PTSD=Posttraumatic stress disorder; AUD=Alcohol use disorder; SES=Socio-economic status; Crime=Physical assault; M \pm SD=Mean \pm standard deviation; OR=Odds ratios; 95%CI=95%confidence intervals; ^a p-values of estimates were corrected for type I error (Bonferroni); ^b Score z-transformed for logistic regressions; ^c Data not available due to too small cell weights; *** p<0.001; ** p<0.01; * p<0.05; ¹ p<0.01 (Bonferroni-corrected); ² p<0.025 (Bonferroni-corrected); ^{ns} not significant (Bonferroni-corrected).