Is there a diagnosis-specific influence of childhood trauma on later educational attainment? A machine learning analysis in a large help-seeking sample

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Abstract

Background: Childhood adversities and trauma (CAT) are associated with poor functional outcome. However, the influence of the single CAT aspects on the risk of a poor functional outcome within different mental disorders has not been investigated so far. Our aims were (i)to predict individual functional outcome based on CAT (ii)to examine whether the prediction power differs within different diagnostic groups (clinical high-risk for psychosis (CHR), psychosis, affective disorders, anxiety disorders) (iii)to compare the specific patterns of CAT experiences, influencing functional outcomes in these groups.

Method: Clinical data of 707 patients (mean age:25.09 years (SD=5.6), 65.5% male) of the Cologne Early Recognition and Intervention Center were assessed with the Trauma And Distress Scale. Functional outcome was estimated by the Social and Occupational Functioning Assessment Scale and school educational attainment. Using machine learning, we generated individualized models to predict functional outcome and to identify specific CAT patterns.

Results: Across the entire sample, the best prediction for the functional outcome achieved a balanced accuracy (BAC) of 0.6. After splitting into the single diagnostic groups, an improvement with best results in the psychosis group (BAC=0.70) was observed. Considering specific CAT patterns, the most predictive items depicted a positive and caring environment – or the absence of these, a positive self-image and experiences of bullying.

Conclusions: Our results indicated that CAT was differentially associated with functional outcome in the various mental disorders. Thus, the importance of mediating variables, that might explain the interindividual differences in the vulnerability to CAT, like resilience factors, appeared to be crucial.

Keywords: childhood maltreatment, abuse, neglect, distress, functioning, machine learning

Introduction

Thirty to 40% of the adult population in Western countries have been exposed to childhood adversities and traumatic experiences (CAT) such as sexual (SA), emotional (EA) and physical abuse (PA), or emotional (EN) and physical neglect (PN) (Scher et al.,2004). CAT appears to substantially influence the future life, contributes to the development of psychiatric disorders and is associated with future impairments in adulthood (Kessler et al.,2010). CAT relates to poor future functional outcome in multiple domains including negative effects on physical health, impaired neurocognitive functioning, financial, educational, occupational and social functioning, and an increase in risky and criminal behavior (Copeland et al.,2018). Thus, CAT is associated with high economic and social costs for the society (Cutajar et al.,2010). In the United States, the estimated lifetime costs per child maltreatment victim cases incurred in 2010 was about $210,012 (Fang et al.,2012). In order to alleviate this high societal and personal burden, it is of high importance to disentangle the differential effects of individual CAT domains on functional outcome with the aim to initiate targeted preventive interventions at an early stage. Interestingly, recent results indicate that CAT domains have a differing impact on various psychiatric diseases (Carr et al.,2013). Considering interrelations of both disorders and CAT domains, a recent analysis based on structural equation modelling pointed out that depressive and anxiety disorders were linked to both PA and EN, whereas manic and psychotic disorders were specifically related to PA and substance dependence to EN (Salokangas et al.,2019). Another study reported EA to be most frequently correlated with personality disorders (Neumann,2017). Trauelsen and colleagues (2015) found, that EA, EN and PA were specifically associated with first episode psychosis, while Thompson and colleagues (2009) reported positive symptom severity in patients with a clinical high-risk for psychosis (CHR) as associated with PA and SA. Furthermore, previous work of our group showed that specific associations between different areas of CAT and perceived stress are existing. CAT areas that reflected a dimension of deprivation, i.e. neglect experiences, were related to a stress network community representing low perceived self-efficacy. In contrast, CAT associated with threat, i.e. experiences of abuse, was specifically associated with a stress network community that reflected perceived helplessness (Betz et al.,2020).

Numerous clinical and psychosocial variables have been identified that are associated with poor functional outcome in mental disorders (Gade et al.,2015). However, associations were typically described on group-level, thus not allowing precise predictions for individual patients. Modern machine-learning techniques allow overcoming this drawback by identifying multivariate patterns that are predictive at the individual level. First studies using machine-learning in patients with recent-onset depression and CHR support the potential of various baseline clinical data in predicting social, clinical and treatment outcomes with accuracies of 65-83% (Koutsouleris et al.,2018). In precision or personalized medicine, such individual-based machine-learning algorithms are thought to enable novel and individualized approaches for risk-stratification in help-seeking populations (Fernandes et al.,2017).

To the best of our knowledge, no study so far investigated whether the individual functional outcome of patients can be predicted merely by the specific patterns of single CAT experiences. Thus, our current study aimed 1) to identify multivariate patterns of CAT that are predictive for future functional outcome on an individual patient level; 2) to investigate the relative contribution of CAT for future functional outcome by comparing prediction accuracy between diagnostic groups; and 3) to compare the specific multivariate patterns of CAT experiences that influence functional outcomes in the different diagnostic groups.

Method

Sample

The sample consisted of N=1708 patients who sought help at the Early Recognition and Intervention Centre for Mental Disorders (FETZ) (Schultze-Lutter et al.,2009) at the Department of Psychiatry and Psychotherapy at the University Hospital in Cologne, Germany, between 2009 and 2013. The FETZ is an outpatient unit that offers patient low-threshold referral, diagnostic evaluation and CHR assessment. After exclusion of patients with missing information regarding CAT (≥ 20% of items), the sample size reduced to n=707 (41.4%) with a mean age of 25.09 years (SD=5.6); 463 (65.5%) were male (Table 1). Diagnostic groups significantly differed in their current functioning (Kruskal-Wallis statistic=32.309, df=4.000, p=<0.001). A comparison of the included and excluded samples is provided in Table S1. All patients gave their written informed consent to use their clinical data for scientific analyses. The study was approved by the ethics committee of the Medical Faculty of the University of Cologne (ID 19-1618_1) and registered at the German Clinical Trials Register (DRKS-ID: DRKS00024469).

Subgrouping according to diagnostic assessment

Diagnosis according to the International Statistical Classification of Diseases and Related Health Problems, Version 10 (ICD-10) (World Health Association,1999) were made by experienced and trained psychologists and psychiatrists based on all available information; clinical diagnoses were also discussed during weekly case conferences with the senior doctor/ psychologist. We classified patients with any type of psychotic disorder under 'psychosis' (F2) including any schizophrenia diagnosis, schizoaffective disorder, cannabis-induced psychosis, brief psychotic disorders, delusional disorder psychotic depression and psychotic bipolar disorder. Patients with CHR, included by Cognitive Disturbances (COGDIS) and Cognitive Perceptive basic symptoms (COPER) according to the Schizophrenia Proneness Instrument (SPI-A) (Schultze-Lutter et al.,2007), and/ or UHR criteria (Phillips et al.,2000) according to the Structured Interview for Psychosis-Risk Syndromes (SIPS) (McGlashan et al.,2010) were classified as 'CHR'. Patients fulfilling a genetic risk and functional deterioration (GRFD) state, defined by a current 30% or greater reduction in the functional disability score of the split version of the Global Assessment of Functioning Scale (GAF-F) (Pedersen et al.,2007) compared with the highest lifetime level of functioning, and having a first-degree relative with a history of any psychotic disorder, or having a schizotypal personality disorder, were also included in the CHR group. Patients with any non-psychotic disorder of the affective spectrum (F3) were classified as 'affective' and patients with any disorder from the anxiety spectrum (F4) were classified as 'anxiety'. If patients fulfilled criteria for more than one diagnostic category, preference was given to the more severe diagnosis respectively the one which is closer to psychosis. Thus, in case patients fulfilled criteria for any psychotic disorder as defined above, they were categorized under 'psychosis'. If patients met the criteria for an affective or anxiety disorder and also the CHR criteria, they were categorized as CHR. If patients met criteria for both anxiety and affective disorders, they were assigned to the disorder group that was clinically more prominent.

Assessments

All assessments were conducted by trained psychiatrists and psychologists. The primary assessment of functioning was based on patients' school educational attainment. A school education level of 3

according to the International Standard Classification of Education (ISCED) (Bundesministerium für Bildung und Forschung,2020) were categorized as high and ISCED equivalents ≤ 2 as low educational attainment, respectively. A school graduation of 3 equals an upper secondary education that directly prepares for tertiary education (such as university) and usually offers an increased range of subject options and streams. A school graduation of 2 equals a lower secondary education, building on primary education, typically including a more subject-oriented curriculum.

The Social and Occupational Functioning Assessment Scale (SOFAS) (Goldman et al.,1992) was used as a secondary measure of functioning. On this clinical observer-rated scale, the patient's level of functioning is estimated from 1 (low) to 100 (high) based on all available information. The SOFAS score at time of assessment (current) and the highest functioning within the last year were recorded. A cut-off value of 70 on the SOFAS was used to separate good from poor functioning (Goldman et al.,1992). To operationalize the construct "functional outcome" for the following machine-learning analysis, we built three different comparisons: First, the differentiation between high and low school educational attainment; second the comparison between a high (>70) or low (≤70) current SOFAS score and third, the comparison between high or low highest-past-year SOFAS score.

For the assessment of CAT, we used the German version of the Trauma And Distress Scale (TADS) (Table S2) that was developed by Patterson and colleagues (2002). The TADS is a retrospective self-assessment instrument for CAT in adult samples with good psychometric properties (Salokangas et al.,2016). It includes 43 items with 25 items focusing on five core domains: emotional neglect (EN, five items), emotional abuse (EA, five items), physical neglect (PN, five items), physical abuse (PA, five items), and sexual abuse (SA, five items). The remaining 18 items include three lie items and 15 items on general adversity/ distress (DI) assessing loss events, discrimination, bullying and guilt feelings (Salokangas et al.,2016). Rating is carried out on a 5-point Likert scale according to the frequency of the experience (0=never to 4=almost always). To control for response bias, some TADS items are worded positively so that low raw scores indicate more pronounced CAT experiences. These items were reversed before calculating the TADS sum score but entered as raw scores in single items analyses. Additionally, the items "I have been bullied at work" and “I did well at school” were removed from the analysis, as they refer to current rather than past experiences.

In order to control our results for the socio-economic status patients’ parents, school leaving graduation and current occupation, separately for mother and father were recorded. School-leaving graduations were recorded according to seven categories (no school-leaving certificate; high school graduation; technical diploma; 10^{th} grade, junior high school; other school-leaving certificate; still at school), also orientated on the ISCED (Bundesministerium für Bildung und Forschung,2020). The occupational status was divided into 9 categories (managers (1); professionals (2); technicians and associate professionals (3); clerical support workers (4); service and sales workers (5); skilled agricultural, forestry and fishery workers (6); craft and related trade workers (7); plant and machine operators and assemblers (8); elementary occupations (9)) based on the International Standard Classification of Occupations (ISCO) 2008 (International Labour Office, Geneva;2010).

Statistical & Machine Learning Analysis

Analyses based on Spearman’s rank correlation test were used to investigate the relationship between TADS total score and functioning (current functioning, highest functioning past year). Mann-Whitney U-

tests were used to test for differences in TADS total scores between patients with high compared to low educational attainment.

To investigate the predictive patterns of CAT as measured by individual TADS items, we employed a machine-learning pipeline based on an elastic-net classifier (Zou and Hastie,2005). By including a flexible regularization term, this algorithm allows binary classification, while, at the same time, controlling the fitting to noisy, un-informative variables. The elastic-net classifier was embedded in a repeated, nested cross-validation framework, including an inner cross-validation and an outer cross-validation with 5 folds and 10 repetitions at both levels. Patients with more than 20% of missing values in the TADS or with missing data in an outcome domain were excluded from the analysis. Preprocessing of features included median imputation of missing values and down sampling of the majority class to balance the distribution in the outcome labels (e.g. equal number of participants with high and low functioning), and normalizing features to a range between 0 and 1. For the elastic-net classifier hyperparameters were tuned to improve classification using random search. 100 iterations were performed for each CV-fold to identify optimal lambda (between 0 and 1) and alpha (between 0 and 1). All preprocessing steps and hyperparameter optimizations were embedded in the CV scheme to allow reliable estimates of classifier performance. Variable importance was estimated by averaging absolute model coefficients across all cross-validation folds. All computations were performed using the mlr package (Bischl B, 2016) in the R language for statistical computation version 4.0.2 (R Core Team,2017).

Results

TADS scores

Association of CAT and functional outcome

Analysis using Spearman's rank correlation test indicated a significant association between TADS total score and current functioning (rho=-0.174, p=0.005) and highest functioning past year (rho=-0.275 p=<0.001) (**Figure 1A, B**). Patients with low educational attainment showed higher TADS total scores as compared to patients with high educational attainment (Mann-Whitney U-test, W=13829, p=<0.001) (**Figure 1C).** There were also significant differences in the TADS sum scores of the different subscales across all diagnostic groups (**Table S3).**

Predictive patterns of CAT

The computed classifiers, based on the TADS single items, distinguished within the three different functional outcome groups only slightly above chance level. The best predictive power was obtained on highest functioning past year (BAC=0.60) followed by educational attainment and current functioning (both BAC=0.59) (**Table 2)**. All three effects remained significant after controlling for age and sex by including them as predictors.

After division into the different diagnostic groups, the pattern of the single TADS items proved to be predictive for functioning (**Figure 2A)**. Educational attainment (low vs. high) was chosen here as main outcome, because it was considered as the most stable prediction of the functional outcome, depicting performance even over a longer period of time. For the CHR group, results were not better than chance (BAC=0.54). Slightly better values could be achieved in the affective spectrum (BAC=0.61) and the anxiety group (BAC=0.65). The best predictive value of BAC=0.70 was found in the psychosis spectrum group (**Table 3, Figure 2A**).

The individual predictive pattern of the TADS subscales revealed a heterogeneous picture (**Figure 2B**). In the psychotic group and the CHR group, the subscales EN, PA and DI were most predictive. However, the results of the CHR group should be viewed with caution here, as the predictive power of the model was not very good. In the affective group, PN, PA and DI and in the anxiety group, PN, DI and EN appeared to be most predictive for the functional outcome. In both groups, particularly PN showed the highest predictive value.

Concerning the predictive pattern of the single TADS items in the different diagnostic groups the highest predictive value was obtained by the item "If I needed treatment someone would always take me to see a doctor or nurse when I was young" (item 31, part of PN, weight 0.18). The item "When I was young, I could make friends easily" (item 43, part of DI, weight 0.22) could be shown to be most predictive for the functioning in the anxiety group. In the CHR group "I felt afraid of someone in my family" (item 42, part of DI, weight 0.33) reached the highest weight for the forecast of the later functional outcome (**Figure 2C**, **Table S4**). Again, due to the poor predictive power of the model for the CHR group, these results should be interpreted with caution.

Discussion

In the present study we examine the differential individual influence of the single CAT domains and distressing experiences on the risk of a poor functional outcome within different mental disorders (CHR, psychosis, affective disorders, anxiety). Our results suggest, that the CAT signature, which is predictive for educational attainment, is specific to the individual diagnosis. This is also indicated by the different feature importance scores. With respect to the content of the most predictive items in the different diagnosis groups, a positive and caring environment – or the absence of these, a positive self-image and experiences of bullying were most influential overall.

Already in the past, the Adverse-Childhood-Events (ACE) study has shown that CAT is associated with poor functional outcome (Felitti et al.,1998). A study by Copeland and colleagues (2018) showed that cumulative CAT was not only associated with a higher rate of psychiatric illness but also with a poorer functional outcome in adults, even after adjusting for a broad range of other risk factors in childhood, like family adversities and hardships. Considering our results, the question arises why prediction of functional outcome by CAT and related distress showed higher accuracy in the psychosis and the anxiety group (BAC=0.70; BAC=0.65), while there was similar the affective (BAC=0.61) and even lower accuracy in the CHR group (BAC=0.54), in comparison to the prediction across the whole sample. One explanation for this finding could be higher heterogeneity in the CHR group. This includes psychiatric comorbidites such as depression and anxiety which are frequently reported in CHR groups (Fusar-Poli et al., 2014). Interestingly, our CHR sample (n=107) showed fewer patients with a comorbid F3 diagnosis (5% vs. 41 %) but more patients with a comorbid F4 diagnosis (25% vs. 15 %) in comparison to a recent meta-analysis (Fusar-Poli et al., 2014). Moreover, recent studies indicate heterogeneity in CHR samples with respect to prodromal symptoms, neurocognition (Healey et al., 2018) and with respect to the trajectory of symptoms and functional domains (Allswede et al., 2020). Another important difference is the younger age of the CHR group (mean: 23.9 years, SD: 4.8 years) compared to the other groups so that it could also be speculated whether the trauma effects on the functional outcome have not yet finally manifested. It is also surprising that the affective group performed less well, since depressiveness as a mediator between CAT and negative outcomes has been shown in the past (Schmidt et al.,2017). It can be discussed whether the severity of depressive symptoms might be neutralized by the fact that there are participants with anxiety symptoms in the affective symptoms group (F3) who have a different phenotype than patients with depression. It could also be speculated whether depressiveness is an important mediator, especially among women, who, however, are less represented in our sample.

Overall, it must be emphasized that CAT was differentially associated with functional outcome in the various mental disorders in our work. Already in the past, the longitudinal Kauai study showed that 30% of the observed children did not develop a mental illness despite of high CAT experiences (Werner,1993). That is in line with further studies revealing, that many victims of CAT show no or only minor long-term psychological impairment (Schulz et al.,2014). Thus, several factors might explain interindividual differences in the vulnerability to CAT. For example, resilience factors appear to be important mediating variables (Lee et al.,2020) and could, if the experiences are not too severe and encounter a sufficient number of protective factors, even increase resilience (Schultze-Lutter et al.,2016). Furthermore, a review of Cotter and Yung (2018) suggested that the association between CAT,

poorer symptomatic and functional outcomes may be based on an insecure attachment style, leading to be less willing to seek help or engage with a therapy/ medication.

Numerous systematic reviews and meta-analyses have previously shown that the different core domains of CAT are significantly associated with mental illness (Agudelo Garcia et al.,2019; Carr et al.,2013). With regard to the specific trauma patterns of our analyses, the domains EN, PA and DI were shown to be most important in the psychosis spectrum and the CHR group (Figure 2B). These results are in line with a previous work found that EN, PA and EA had the greatest effects on a first psychotic episode, even after controlling for the effects of other CAT domains (Trauelsen et al., 2015). A work of Salokangas and colleagues (2019) that also considered co-occurrence of both CAT domains and disorders of different diagnostic categories revealed that manic and psychotic disorders as well as depressive and anxiety disorders were related to PA; the latter two also to EN. With regard to CHR patients, Thompson and his group (2009) showed PA and SA to be associated with positive symptom severity in CHR individuals. Trauma history and number of traumatic events were significantly associated with positive, general and affective symptoms in CHR individuals (Loewy et al.,2019). Remarkably, SA played only a minor role in the prediction of functional outcome in our sample, although in the past it was often considered as one of the most important trauma domains (Hailes et al.,2019). This might be due to the fact that the prevalence of SA was reported to be higher in women (World Health Organization (WHO),2020), whereas our sample consisted of a larger number of men.

It should also be emphasized that the DI subscale, which is not a traditional CAT subdomain has shown to be a crucial factor in the prediction of functional outcome in all diagnoses. It should be therefore considered that traumatic events, which are reflected by the DI scale, like loss events, discrimination, bullying and experiences of guilt, might be more crucial for the prediction of the later functional outcome. Thus, a broader concept of CAT, that goes beyond the original five core domains (EA, EN, PA, PN, SA), might be reflected by our results.

In our analyses PN had the greatest impact on the later functional outcome in patients from the affective and the anxiety spectrum. Additionally, PA was especially predictive for the affective spectrum and EN for the anxiety spectrum group. In a path analysis of Salokangas and colleagues (2019) it was demonstrated that, after considering co-morbidity and co-occurrence of CAT domains, only PA and EN were directly related to the diagnosis of depressive and anxiety disorders. However, it should be noted that their study was about the association with diagnoses and not with the level of function. A recent meta-analysis revealed all subdomains of CAT as highly associated with depression in adulthood. The same analysis showed the subdomains PA, PN, EN and SA as significantly associated with anxiety disorders. In contrast to our work, the lowest correlations for both anxiety and depression were found for neglect. The authors discussed this critically in view of the fact that neglect (PN and EN) showed up in their work as the least studied forms of CAT (Gardner et al.,2019).

These findings could significantly improve the treatment of functional impairments. Specific CAT patterns could be targeted in different diagnostic states to achieve an improvement of the functional level. Moreover, Marshall and colleagues (2018) emphasized the potential importance of special preventive measures, such as therapeutic intervention aimed at sufferers of past abuse, neglect and poor parenting to prevent ‘trans-generational patterns’ continuing with their own children.

Strengths and Limitations

Major strength of our study is the large and rather young sample, which was not recruited according to specific study criteria and thus reflects everyday conditions in an early detection center and the possible successful prediction of functional outcome using CAT. Moreover, functioning seems to be a good variable to study when represented by educational level. However, the precondition here is that the (young) age of the sample allows an evaluation of education. However, some important limitations might be considered. As do most CAT assessments, the TADS retrospectively assesses CAT, thus, running the risk of a "recall bias" depending on the individual's current mental health situation (Colman et al., 2016). Yet, as the sample with the second lowest mean level of current functioning, the CHR group, displayed the poorest predictive ability of CAT and distressing experiences, such a systematic recall bias seems less likely. Another possible limitation is the non-assessment of factors as the age at onset, or the frequency and the extent of the suffering associated with exposure to CAT, which have been shown to be important (Teicher et al.,2016). It should also be critically considered that even the highest predictive power of 0.70 achieved in psychosis patients is to be regarded as rather weak in general. In the future, a further improvement of the prediction could possibly be achieved by taking genetic, brain-structural or environmental factors into account. In this context, it is important to consider that CAT can have different adverse effects on individuals, affecting brain development, cognition, interpersonal behavior and clinical symptoms. (Teicher et al., 2016). Additional unmeasured variables, such as genetic risk and neighborhood environmental factors, may account for aspects of observed associations (Cotter et al.,2018). Furthermore, it can be considered that by dividing the psychosis group into the 6 psychosis types according to ICD-10 (World Health Association,1999), a lower diversity of CAT influences and thus a better classification might be achieved. Finally, boundaries between good and low school qualifications were somewhat arbitrary despite reflecting the two main different educational categories according to the ISCED.

Implications for the future

Our work has demonstrated the role of individual aspects of CAT in different psychiatric conditions for achieving a good level of functioning in later life, thus providing a clear target for early interventions in the framework of child-focused public health efforts to ameliorate long-term functional impairment. However, in order to ensure the successful application of such therapeutic measures, the predictions of functional outcome based on adverse experiences must be further improved in the future. Additionally, there is increasing evidence that routine evaluation of CAT history should be adopted for patients presenting to mental healthcare services in order to identify those who may require more intensive support and additional treatment (Hudziak,2009). In the future, suitable methods, such as structure equation models and longitudinal studies should be used to investigate the exact relationship between CAT and functional outcome, against the background of mediating variables and resilience factors. Here, there are already first cross-sectional studies that have examined meditating variables, such as attachment style and coping strategies using structural equation modeling analyses (Shapiro and Levendosky, 1999).

Figures

Figure 1: Association between TADS sum score and functioning. Linear regression analyses indicate an association between TADS total score and current functioning (A) and highest functioning past year (B). A Mann-Whitney U-test indicates higher TADS total score in patients with low as compared to high educational attainment.

Figure 2: Performance analysis of machine-learning models for prediction in different diagnostic subgroups **(A).** Feature importance of predictors is depicted averaged across TADS domains **(B)** and at the level of individual items **(C).** Abbreviations: F2; any type of psychotic disorder, including any schizophrenia diagnosis, schizoaffective disorder, cannabis-induced psychosis, brief psychotic disorders, delusional disorder, psychotic depression, and psychotic bipolar disorder, F3; non-psychotic disorders of the affective spectrum, F4; any disorder from the anxiety spectrum, CHR; patients with a clinical high-risk for psychosis.

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Table 1: Sociodemographic and clinical data of the analyzed sample (N=707)

	total	psychotic	affective	anxiety	CHR	other	Comparison[1]
n	707	51	204	82	107	263	-
Males, n (%)	463 (65.5)	38 (74.5)	126 (61.8)	59 (72)	68 (63.6)	172 (65.4)	X-squared=4.802, df=4.000, p=0.308
mean age (SD)	25.1 (5.6)	26.5 (6.9)	25.4 (5.7)	25.1 (5.5)	23.9 (4.8)	25.1 (5.5)	F=2.173, df=4.000, p=0.070
median current functioning (IQR)	55.0 (22.0)	45.0 (12.2)	59.0 (20.0)	65.0 (21.0)	51.0 (16.5)	55.0 (20.0)	Kruskal-Wallis statistic=32.309, df=4.000, p=<0.001
median highest functioning past year (IQR)	65.0(25.0)	58.0 (35.0)	65.0(22.0)	71.0(28.0)	65.0(17.8)	65.0(23.5)	Kruskal-Wallis statistic=5.369, df=4.000, p=0.251
educational attainment (high / low)[2], n (%)	363 (51.3) / 344 (48.7)	24 (47.0) / 27 (52.9)	112 (54.9) / 92 (45.0)	42 (51.2) / 40 (48.8)	43 (40.2) / 64 (59.8)	142 (54.0) / 121 (46.0)	X-squared=7.479, df=4.000, p=0.113

[1]Based on Chi-Square test for categorical variables, ANOVA for continuous variables and Kruskal-Wallis rank sum test for ordinal variables.

[2]school education level of 3 according to the International Standard Classification of Education (ISCED)(29) and ISCED equivalents ≤ 2 were categorized as high and low educational attainment

Abbreviations: F2; any type of psychotic disorder*,* including any schizophrenia diagnosis, schizoaffective disorder, cannabis-induced psychosis, brief psychotic disorders, delusional disorder psychotic depression, and psychotic bipolar disorder, *F3;* non-psychotic disorders of the affective spectrum*, F4;* any disorder from the anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders spectrum*, CHR;* patients with a clinical high-risk for psychosis.

Table 2: Performance of predictive models based on the elastic net algorithm predicting educational attainment and psychosocial functioning in the total sample (N=707).

Binary outcome	n	BAC	TPR	TNR	TP	FP	TN	FN	PPV	NPV	AUC	p
educational attainment	707	0.59 (0.05)	0.52 (0.07)	0.67 (0.07)	17.80	12.10	24.20	16.60	0.60	0.59	0.63	<0.001
highest functioning past year	454	0.60 (0.06)	0.52 (0.09)	0.68 (0.10)	14.68	5.60	11.70	13.42	0.73	0.47	0.63	<0.001
current functioning	577	0.59 (0.09)	0.49 (0.08)	0.68 (0.14)	23.52	3.24	6.86	24.08	0.88	0.22	0.61	<0.001

Abbreviations: TP = True positive, TN = True negative, FP = False positive, FN = False negative, BAC = Balanced Accuracy, PPV = Positive Predictive Value, NPV = Negative Predictive Value, AUC = Area-under-the Curve

Table 3: *Prediction of educational attainment in the four diagnostic groups by single CAT and distressing experiences*

diagnosis	n	BAC	TPR	TNR	TP	FP	TN	FN	PPV	NPV	AUC	p
F2	51	0.70 (0.20)	0.68 (0.26)	0.72 (0.30)	1.78	0.70	1.70	0.92	0.78	NaN	0.72	<0.001
F3	204	0.61 (0.10)	0.47 (0.17)	0.74 (0.14)	4.34	2.86	8.34	4.86	0.61	0.64	0.64	<0.001
F4	82	0.65 (0.13)	0.56 (0.22)	0.74 (0.17)	2.24	1.10	3.10	1.76	0.68	0.66	0.68	<0.001
CHR	107	0.54 (0.12)	0.47 (0.20)	0.61 (0.21)	2.96	1.70	2.60	3.44	0.64	0.44	0.60	0.079

Abbreviations: TP = True positive, TN = True negative, FP = False positive, FN = False negative, BAC = Balanced Accuracy, PPV = Positive Predictive Value, NPV = Negative Predictive Value, AUC = Area-under-the Curve, F2; any type of psychotic disorder, including any schizophrenia diagnosis, schizoaffective disorder, cannabis-induced psychosis, brief psychotic disorders, delusional disorder, psychotic depression, and psychotic bipolar disorder, F3; non-psychotic disorders of the affective spectrum, F4; any disorder from the anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders spectrum, CHR; patients with a clinical high-risk for psychosis.

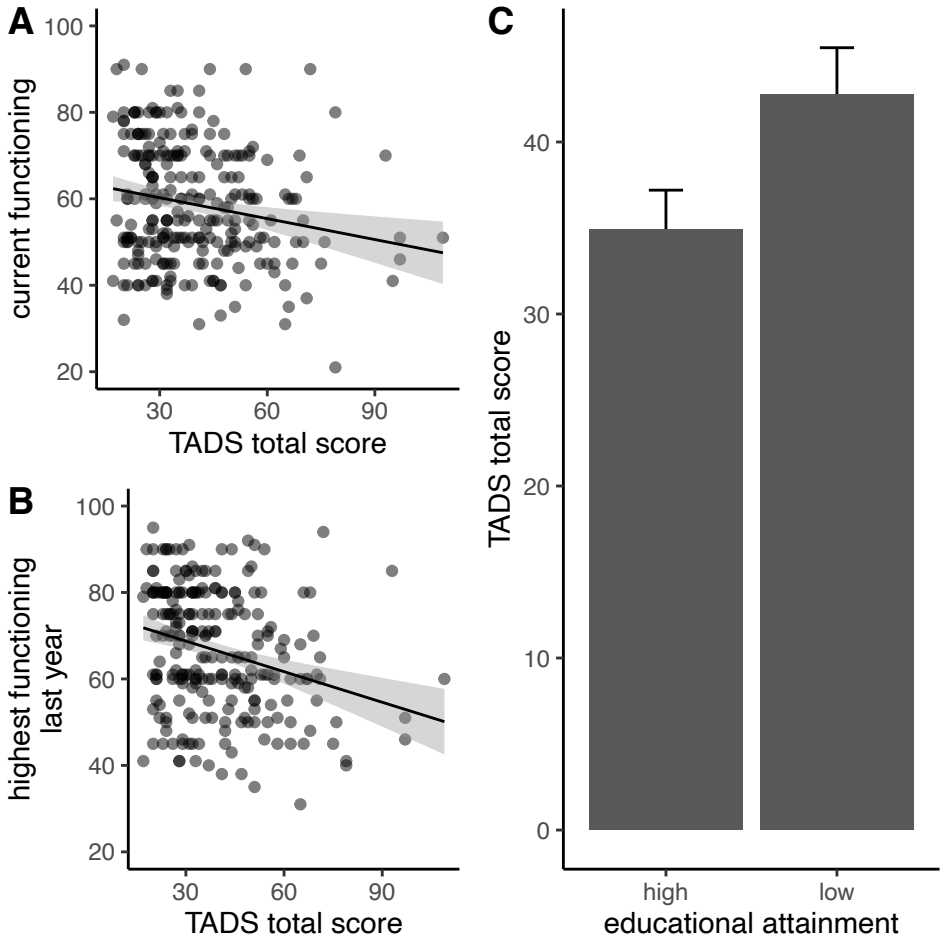

Figure 1: *Association between TADS sum score and functioning. Linear regression analyses indicate an association between TADS total score and current functioning (A) and highest functioning past year (B). A Mann-Whitney U-test indicates higher TADS total score in patients with low as compared to high educational attainment.*

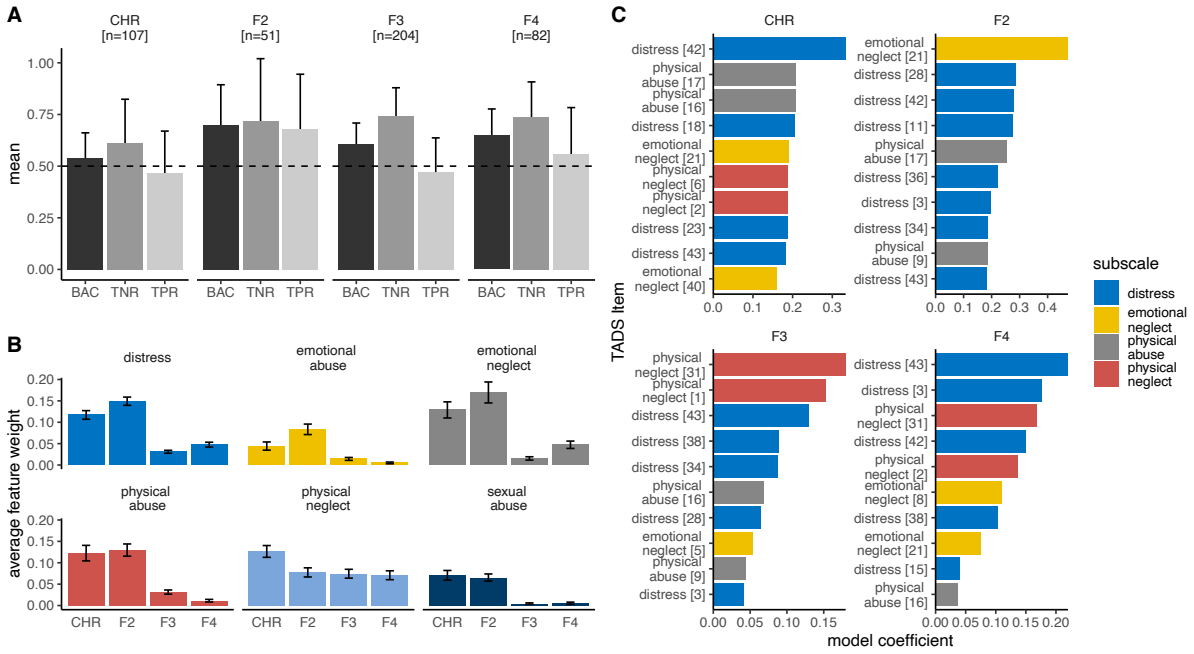

Figure 2: *Performance analysis of machine-learning models for prediction in different diagnostic subgroups* ***(A).*** *Feature importance of predictors is depicted averaged across TADS domains* ***(B)*** *and at the level of individual items* ***(C).*** *<u>Abbreviations:</u> F2; any type of psychotic disorder, including any schizophrenia diagnosis, schizoaffective disorder, cannabis-induced psychosis, brief psychotic disorders, delusional disorder, psychotic depression, and psychotic bipolar disorder, F3; non-psychotic disorders of the affective spectrum, F4; any disorder from the anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders spectrum, CHR; patients with a clinical high-risk for psychosis.*

Supplementary Material

to

Is there a diagnosis-specific influence of childhood trauma on later functional outcome? A machine learning analysis in a large help-seeking sample

by

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Table S1: Comparison of the included and excluded sample

	included patients	excluded patients	comparison[1]
n	707	1001	-
f/m	242/463	322/603	X-squared=0.023, df=1.000, p=0.880
mean age (sd)	25.09 (5.59)	24.74 (5.79)	t=-0.348, df=1516.651, p=0.223
median TADS (IQR)	245.00 (147.00)	259.00 (140.00)	W=2988.500, p=0.573
median current functioning (IQR)	55.00 (22.00)	55.00 (18.00)	W=213370.000, p=0.719
median highest functioning past year (IQR)	65.00 (25.00)	65.00 (20.50)	W=128569.500, p=0.060

[1]Based on Chi-Square test for categorical variables, two-sample t-test for continuous variables and two-sample Mann-Whitney-U test for ordinal variables.

Table S2: Trauma And Distress Scale (TADS) (Patterson et al. (2002)

TADS	Statement	Never	Rarely	Sometimes	Often	Nearly Always
1	When I was young, I felt safe and protected by someone					
2	When I was young, I was often hungry					
3	I was bullied at school					
4	I often wear ragged or dirty clothes to school					
5	When I was young, I felt valued or important					
6	My parents/caregivers were often drunk, stoned, or wasted					
7	I have been bullied at work*					
8	My family was emotionally warm and loving					
9	When I was young, I was hit so hard that it left marks, cuts, or bruises					
10	I felt rejected by my parents/caregivers					
11	When I was young, there was an adult I could confide in					
12	When I was young, I was humiliated by people in my family					
13	When I was young, my family looked after each other					
14	I believe that I am a bad person					
15	I believe that somebody died because of me					
16	I have experienced serious physical assault					
17	Adults noticed cuts, bruises, or marks from when I was beaten					
18	My childhood was perfect					
19	I am bothered by a very shameful secret					
20	I think I was physically abused when I was young					
21	I respect myself					
22	When I was young, someone touched me or tried to make me touch them in a sexual way					
23	I have had experiences that I feel very guilty about					
24	I have been involved in life-threatening situations					
25	I was forced to keep secrets about someone sexually interfering with me when I was young					
26	When I was young, I felt hated by a member or members of my family					
27	My family was the greatest ever					
28	Other people have acted badly because of me					
29	When I was young, I felt like the odd one out in my family					
30	I have experienced sexual assault					
31	If I needed treatment someone would always take me to see a doctor or nurse when I was young					
32	I feel that I was put down, criticized, and made to feel inferior when I was young					
33	Someone sexually molested me when I was young					
34	I feel responsible for harm and injury to another person					
35	When I was young, I had friends I could talk to about personal problems					
36	I have experienced harassment/persecution from other ethnic groups					
37	I did well at school*					
38	I have experienced the loss of somebody who was very important to me					
39	I believe that I do not deserve to do well in life					
40	My family was supportive and encouraging when I was young					
41	I believe that I was sexually used when I was young					
42	I felt afraid of someone in my family					
43	When I was young I could make friends easily					

Table S3: Dunn's post-hoc test comparing median current functioning between diagnostic groups:

Comparison	Z	P.adj
CHR - F2	2.3465	0.0227
CHR - F3	-2.9481	0.0048
F2 - F3	-4.6680	<0.0001
CHR - F4	-3.0261	0.0050
F2 - F4	-4.6341	<0.0001

A) Kruskal-Wallis rank sum test for differences in TADS subscales between diagnostic groups:

TADS subscale	statistic	df	p-value
distress	8.23	4	0.0836
emotional abuse	26.78	4	<0.0001
emotional neglect	36.69	4	<0.0001
physical abuse	12.37	4	0.0148
physical neglect	11.51	4	0.0214
sexual abuse	8.45	4	0.0764

B) Post-hoc analysis using Dunn's test and Benjamini-Hochberg correction for multiple comparisons for differences in TADS subscales between diagnostic groups

TADS subscale	Comparison	Z-value	adj. p-value
distress	CHR - F2	2.75	0.0359
emotional abuse	CHR - F2	3.11	0.0076
emotional abuse	CHR - F3	2.46	0.0422
emotional abuse	CHR - F4	5.00	<0.0001
emotional abuse	F3 - F4	3.38	0.0037
emotional neglect	CHR - F4	5.00	<0.0001
emotional neglect	F3 - F4	4.45	<0.0001
physical abuse	CHR - F4	2.76	0.0286
physical abuse	F2 - F4	2.79	0.0317
physical neglect	CHR - F4	2.77	0.0334
sexual abuse	CHR - F3	2.74	0.0369

Table S4: Weights of the single TADS items for the prediction of functional outcome in the single diagnostic groups

TADS item	Statement	TADS domain	F2	F3	F4	CHR
1	When I was young, I felt safe and protected by someone	PN	0.0515	**0.1528**	0.0325	0.0811
2	When I was young, I was often hungry	PN	**0.1292**	0.0109	**0.1368**	**0.1878**
4	I often wear ragged or dirty clothes to school	PN	0.0410	0.0172	0.0139	**0.1147**
6	My parents/caregivers were often drunk, stoned, or wasted	PN	0.0436	0.0111	0.0021	**0.1888**
31	If I needed treatment someone would always take me to see a doctor or nurse when I was young	PN	**0.1216**	**0.1797**	**0.1685**	0.0599
9	When I was young, I was hit so hard that it left marks, cuts, or bruises	PA	**0.1853**	0.0446	0.0015	**0.1153**
17	Adults noticed cuts, bruises, or marks from when I was beaten	PA	**0.2536**	0.0013	0.0164	**0.2089**
16	I have experienced serious physical assault	PA	0.0868	0.0689	0.0377	**0.2087**
20	I think I was physically abused when I was young	PA	0.0400	0.0353	0.0000	0.0316
24	I have been involved in life-threatening situations	PA	0.0824	0.0070	0.0009	0.0480
5_r	When I was young, I felt valued or important	EN	0.0628	0.0541	0.0209	**0.1157**
8_r	My family was emotionally warm and loving	EN	0.0934	0.0004	**0.1095**	0.0832
13_r	When I was young, my family looked after each other	EN	**0.1446**	0.0010	0.0012	0.0945
21_r	I respect myself	EN	**0.4725**	0.0034	0.0757	**0.1902**
40_r	My family was supportive and encouraging when I was young	EN	0.0749	0.0182	0.0295	**0.1607**
10	I felt rejected by my parents/caregivers	EA	0.0364	0.0061	0.0053	0.0597
12	When I was young, I was humiliated by people in my family	EA	**0.1598**	0.0154	0.0017	0.0331
14	I believe that I am a bad person	EA	0.0759	0.0302	0.0049	0.0324
26	When I was young, I felt hated by a member or members of my family	EA	0.0412	0.0011	0.0056	0.0509
32	I feel that I was put down, criticised, and made to feel inferior when I was young	EA	**0.1040**	0.0187	0.0071	0.0457
22	When I was young, someone touched me or tried to make me touch them in a sexual way	SA	0.0668	0.0028	0.0177	0.0381
25	I was forced to keep secrets about someone sexually interfering with me when I was young	SA	0.0940	0.0072	0.0000	0.0162
30	I have experienced sexual assault	SA	0.0666	0.0022	0.0002	**0.1336**
41	I believe that I was sexually used when I was young	SA	0.0263	0.0090	0.0082	**0.1298**
33	Someone sexually molested me when I was young	SA	0.0733	0.0012	0.0003	0.0357
3	I was bullied at school	DI	**0.1988**	0.0408	**0.1770**	**0.1553**
11	When I was young, there was an adult I could confide in	DI	**0.2763**	0.0026	0.0011	0.0376
15	I believe that somebody died because of me	DI	**0.1354**	0.0007	0.0406	0.0617
18	My childhood was perfect	DI	0.0965	0.0044	0.0343	**0.2050**
19	I am bothered by a very shameful secret	DI	0.0312	0.0150	0.0021	0.0428
23	I have had experiences that I feel very guilty about	DI	**0.1255**	0.0305	0.0000	**0.1870**
27	My family was the greatest ever	DI	0.0368	0.0008	0.0142	0.0332
28	Other people have acted badly because of me	DI	**0.2868**	0.0641	0.0025	0.0727
29	When I was young, I felt like the odd one out in my family	DI	0.0579	0.0093	0.0019	0.0674
34	I feel responsible for harm and injury to another person	DI	**0.1855**	0.0876	0.0049	**0.1510**
35	When I was young, I had friends I could talk to about personal problems	DI	0.0921	0.0042	0.0023	0.0645
36	I have experienced harassment/persecution from other ethnic groups	DI	**0.2235**	0.0064	0.0034	0.0950
38	I have experienced the loss of somebody who was very important to me	DI	0.0903	0.0889	**0.1043**	0.0746
39	I believe that I do not deserve to do well in life	DI	0.0869	0.0082	0.0046	**0.1090**
42	I felt afraid of someone in my family	DI	**0.2800**	0.0019	**0.1502**	**0.3336**
43	When I was young, I could make friends easily	DI	**0.1840**	**0.1300**	**0.2199**	**0.1827**
37	**I did well at school**	**DI**	**excluded from analyses**			
7	**I have been bullied at work**	**DI**				

EA= Emotional Abuse, EN = Emotional Neglect, PA=Physical Abuse, PN= Physical Neglect, SA= Sexual Abuse, DI= Distress, CHR= Clinical high-risk for psychosis, r= item reversed; ≥0.1 are in **bold**

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Author contributions

MR, CD, TH; Screening, recruitment, rating, examinations, implementing examination protocols of the study. JK, NP, MG, JD, LD, NGH, TH; Methodology, formal analysis, data curation. KV, FSL, JK; Project administration, supervision. SR, JK, FSL, JK, KV; Review and editing. TH; Conceptualization, methodology, formal analysis, writing, screening, recruitment, rating.

Declaration of interest

None

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