Research report

The impact of childhood adversity on suicidality and clinical course in treatment-resistant depression

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ABSTRACT

Background: Childhood adversity is a risk factor for the development of depression and can also affect clinical course. We investigated this specifically in treatment-resistant depression (TRD).
Methods: One hundred and thirty-seven patients with TRD previously admitted to an inpatient affective disorders unit were included. Clinical, demographic and childhood adversity (physical, sexual, emotional abuse; bullying victimization, traumatic events) data were obtained during admission. Associations between childhood adversity, depressive symptoms and clinical course were investigated.
Results: Most patients had experienced childhood adversity (62%), with traumatic events (35%) and bullying victimization (29%) most commonly reported. Childhood adversity was associated with poorer clinical course, including earlier age of onset, episode persistence and recurrence. Logistic regression analyses revealed childhood adversity predicted lifetime suicide attempts (OR 2.79; 95% CI 1.14, 6.84) and childhood physical abuse predicted lifetime psychosis (OR 3.42; 95% CI 1.00, 11.70).
Limitations: The cross-sectional design and retrospective measurement of childhood adversity are limitations of the study.
Conclusions: Childhood adversity was common amongst these TRD patients and was associated with poor clinical course, psychosis and suicide attempts. Routine assessment of early adversity may help identify at risk individuals and inform clinical intervention.

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1. Introduction

Over the past three decades a consistent body of research has found childhood abuse to be an important psychosocial risk factor for the development of depression and has also been associated with a poorer clinical course of depression, including earlier illness onset (Brodsky et al., 2001; Gladstone et al., 2004; Gamble et al., 2006), greater severity of symptoms (Gamble et al., 2006; Wiersma et al., 2009) and co-morbidity (Gladstone et al., 1999; Bernet and Stein, 1999; Wiersma et al., 2009).

Childhood abuse may also be related to specific subtypes of depression, having been associated with the presence of psychotic features both in those with MDD (Gaudiano and Zimmerman, 2010) and bipolar disorder (Hammersley et al., 2003).

Both epidemiological (Asgeirsdottir et al., 2011; Joiner et al., 2007) and clinical studies of patients with MDD (Brodsky et al., 2001; Zisook et al., 2011) and bipolar disorder (Leverich et al., 2002) have reported associations between childhood abuse and suicidal behaviours. Whilst some have suggested this association may be moderated by the presence of borderline personality disorder (BPD) (Gladstone et al., 1999; Zlotnick et al., 2001), others have reported higher rates of suicide attempts in maltreated MDD patients even when adjusting for BPD (Brodsky et al., 2001). Thus, the relationship between early adversity, BPD and suicidal behaviour remains unclear.

Many previous studies have focused primarily on childhood physical or sexual abuse (Martins et al., 2011); however, a growing body of research suggests emotional abuse to be particularly associated with the clinical course of depression (Bernet and Stein, 1999; Etain et al., 2010; Liu et al., 2009), including chronicity (Brown et al., 2007) and suicidal behaviours (Gibb et al., 2001). Broadening the definition of childhood adversity to encompass negative experiences other than childhood abuse may also be important. For instance, childhood bullying victimization has been

associated with depression, anxiety, social isolation, psychosis and suicidal behaviour (Arseneault et al., 2010; Roeger et al., 2010; Klomek et al., 2009). As bullying often occurs alongside other abusive experiences, measuring and controlling for multiple types of adversity is likely to be important (Fosse and Holen, 2004).

In a recent meta-analysis Nanni et al. (2011) found that exposure to childhood maltreatment doubled the risk of both depressive episode recurrence and persistence. This is important considering the substantial health care costs associated with both childhood adversity and chronic depression (Walker et al., 1999; Rost et al., 1998).

An estimated 20–40% of depressed patients experience treatment-resistant depression (TRD), typically defined as a failure to respond to at least one adequately prescribed antidepressant medication (Sackheim, 2001). TRD is associated with a high disease burden and poses a significant clinical and public health challenge (Greden, 2001). TRD patients experience a more severe and protracted course of illness (Üstün and Kessler, 2002), have a higher risk of self-injurious behaviours (Dunner et al., 2006) and higher rates of co-morbid physical and mental health problems. TRD is also associated with greater social impairment (Kennedy and Paykel, 2004) and service utilisation (Crown et al., 2002).

Investigating factors associated with TRD and its clinical course could further our understanding of the condition and help to improve treatment outcomes. To date there has been little investigation into associations between childhood adversity and TRD; thus, in this study we aim to further investigate:

(i) The prevalence of childhood adversity when defined broadly to include abuse, traumatic life events and bullying victimization in patients with TRD.
(ii) Associations between childhood adversity and clinical course of TRD, including psychotic symptoms and suicide attempts.

2. Methods

2.1. Participants

This cross-sectional study included 137 patients previously admitted to the National Affective Disorders Unit, a specialist inpatient unit for adults with complex affective disorders (see Wooderson et al., 2011 for details). All participants gave informed consent to participate and the study was approved by the local ethics committee.

Information regarding medication history was obtained by clinical interview at admission to the unit and referring to case notes. Treatment resistant depression was defined as failure to respond to at least one prior adequate trial (both dose and duration) of one major class of antidepressant (Sackheim, 2001). Regarding previous antidepressant trials, participants had received a range of 1–19 and a median of 5 (IQR=3–8). Participants had also received a median of 12 (IQR=7–17) adequately implemented psychiatric medication trials prior to admission, and 85% of patients had previously been treated with mood stabilisers, 80% with an antipsychotic, 42% with one or more other augmentation strategy, and 62% with anxiolytic/hypnotic medications. In addition, almost two thirds of participants had previously received ECT therapy, further signifying this as a particularly difficult-to-treat cohort.

2.2. Assessment

2.2.1. Diagnosis, symptoms and suicidality

Diagnosis was established using International Classification of Diseases (ICD-10) (WHO, 1992) definitions after a full, longitudinal clinical assessment including access to old case notes and the use of appropriate standardised interviews (Mini-International Neuropsychiatric Interview; Structured Clinical Interview for DSM-IV, axis I and II versions). Depressive symptom severity was also routinely measured using the 21-item clinician-rated Hamilton Depression Rating Scale (Ham-D; Hamilton, 1960). Suicide attempts were defined as severe life threatening acts that occurred in the context of suicidal ideation or intent to end one's life.

2.2.2. Childhood adversity

Information regarding childhood (< 18 years) adversity was obtained using all available sources, including clinical interviews and the Intrusive Memory Protocol (n=63) (Brewin et al., 1996). Using the criteria outlined in the Early Trauma Inventory (Bremner et al., 2000), two raters (CT & KM) independently coded for the presence/absence of childhood physical abuse (CPA), sexual abuse (CSA), emotional abuse (CEA) and traumatic events (CTE; e.g. parental separation or divorce, death of a relative/friend). Childhood bullying victimization (CB) was also coded to capture peer abuse. Discrepancies between raters were resolved through discussion with a third independent rater (AJC). Group comparisons were conducted between those who had experienced any childhood adversity (at least one type of adversity) and those who had not, in addition to comparing each of the five subtypes of adversity.

Measures of CPA, CSA and CEA were validated in a subgroup of 32 patients who also underwent interview using the Childhood Experience of Care and Abuse scale (CECA; Bilfulco et al., 1994). Good reliability was found between our childhood adversity data and the CECA data, using Cohen's Kappa as follows: CPA κ=0.78; CSA κ=0.88; CEA κ=0.59.

2.2.3. Depression severity

Depressive symptoms were assessed at admission using the Ham-D as the primary measure. A subgroup of participants also completed the self-rated 21-item Beck Depression Inventory at admission (BDI; Beck et al., 1961).

2.3. Analyses

Analyses were conducted on both the whole sample of patients with TRD and confined to those with a primary diagnosis of unipolar TRD (i.e. ICD-10 Depressive Episode or Recurrent Depressive Disorder – hereafter termed Major Depressive Disorder (MDD) for comparative purposes). Due to small sample sizes, patients with bipolar depression or secondary depression were not analysed separately.

Data were analysed using SPSS 15.0 for Windows software. Analyses of differences between diagnostic groups were conducted using Pearson Chi-squared, ANOVA or Kruskal Wallis tests, with Bonferroni corrected post-hoc tests. Pairwise group comparisons exploring associations between adversity and demographic (e.g. age, gender, marital status, years of education) or clinical variables (including illness duration, duration of admission, number of previous depressive episodes) were conducted using either t-tests or Mann–Whitney U tests for continuous data, and Pearson Chi-squared or Fisher's exact tests for categorical data, as appropriate.

Logistic regression modelling was used to further investigate clinical factors significantly associated with childhood adversity, namely the experience of psychotic symptoms and history of suicide attempts, whilst controlling for other clinical and demographic variables. All variables reaching a p value≤0.1 were entered into a fully adjusted multivariate model. Odds ratios with 95% confidence intervals and significant figures are reported. All tests were two-tailed and significance level was set at 0.05.