

Bipolar Disorder, Depression and Childhood Adversity

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Abstract

Childhood adversity is related to an increased risk of developing mental disorders such as major depression, bipolar disorder, schizophrenia and substance abuse, post-traumatic stress disorder, substance abuse, affective problems, anxiety, personality disorders, and suicide. Bipolar disorder and depression are mental disorders that have been particularly associated with childhood abuse. The fact that there is a link between affective illnesses and childhood adversity emphasizes the need for proper assessment for bipolar disorder when these patients present with either depression or mood instability, and that these conditions, when identified, require effective treatment.

Key words: bipolar disorder, childhood adversity.

Introduction

Childhood abuse is known to cause significant negative effects on the mental wellbeing of children as they grow up, which persist as the child goes through their teenage years and enter adulthood (1). The prevalence of childhood abuse is unfortunately not rare, with sexual abuse being shown to be as high as 8% in a nationally-representative sample in England, with a prevalence of re-victimization as high as 2% (2). Child abuse can take various different forms and be of varying severity. Etain et al. 2008 (18) described the most detrimental environmental stresses as including emotional and physical parental abuse, multiple violent episodes and sexual abuse. Sexual abuse, in particular, has been shown to result in the greatest risk of developing all types of psychopathologies later in life (3). The experience of severe traumatic events during childhood is known to be associated with poor functioning, cognitive deficits and a number of psychiatric conditions in adulthood (4)(5). While the link between childhood abuse and mental health problems in adulthood is well established, what is more uncertain is the mechanism by which this downstream effect takes place. This mechanism could be via a latent effect, whereby the childhood adversity results in long-lasting biological, psychological and/or sociological damage, irrespective of later circumstances. Alternatively, there could be a pathway effect, whereby the childhood adversity results in unhealthy exposures during adulthood that in turn result in mental health problems (6-9). Bipolar disorder and depression are two examples of mental illness with a demonstrated link to child abuse. The link will be explored in this article.

Impact of childhood adversity in adulthood

There is much interest in understanding the effect of child abuse when the child grows and develops. A systematic review of prospective evidence of associations between poor parent-child relationships and common psychiatric disorders in later life reported that abusive relationships predicted depression, anxiety and PTSD (10). The same review further demonstrated that maternal emotional unavailability in early life predicted suicide attempts in adolescence. Epidemiological studies and clinical trials have gone on to show that childhood stress is related to an increased risk of developing mental disorders such as major depression, bipolar disorder, schizophrenia & substance abuse, post-traumatic stress disorder, substance abuse, affective problems, anxiety, personality disorders, and suicide (11,12) (3). It was concluded that there is robust evidence of the role of the environment,

specifically adverse childhood experiences, in various aspects of mental disorders (1). In the study by Chou (2), childhood abuse was significantly associated with mixed anxiety and depression, generalized anxiety disorder, eating disorders, post-traumatic stress disorder, and suicidal ideation. Similarly, re-victimization was significantly associated with mixed anxiety and depression, phobia, post-traumatic stress disorder and suicidal ideation.

Childhood adversity also increases the risk and severity of psychotic symptoms in adult life (12,13). Hence, many psychiatric patients with a history of childhood trauma will have worse outcomes when mentally disordered and higher rates of clinical disorders than those without such history (14,15) (17) (3).

Childhood abuse and bipolar disorder

Bipolar disorder (BPD) is a mental disorder that has been particularly associated with childhood abuse. 30-50% of those with of BPD report having endured traumatic childhood events, most commonly emotional abuse (18) (12) (19, 20). When comparing the rates of emotional abuse in these patients with sufferers of major depressive disorder the rates are higher for those with BPD (21). Conus et al. (22) reported that a history of childhood trauma in BPD patients is associated with recurrent depressive symptoms in adulthood, and also lower premorbid functional levels and reduced compliance to treatment. Furthermore, patients who suffered sexual and physical abuse present with more severe mania symptoms (23). One theory for this link between BPD and childhood trauma is that the trauma triggers the first episode of BPD, which is indeed often associated with psychosocial stressors (24). A history of physical or sexual abuse is associated with an earlier onset of BPD, increased comorbidity and higher rates of suicide attempt (25). Furthermore, these patients also present with higher rates of substance abuse, anxiety comorbidity, post-traumatic stress disorder and depressive symptoms of higher intensity, particularly women, when compared to patients without trauma (18) (17). Men with BPD are, however, more often exposed to sexual and physical abuse than men with major depressive disorder (21).

Childhood abuse and depression

Depression is another mental illness that has been shown to be associated with preceding adverse life events such as child abuse. Johnson (26) showed that subjects who have experienced negative life events take three times longer to show recovery in mood disorders. The symptoms of these patients may also be more severe usually with a higher risk of suicide attempt and the need for more health services in adulthood (12) (17). Schoedl et al. (27) were able to support this with their finding that depressive symptoms are more severe among those who were abused as children under the age of 12 than those abused after that age.

Other issues that need to be considered are that children who have a psychiatric disorder are more susceptible to experience a traumatic episode (18), and that there is a possible genetic factor that plays a role. Individuals who have genetic risks and a history of trauma seem to show an earlier development of mental disorder compared to those without genetic risks (19). These patients often have difficulties with interpersonal relationships and they tend to be more isolated, more refractory to treatment and at greater risk of recurrent mood episodes (12).

More research to establish the nature between child abuse and depression fully will be useful in the future but the data thus far suggests that childhood trauma is indeed associated with an increased severity of mental disorders like depression and the effect of such an adverse event can be long-lasting and persistent (12) (17).

Neurobiological changes associated with childhood abuse

In order to be able to understand the link between mental disorders such as bipolar disorder and the trauma of childhood abuse, it is important to understand the associated neurobiological changes.

Studies have provided evidence that adverse events in childhood can have important effects on the plasticity, morphology, physiology and functioning of the brain. Some of the neurostructural changes demonstrated include the reduction of the volume of the hippocampus and corpus callosum following trauma at an early age (1). Patients with a family risk of depression who have a history of emotional abuse have been shown to have significantly smaller left and right hippocampal heads. Voxel based morphometry has also shown smaller dorsolateral prefrontal cortices, medial prefrontal cortices and anterior cortex cinguli in these patients. Hence high-risk individuals for depression have reduced volume of brain regions related to emotional processing when they additionally suffered childhood abuse, demonstrating that genetic and environmental factors such as childhood trauma influence brain structure possibly via epigenetic mechanisms and thus structural anomalies may precede the onset of the illness (28). Additionally, common genetic variation of the serotonin transporter-linked polymorphic region (5-HTTLPR) has been related to depressive symptoms, in particular after stressful life events. Gender modulates the interactive effect of the 5-HTTLPR genotype and childhood adversity on hippocampal volume. While the short-allele is associated with hippocampal volume independent of childhood adversity in women, men only have smaller hippocampi if they carry the risk allele and experienced severe childhood adversity (29). Gene polymorphisms may also interact with childhood adversity to affect the size of the hippocampus and the occurrence of major depressive disorder. One of the polymorphisms found to be associated with major depressive disorder is the Val66MET polymorphism of brain-derived neurotrophic factor (BDNF). In a study it was shown that MDD patients had smaller hippocampal volumes, both in the left and right hemispheres ($F = 5.4$, $P = 0.022$). There was a significant interaction between BDNF allele and history of childhood adversity ($F = 6.1$, $P = 0.015$): Met allele carriers showed significantly smaller hippocampal volumes when they did have a history of childhood adversity, both in patients and controls. Hence stress-gene interactions are relevant for hippocampal volume reductions. Subjects exposed to early life adversity developed smaller hippocampal volumes when they carry the Met-allele of the BDNF polymorphism (30).

Emerging evidence appears to indicate that the neurobiological effects of stress may vary at different developmental stages (1). Differences in brain image findings in studies with adults and children can also be attributed to differences in brain maturation (1). It is suggested that colossal abnormalities in children with PTSD are due to atrophy or neurodevelopmental deficits that result from traumatic experiences (31). Preclinical evidence shows that very early life experiences can dramatically impact the morphometry of the corpus callosum (32). Myelination of the corpus callosum begins between the ages of 6 months and 3 years and continues into the third decade of life (33-35)(1). As well as the effects of stress and glucocorticoids on cell proliferation in the hippocampus (36), glucocorticoids have been shown to inhibit the proliferation of the oligodendrocyte precursor throughout the brain (37). Given the role of oligodendrocyte precursors in myelination, prenatal glucocorticoid exposure is associated with reduced myelination of the corpus callosum and hence reduced myelin sheath thickness (38). Because of the rostral-to-caudal myelination sequence, it is suggested that different regions of the corpus callosum might have different windows of opportunity for vulnerability to early experiences (33)(1). Another possibility, however, is that abnormalities in corpus callosum morphology are due to genetic developmental factors which predispose individuals to develop PTSD after exposure to trauma (39).

Conclusion

The above review clearly demonstrates the relationship between childhood adversity and affective disorders, including bipolar disorder and major depressive disorder. It also demonstrates what is known of the underlying neurobiology. The fact that there is a link between affective illnesses and childhood adversity emphasises the need for proper assessment for bipolar disorder when these patients present with either depression or mood instability, and that these conditions, when identified, require effective treatment.

GP Comment

What have I learned from this paper?

This review shows us that the impact of abuse in early life can be long-lasting. Childhood adversity is a risk factor in the development of a range of mental health disorders, including bipolar affective disorder, and can also lead to increased severity. This reminds us of the importance of taking a history of childhood experiences during the psychiatric assessment.

Dr Jenny Hopwood, GP Trainee.

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